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CONTENTS

THE PREVALENCE OF STAPHYLOCOCCAL INFECTIONS IN AN EMERGENCY HOSPITAL FOR CHILDREN - A RETROSPECTIVE STUDY

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Abstract

Introduction: Infection is a matter of highest importance in pediatric pathology, and still remains a major cause of morbidity and mortality, despite the progress made Rational use of antibiotics is an essential part of patient safety and requires guidance and close supervision. Aim was to identify resistance phenotypes of strains of staphylococci in the pediatric population in our hospital. Material and methods: retrospective study, based on analysis of patients' records, those who were taken cultures between the aforementioned period. Isolation of germs was done on selective and non-selective media suitable and staphylococcal strains identification was done by conventional methods. All data was collected in Microsoft Excel. Results: Most of the cultures positive for Staphylococcus came from biological material collected from the nasal passages and larynx. There were no strains resistant to vancomycin, teicoplanin and linezolid. Best rate of sensitivity to antibiotics have had MSSA strains identified in pathological products from abscesses and wounds. The best results were presented to netilmicin. Conclusions: Our study showed that Isolated Staphylococcal strains are most frequent from all positive cultures. More than 75% of the isolated MSSA strains are resistant to more then two antibiotics. Identification and knowledge of these phenotypes of resistance is useful in initiating empiric therapy, especially in critical situations when etiological treatment cannot be delayed.

Key words: stphiloccocus aureus, antibiotic resistance, child

Introduction - The purpose of the paper

Infection diseases represent a matter of highest importance in pediatric pathology, and still remains a major cause of morbidity and mortality, despite the progress made in its prevention and treatment. Staphylococcal infection is one of the most frequently isolated nosocomial pathogens from intensive care unit patients [1] due to the increased ability of the bacteria to adapt to environmental factors [2], patient population diversity and the alarming rate of acquisition of new mechanisms of antibiotic resistance.

The value of antibiotics for human health is immeasurable. They have changed the life expectancy in the last 50 years and a plausible estimate of the increase in life expectancy attributable to antibiotics might be 2 to 10 years. [3] However, rational use of antibiotics is an essential part of patient safety and requires guidance and close supervision. Given the association between antibiotic use and selection of resistant germs, the frequency of inappropriate use of antibiotics is used as a surrogate marker of the impact of antimicrobial resistance that can be avoided.

The prevalence of staphylococcal infections, especially those caused by strains of MRSA in hospital, varies widely according to geographical areas. [4] MRSA infections are associated with a higher mortality than those due Methicillin susceptible S. aureus (MSSA) [5], which is explained by the greater resistance of MRSA strains to antibiotics, leading to an initial empirical treatment that most often will prove to be ineffective with negative effects on disease progression. [6].

The aim of this study was to identify resistance phenotypes of strains of staphylococci in the pediatric population in a Romanian pediatric referral hospital area.

Material and method

Design: retrospective study, based on analysis of patients' records between 01.06.2007-01.10.2007, a randomly chosen period of time. We collected the data from the Central Laboratory from Emergency Hospital for Children "Louis Ţurcanu" Timisoara using all the cultures that were performed in that arbitrary period.

Patients: We included all patients with signs or symptoms of infection, who were taken cultures between the above-mentioned interval of time.

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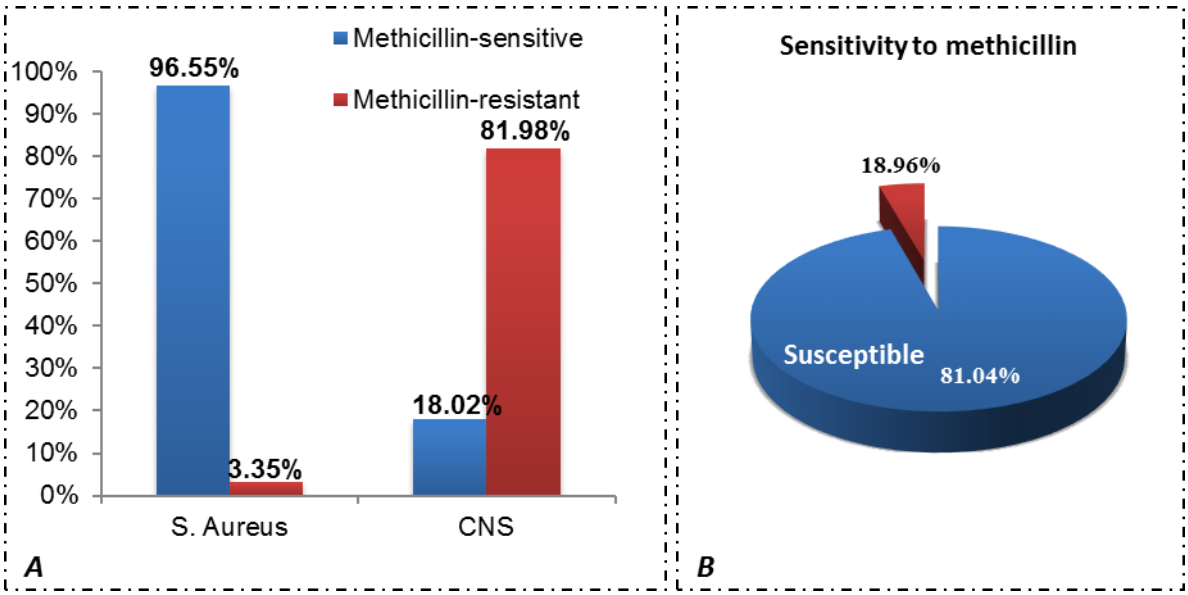

Fig. 1. The percentage of staphylococcal strains according to methicillin resistance

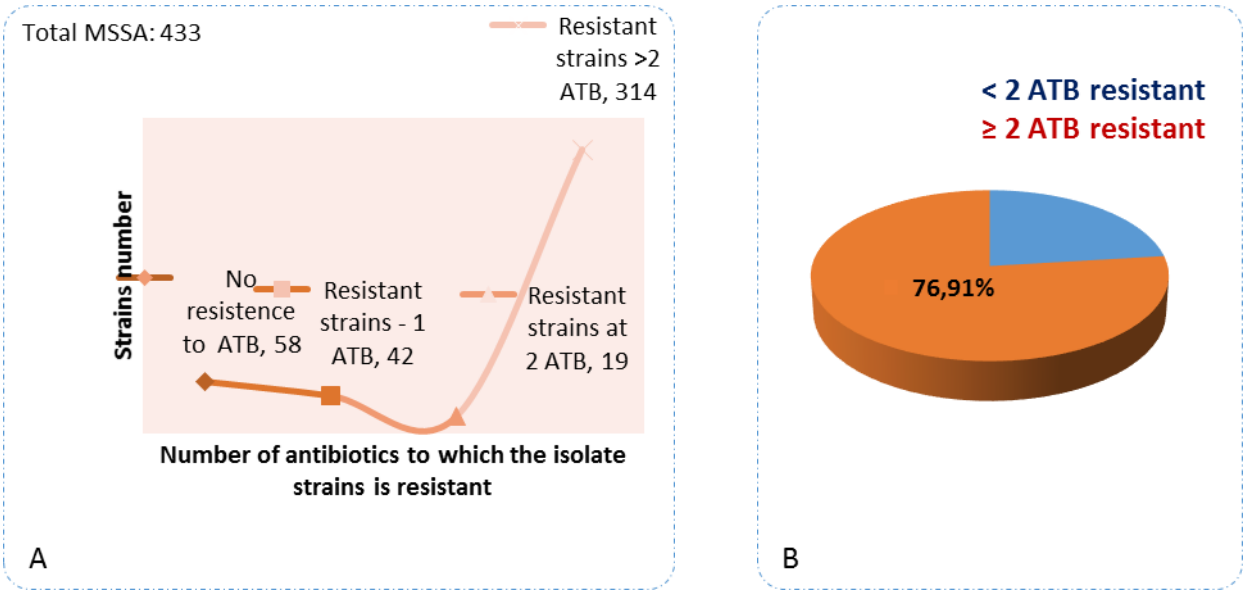

Fig. 2. Multi-resistant strains of MSSA

Isolation of germs from the pathological products was done on selective and non-selective media. Staphylococcal strains identification was done by conventional methods on Blood Agar media and MacConkey agar was used for the isolation of gram-negative enteric bacteria. Blood cultures were taken on Oxoid Signal blood culture system. Urine cultures were taken using urine bags (West spring) and urinary Foley catheter. The diagnosis of a urinary tract infection was confirmed by obtaining a urine culture with greater than 100000 colony forming units (CFU)/mL of one type of bacteria. For samples collected using a Foley catheters and urine bags, results of 1000 to 100000 CFU/mL were considered significant. We have started with the identification of antibiotic susceptibility of Staphylococcus strains isolated from different cultures taken from inpatients and outpatient who addressed our hospital during the study period.

Statistical analysis: all data was collected in a Microsoft Excel table. Statistical analysis was performed using Microsoft Excel 2007.

This study was approved by the Ethics Committee of "Louis Turcanu" Emergency Hospital for Children, Timisoara

Results

During the study, from a total of 7464 bacterial cultures, were isolated a number of 946 bacteria. Out of cultures analyzed - 559 (7.49 % of total pathological products) belonging to the Staphylococcus strains.

Staphylococcal strains isolated - 59% of all positive cultures, were the most frequent bacterial agents identified. From the statistical study we noted that the incidence of clinical entities rendering significantly different. We found that the most frequent staphylococci were isolated from respiratory tract (65%), followed by positive cultures from skin and soft tissue infections (Table 1).

We discovered that staphylococcal strains have frequently been isolated from the nasal swab and throat, representing 64.05% of positive cultures. In terms of skin and soft tissue infections in the sample studied, we found that a percentage of 8.05% of staphylococcal strains were isolated from the skin of the perianal area, groin and underarms. Staphylococcus isolated in the secretions from ear, conjunctiva, and umbilicus, and also from penis and vaginal parts accumulates a rate of 16.99%. In other products taken from the skin and soft tissue infections (wounds, pustules, abscesses) staphylococci were present in an amount of 5.72% of the total.

In regards to isolated staphylococcal species, we found that 448 strains, representing 80.14%, belong to the genus Staphylococcus aureus strains and 111, representing 19.86%, belong to coagulase-negative staphylococci (CNS). We noticed that the ratio between S. aureus and CNS was 4-1.

Resistance to methicillin has been studied for all the samples were the staphylococci existed. We found that 433 (representing 96.55%) of strains belonging to MSSA and only 15 (3.35%) strains were resistant to this antibiotic (MRSA). From the population of coagulase-negative staphylococci, 91 strains (81.98%) are resistant to methicillin and only 20 strains (18.02%) were susceptible to methicillin administration (Fig. 1A).

At the same time, regardless of the species of Staphylococcus, it appears that the susceptibility to meticillin is 81.04%, all the rest are resistant (Fig. 1B).

The MSSA population (433 strains) selected from all samples has revealed a sensitivity of 100% to glycopeptides (vancomycin and teicoplanin) and to the backup antibiotic (linezolid). Sensitivity to aminoglycoside study showed that 91.21% of the strains were sensitive to netilmicin. Testing strains to third generation cephalosporin's, showed that among strains of MSSA, 55.38% were susceptible to ceftriaxone. Percentage of moderately low sensitivity was found to combinations: amoxicillin / clavulanic acid and trimethoprim / sulfamethoxazole. Testing against oxacillin showed an increased level of resistance (54.62%). Average percentage of MSSA strains resistant to the antibiotics tested is 35.08% (Table 2).

Analyzing the association of antibiotic resistance in the same MSSA strains, we saw the presence of a total of 333 strains resistant to more than one antibiotic, the resistance being noticed for up to 9 antibiotics even for the same strain. A percentage of 76.91% of multidrug-resistant strains are identified (Fig. 2 A, B).

Differentiating the cases in relation to the primary site of staphylococcal infection, the sensitivity to the same antibiotic of the MSSA strains will be different and will depend on pathological product from which it was isolated. The percentage of antibiotic sensitivity was higher in the population of MSSA from the throat (62.54%) compared to the ones in the nasal passages (52.49%). In the conjunctivas secretion harvested and those from the external ear canal, MSSA isolates show a very low percentage (35.37%) of sensitivity to majority of the antibiotics. Althought there were no strains of MRSA isolated in these products, MSSA has a high resistance to most of the antibiotics tested. Netilmicin was the only antibiotic with good coverage (sensitivity of 88.98%) on the MSSA. Best rate of sensitivity to antibiotics have had MSSA strains identified in pathological products from abscesses and wounds (73.42%) and this strains are most susceptible to aminoglycosides tested (Table 2).

Table 1. The isolated staphylococcal strains share.

Site of infections	Number of bacterial strains isolated (%)
Respiratory tract infections	***363 (***64.94 %)
Skin and soft tissue infections	172 (30.77 %)
Medical device-associated infections	12 (2.15 %)
Systemic infections	7 (1.25 %)
Urinary tract	5 (0.89 %)
Species	**No. bacterial strains (%)**
Staphylococcus aureus	448 (80.14 %)
Coagulase-negative staphylococci	111 (19.86 %)

Table 2. MSSA sensitivity.

Antibiotic	Methicillin-sensitive S. aureus sensitivity				
	all samples studied	nasal swabs	pharyngeal exudate	conjunctiva secretions and ear	abscesses and wounds
Sensitivity rate	64.92 %	52.49 %	62.54 %	35.37 %	73.42 %
OX	45.38 %	35.71 %	65.78 %	28.33 %	69.23 %
AUG	67.78 %	67.88 %	68.10 %	59.52 %	71.42 %
CFP	55.38 %	57.50 %	48.48 %	52.79 %	71.42 %
RO	50.12 %	44.81 %	67.24 %	18.82 %	69.23 %
NET	91.21 %	92.55 %	88.59 %	88.98 %	92.30 %
GEN	51.06 %	46.87 %	69.29 %	20.83 %	85.71 %
K	28.33 %	24.20 %	37.06 %	17.85 %	53.84 %
E	27.01 %	23.07 %	38.88 %	8.82 %	50.00 %
BIS	60.14 %	61.18 %	69.64 %	26.90 %	83.33 %
CIP	67.55 %	71.16 %	71.42 %	41.67 %	84.61 %
TOB				24.61 %	
FEP					23.07 %
TZP					84.61 %
CES					91.66 %
IMP					83.33 %
MER					87.50 %
VA	100 %				
TEC	100 %				
LZD	100 %				

OX-oxacilin; AUG-amoxicillin-clavulanate; CFP-cefoperazone; RO-ceftriaxone; Net-netilmicin; GEN-gentamicin; K-kanamycin; E-erythromycin; BIS-thrimetoprim-sulfamethoxazole; CIP-ciprofloxacin; TOB-tobramycin; FEP-cefepime; TZP-piperacillin-tazobactam; CES-cefoperazone-sulbactam; IMP-imipenem; MER-meropenem; VA-vancomycin; TEC-teicoplanin; LZD-linezolid

Discussion

Infections caused by staphylococci will spread easily through interpersonal contact, most often occurring in the first instance by direct colonization, producing or not overt infection, depending on demographic factors and host susceptibility to infections.

In this study, following statistical analysis we obtained a procent of 3.35% of MRSA strains of S. aureus population tested (448 positive cultures for S. aureus). For a correct appreciation of the report MRSA / MSSA ratio it is important to study relevant strains isolated from pathological products [8]. For this reason, we excluded from this analysis isolates from throat and nasal secretions, skin, axillary, inguinal and perianal areas, as staphylococcal strains in these regions are frequently colonized and may not reflect an infection. Thus we obtained a rate of 9.37% MRSA (9 strains of all 96 remaining pathological product which was isolated Staph. aureus), a percentage of 2.7 times lower than that reported by Romania in 2007 by the network European antibiotic resistance surveillance -EARS-Net (26%). [13]

In our study, most cultures positive for Staphylococcus came from biological material collected from the nasal passages and larynx. In most studies, these places are cited as anatomical areas usually colonized. The primary location of staphylococci to this level is associated with the development of bacteremia [9].

Resistance to antibiotics was prevalent in strains harvested from the conjunctival secretion and the external ear canal as MSSA isolates susceptibility showed a very low percentage (35.37%). Testing tobramycin, the aminoglycoside antibiotic commonly used in external infections of the eye and ears showed a very low sensitivity of MSSA (24.61%).

Best rate of sensitivity to antibiotics have had MSSA strains identified in pathological products from abscesses and wounds (73.42%). For abscesses or carbuncles, some studies have emphasized the extreme importance of drainage, antibiotic therapy beeing only adjuvant or it can be a first line of treatment in case of afebrile children [10]. The antibiotic may be administered topically together with a strict hygiene of the skin [11].

The best results were presented to netilmicin, but widespread use of this antibiotic, unless really needed as in severe infections, in Intensive Care Unit (ICU) or hematology oncology cases, could lead to the selection of staphylococcal strains resistant to this antibiotic. Netilmicin, when used routinely for mild infections, will lead to unwanted adverse effects.

There were no strains resistant to vancomycin, teicoplanin and linezolid. MRSA and the coagulase-negative

staphylococci resistant to Methicillin were all sensitive to gliopeptide and linezolid. Linezolid has limited clinical experience in pediatric infectious pathology [11].

In assessing the results, we took into account that methicillin-resistant S. aureus (MRSA), according to Clinical and Laboratory Standards Institute (CLSI) 2006 show resistance to all penicillins, all combinations betalactamine / beta-lactamase inhibitors, cephem (cephalosporins) and carbapenems. These, although they may be active in vitro, are not clinically effective. To these antibiotics MRSA strains are usually reported as being resistant [7].

The data cited by the literature was similar to the results of the current study, most of the SCN were resistant staphylococci and vancomycin was the recommended empiric treatment in infections with these pathogens. The combination of rifampicin or gentamicin with vancomycin may increase efficacy [12].

The restriction in prescribing these antibiotics and medical education could prevent or reduce antimicrobial resistance.

Medical care increases the risk of acquiring a staphylococcal infection, particularly multidrugresistant strains to antibiotics. According to statistics from the literature, [14] [15] staphylococcal infection was the most common cause of infection associated with mechanical ventilation, surgical wound infection and bacteremia due to intravenous devices. [16, 17, 18]

Identification and knowledge of these phenotypes of resistance was useful in initiating empiric therapy, especially in critical situations when etiological treatment cannot be delayed.

As empirical antibiotic management strategies we suggested using netilmicin, amoxicilline-clavulanate or trimethoprim/sulfamethoxazole (TMP/SMX). For patients with history of allergies or severe infection, looks like the empiric treatment should have been gentamicine.

In conjunctivae or ear infections caused by MSSA, as initial therapy we used empirical netilmicin or amoxicilline-clavulanate.

In the empirical treatment of skin staphylococcal infection (abscess, wound) gentamicin and oxacillin or netilmicin can be used and in severe infections, polymicrobial or in case of allergy to β-lactams then vancomycin ± gentamicin or vancomycin + imipenem.

The lack of alternatives for empirical treatment was an important risk factor for selecting strains resistant to tobramycin and amoxicillin / clavulanic acid, and raises the question of their use as antimicrobial therapy in some situations. The best results in vitro had shown netilmicin, but widespread use of this antibiotic may lead to selection of resistant staphylococcal strains. TMP/SMX can be a good alternative, per os.

We did not test Clindamycin because, despite some studies that provide in soft tissue infections this substance, in other two recent papers from our country the efficiency was disputable [19]. Although the literature cites the emerging number of strains resistant to vancomycin and linezolid, during our study period there were no strains isolated to be resistant to these antibiotics.

Conclusions

Most staphylococci were isolated from the respiratory tract, followed by those of the skin and soft tissues. The strains of Staphylococcus aureus were 4 times more frequently isolated then the strains of coagulase-negative staphylococci. Most of the staphylococcal strains isolated were susceptible to methicillin. More than 75% of the isolated MSSA strains were resistant to more then two antibiotics. The highest levels of sensitivity were noted to netilmicin, and it may be a treatment option in some cases, in view of the high sensitivity in vitro to this drug. Oxacilin was not an option for hospitalized patients with those strains. Glycopepdides were still an option in our severe cases.

Limitation of our study: data collected from a single Hospital, and the sole period of time, randomly, without a separation between the hospital wards, and between different age groups.

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THE BEST VEGETABLE OIL FOR PRETERM AND TERM INFANT MASSAGE

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Abstract

Although is incompletely developed, in a full process of maturation for months after birth, neonatal skin has important developmental roles and in preventing morbidity. Ancient practice, oil massage of the infant has multiple benefits but recent studies are demonstrating that not all oils are suitable for infant massage. The paper is reviewing the neonatal skin characteristics and functions, the benefits of oil massage, and the role of emolients in neonatal skin care, presenting the the effect of different vegetable oils used for preterm and term infants' massage. Composition of vegetable oils must be known before recommending or using a certain vegetable oil for infant massage, since not "everything natural is good or safe for children". More studies are needed to establish the biological value of the vegetable oils in neonates, to clearly delineate which vegetable oil is the best in terms of efficiency and safety for infant massage.

Keywords: neonatal skin, vegetable oil, oil massage, sunflower oil, preterm infant

Introduction

The neonatal skin is structurally and functionally immature both in preterm and term infants and has multiple protective roles, having an important role for morbidity and mortality prevention in infants. Therefore, neonatal skin care must address these important characteristics of the neonatal skin and limited cutaneous skin barrier functionality, aiming to maintain skin integrity, to avoid exposure to harmful chemical agents, and to prevent toxicity.

Purpose

The aim of the paper was to review the scientific proofs regarding the best option for oil massage of the newborn.

Material and method

The authors reviewed the published literature regarding neonatal skin maturity and function in preterm and term infants and use of oil massage for neonatal skin care. The use of emolients and vegetable oils for massaging preterm and term neonates was also reviewed as regards effects and recent controversies related to vegetable oils content as these aspects are less known for clinicians and different fatty acid content may have beneficial or harmful effects on the neonatal skin. The search for relevant papers used the major databases and search engines on medicine, biomedicine, chemistry, and multidisciplinary (as for example Pubmed, Medline Plus, Pubchem, Scopus).

Results

A. The neonatal skin

The skin is a complex, dynamic organ with multiple vital functions: physical barrier between the body and environment, body temperature regulation, immunity and protection against pathogen invasion and ultraviolet radiation, gas exchanges, sensorial perception. (1-8). Development of the aqueous barrier of the skin begins during the first trimester of the pregnancy and is finalized by 34 weeks of gestation. (2,8-10), maturation of the epidermal cells continues during the entire pregnancy while the corneous stratum and the dermal-epidermal undulations are seen at 34 weeks gestation when the cutaneous barrier maturation is almost complete. (9,11-14) Even in term infants, with a normal functioning of the cutaneous barrier, an increased tendency to irritation and allergic dermatitis is described, presumably due to increased percutaneous absorption and an incompletely developed functionality. (15,16)

Cutaneous barrier functionality is also influenced by the environment and by the dramatic changes occurring during transition from the aqueous intrauterine environment to the colder, drier, and extremely variable extrauterine environment. Initial studies suggested that functional adaptation of the skin to adult functionality takes weeks to months (17) but recent studies demonstrated that maturation may take up to 12 months. (9,18-21) Therefore, the neonatal skin is very sensible, thin, and fragile, prone to increased transepidermal water loss, abnormalities of the fluid and electrolytes homeostasis, excessive bacterial proliferation, vulnerable to trauma, and increased sistemic toxicity (due to increased absorption of chemicals applied on the skin, increased body surface/body weight ratio, and immature systems for drug metabolization). (2,4,13,22-26)

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A thinner skin, with weaker cohesion between dermis and epidermis, increased vascularization, and a less efficient skin barrier are mounting all this risks in the preterm infant (4,27) suggesting that efficiency of the cutaneous barrier functionality is critical for decreasing the neonatal morbidity and mortality, especially in low birth infants. (4,5,28,29) The skin of the preterm infant is comparable with the term infant's skin only 2-3 weeks after birth. (2,30) There are studies showing that during the late neonatal period 50% of the neonatal deaths are related to infections and an incompetent skin barrier is the major predisposing factor for neonatal sepsis. (31,32)

The main factors supporting the neonatal cutaneous skin barrier function are: a more neutral skin pH - protecting against infections and water loss (4,5,8,22) -, epidermal lipids - important for maintaining the skin integrity but with lower concentrations in newborns due to decreased activity of the sebum producing glands and increased water content of the skin (4), natural emolient factors of the stratum corneous - acting as lubricating agents (9) -, and antimicrobial peptides produced by keratinocytes (5) -. Another important factor to consider in neonates is the unique adaptive flexibility of the cutaneous barrier allowing optimization of the growth and skin development, thermal regulation, transepidermal water loss, and protective mechanisms. (2,8,21)

Neonatal skin care must address these important characteristics of the neonatal skin and limited cutaneous skin barrier functionality, aiming to maintain skin integrity, to avoid exposure to harmful chemical agents, and to prevent toxicity.

B. Massage during neonatal period

During the last two decades a great emphasis was put, in neonatology, on developmental care of the preterm infant. Touch is recognized as one of the principle of the developmental care (33) therefore massage of the newborn, especially of the preterm infant, was more and more integrated in this modern type of care, in neonatal units and at home. Moderate pressure massage, by kinesthetic tactile stimulation, stimulates infant growth and development (34-37), brain development, reduces the stress level, and decreases the risk for retinopathy of prematurity (38,39).

C. Oil massage during neonatal period

First introduced in China, in the 2nd century B.C. (40), oil infant massage is a routine practice in many of the countries of the Indian subcontinent and Mediterranean area. (5,41,42) Studies performed in the latest years have undoubtedly demonstrated numerous benefits of the neonatal oil massage: improved skin status and prevention of cutaneous lesions (25,28,42), improved thermoregulation (25,41), increased weight gain (due to increased vagal activity, improved gastric motility, increased level of insulin-like growth factor 1 (10,37), and by preserving warmth and energy (43)) (44-49), better sleep/arousal pattern (44-46)], improved sympathetic central nervous system development (44,45), decreased stress levels, better coordination of respiration with heart activity (50), improved motor and emotional development (46-49,51), increased oxygenation (52), decreased nosocomial infections and mortality rates (25,37,44-46,52,53), increased bone density (46), better skin nutrition (due to lipids absorption through the skin) (47,48), decreased hospitalization in the intensive care units (44,45), reduced hospitalization costs. (54) Most of these benefits are seen with simple massage but oil massage is more efficient. (55)]. Also, applying oils immediately after bath, on the wet skin is more efficient. (4) Compared to simple massage, oil massage is associated with decreased motor activity, decreased stress behaviors, increase vagal activity, and increased salivary cortisol level. (35,56) However, experts are cautioning against vigorous massage, even with oils, since it increases the risk for rashes, skin lesions, bacterial colonization, and infections. (28,41,55) Some of the adverse effects of the oil massage of the newborn are related to the used oils. (41)

Common name	Sistematic abreviation	Olive oil	Sunflower oil	Soy oil	Rapeseed oil	Sesame oil	Peanut oil
Palmitic acid	16:0	11.5; 12.22	6; 6.6; 7.31	10; 12.13; 5.80; 11.1	4; 3.36; 5.15; 3.73	8.5; 11.2; 10.2; 5.14	8.75; 10; 6.23; 14.1
Stearic acid	18:0	2.5	3.08; 5; 3.75	3.49; 5; 8.28; 5.6	1.5; 2; 1.66; 3.49;	4.5; 5.22; 5.42; 5.14	2.14; 3; 2.95; 2.7
Arahidic acid	20:0	0.5	0.5; -; -	0.5; -; -;-	0.5; 0.67; -; -	-; 0.5; -:-	1.05; 1.5; -; 1.6
Oleic acid	18:1(9)	74.37; 75.5	17.31; 23; 29.5	21; 23.41; 31.5; 22.6	61.6; 63; 65.3; 50.95	41.91; 42; 43.0; 39.65	41; 60.21; 68.49; 49.1
Linoleic acid	18:2(9,12)	7.5; 9.84,	63; 73.31; 59.2	53; 54.18; 45.00 ; 47.2	20; 20.38; 19.8; 39.75	40.08; 4.5; 41.1; 44.73	35.5; 21.28; 18.28; 27.4
Linolenic acid	18:3(9,12,15)	0.59; 1.0	<0.5; -; 0.07	0; 6.5; 5.49; 5.7	8.47; 9; 7.86; 0.34	0; -; 0.14; 0.56	0; 0.54; 0.05; -
References		(97,104)	(97,104,105)	(97,104,108,109)	(97,104,105,108)	(97,104,105,108)	(97,104,105)

Table 1. Reported fatty acid composition of some vegetal oils

Vegetable oil	Oleic acid	Linoleic acid	References
	18:1(9)	18:2(9,12)	
Mustard	9.26	13.79	(101)
Safflower	12.59; 12	77.54; 78	(97,104)
Corn	24.9; 39.65; 32.5; 27.5; 27.65; 28.6	33.6; 44.73; 52; 55.7; 57.21; 55.6	(97,103,104,108,111)
Wheat germs	17.42; 20; 14.36	56.72; 52; 61.62	(97,104)
Walnut	16.8; 16; 22.65, 28.3	58.35; 59; 55.13; 53.8	(97,103,104)
Pumpkin	36.5; 28.7; 24; 25.9;	44.46; 59.5; 54; 50.9,	(103,104,105)
Rice bran	40.4	36.1	(104)
Argan	45.1	34.2	(113)
Grapeseeds	62.26	6.22	(114)

Table 2. The oleic and linoleic acid content of some oil

D. Emolients during the neonatal period

Emolients are acting by softening the skin, establishing it's elasticity and homeostasis, lubricating and humidifying the skin, preventing transepidermal water loss, and preserving the skin integrity. (2,4,5,22,57) There are studies demonstrating also that emolients may prevent atopic dermatitis (4,58), nosocomial infections, and neonatal mortality. (59,60) On the surface of the skin, emolients are leaving a lipid film that fills the spaces between corneocytes, facilitating their adherence to the corneous stratum, humidifying and occlusive effects that prevent water loss. (61) Oils applied on the skin are offering lipids to keratinocytes, lipids that are transported by the cell membrane and metabolized into the cells (59) and used to build a functional epidermal barrier. (62) Oils must not be used in dermatoses, skin inflammatory lesions, and in flexure areas due to the occlusive effect. (4) Emolients that are not irritant for the skin, containing lipids known to improve skin barrier are recommended in preterm and term infants. (4,29,63) Some are recommending mineral oils on the maturing skin arguing that mineral oils are more stable, semi-occlusive, not miscible with water, and with longer term of validity. (5,64) Unfortunately, there are no long-term studies evaluating the use of emolients in the neonatal period. (5) A recent systematic review based on 8 studies developed in developing countries evaluating emolient use compared to routine skin care in the first 96 hours of life for a minimum of one week, in infants less than 37 weeks gestation, showed that emolients decreased the mortality rate by 27%, the infection rate by 50%, improved weight gain without significant impact on height and cranial circumference in the first month of life. (65) An even more recent meta-analysis of 18 eligible trials, comprising 3089 infants, evaluating topical emolients showed no difference as regards the rate of invasive infections (relative risk of 1.13 [95%CI 0.97-1.31]) and the mortality rate (relative risk of 0.8 [95%CI 0.5-1.03]). (66) Another meta-analysis, evaluated topical ointments effect against nosocomial infections, applied in the first 96 hours of life in 1304 preterm infants aged less than 37 weeks gestation and found that the procedure increased the risk of infections with coagulase-negative Staphylococcus, the risk for any infection, and for nosocomial infections (relative risks of 1.31, 1.19, and 1.20, respectively) but authors evaluated only 4 trials and speculate that the results may be due to contamination of the ointments and/or occlusive effect of the ointment delaying the skin maturation. (67)

E. Vegetable oils used for massaging newborns and preterm infants and their effects - current knowledge and controversies

Massage with vegetable oils in the neonatal period have demonstrated that some of them may increase the skin integrity and decrease the risk of dermatitis (57,68) but controversies related to efficiency in at risk neonates are persisting. Cutaneous and systemic benefits of the oils are based on the oil's composition (25), some of them having even toxic effects after skin absorption or delaying the healing of a compromised cutaneous barrier. Adverse effects are seen mostly in preterm infants. (25,41,42) Recent studies have shown that, applied on the skin, the oils are penetrating the corneous stratum and oils containing even low concentrations of oleic acid (over 25%) may disrupt the protective skin barrier, penetrate the dermis-epidermis junction, affecting it's permeability and integrity. (69-71) Some unsaturated free fatty acids (like oleic acid) may act as facilitators for skin permeability, thus favoring contact dermatitis. (72-74) Triacylglycerols (triglycerides) do not cross the skin but lipases from the resident cutaneous flora can break triacylglycerols into glycerol (important skin humidifier (75)) and free fatty acids. (76) Vegetable oils have a variable composition in essential fatty acids, some of them having negative effects on the cutaneous barrier due to increased concentration of oleic acid (as olive, soy, and mustard oils). (5) The benefits of the vegetable oils may be due to fatty acids effects on the lipid structures of the cutaneous barrier. (25,41) A theory suggests that fatty acids from the oils are absorbed in the blood and thus modulate the barrier function and other aspects of the immune function from other entrance gates of the pathogen agents (gastrointestinal and pulmonary mucosa), a theory based on the fact that the deficit of essential acids is associated with increased risk of translocation of intestinal bacteria (77) and

that various diets with essential fatty acids can modulate inflammation, improve intestinal barrier functioning, decrease the rate of infections originating in the gut, improve pulmonary function, and mortality rates. (28,78) Oils containing medium chain triacylglycerols have the potential to improve the nutrition of the preterm infants, as these oils can be absorbed through the skin. (35,36) The recent meta-analysis performed by Clemison and McGuire (66) on 11 studies, comprising 1184 infants, mostly premature infants, evaluated the use of vegetable oils and found no significant difference as regards the incidence of invasive infections and mortality rate but significantly increased weight gain, liner growth, and better growth of the cranial circumference, concluding that topical vegetable oils are improving growth and cautioning that the analyzed studies weren't blinded.

Sunflower oil is cheap and universally available and therefore the most studied oil for infant massage in the latest years. Sunflower oils contain only 16-19% oleic acid and 68-72% linolenic acid (79), reflecting the cutaneous lipids, and very similar with the human sebum of the skin, and demonstrates regenerative, reparative, and humidifying effects, improving the cutaneous barrier when applied on the neonatal skin. (80) Sunflower oil has also the capacity to restore the intracellular lipids. (81) Oils containing triacylglycerols, as sunflower oil, may interact directly with proteins in the skin, decreasing the risk of irritation due to surfactants. (82) Glycerol trioleate in the sunflower oil binds to proteins from the stratum corneous increasing their flexibility more than mineral oils. (83) Comparative studies demonstrated that sunflower oil is superior to olive, mustard, and soy oil as regards rapidity of healing the cutaneous barrier, toxicity, and contact dermatitis risk. (4,63,84) A randomized controlled study compared sunflower oil massage to simple massage and no intervention in 69 preterm infants less than 1500 g birth weight and less than 37 weeks gestation in the first 10 days of life and found a better weight gain and no influence on the neurodevelopmental scores at 10 days of life. (43) Another randomized controlled trial on 22 premature infants, with birth weights of 1500-2500 g, compared oil massage versus standard care in the first 10 days of life and found decreased skin pH, decreased regional water losses, no significant effect on the sebum production, concluding that sunflower oil may insignificantly support the maturation of the skin barrier in preterm infants but the results may have been influenced by the lower gestational age of the infants assigned to sunflower oil massage group. (85) A comparative study of sunflower oil massage versus petroleum found similar results in decreasing the nosocomial infection and mortality rate. (52) The antibacterial effects of the sunflower oil are supported by some trials (most of them coming from developing countries) (28,52,60) and denied by other studies, most of them developed in industrialized countries. (66,67) A comparative study of sunflower oil massage versus coconut oil versus only massage in preterm infants showed that sunflower oil was more efficient in improving oxygenation and reducing the stress levels. (50) In term infants, oil massage with sunflower or olive oil showed that oils improved skin hydration but the structure of the cutaneous lipid lamellae was insignificantly influenced, implicating that oils may affect the cutaneous barrier functioning. (74)

Olive, mustard, and soy oil are oils with increased content of oleic acid and, in the light of the results of the recent studies, have the potential to disrupt the cutaneous barrier, predisposing to skin lesions. (5,71,86) Olive oil, although one of the most recommended for the skin care of the newborn even in neonatal units and maternity hospitals (87), contains 55-85% oleic acid and should be avoided in preterm and term newborns. (82,88-90) Increased risk for atopic dermatitis and exacerbation of atopic dermatitis were reported with olive oil use. (2) Mustard oil was used mostly in India but its use is now restricted due to demonstrated negative effects - increased cutaneous water loss, delayed functional maturation of the skin barrier, ultrastructural changes of the keratinocytes -, and increased risk for irritative reactions. (55) Allylisothiocyanate, the main antigen contained in mustard oil, has the potential to induce contact dermatitis. (91,92) Hypersensitivity to mustard oil was also reported. (93) Limited clinical data are available for the use of other vegetable oils for massage in the neonatal period. Coconut oil is not hydrogenated, contains 92% saturated fats and no cholesterol, and is, in fact, a mixture of short and medium chain fatty acids, especially lauric acid (44%) and miristic acid (16.8%). (35,55) Some authors are suggesting that coconut oil can be used in preterm infants as an alternative to sunflower oil but evidence is less supportive as for sunflower oil. (55,82) Safflower oil is rich in essential fatty acids and massage with safflower oil increases the triacylglycerols and essential fatty acids (linolenic and arachidonic acid) levels while massage with coconut oil increases the level of saturated fats mostly in term neonates. (35,86) Sesame oil massage, versus herbal oil, mustard oil, and mineral oil, was more efficient in improving growth parameters and sleep in newborns. (48) Other oils that have been recommended based on their increase content of linolenic acid content are grape seeds oil (55,86) and almond oil. (65)

Experts are advising also on some practical points of using vegetable oils for massage in preterm and term infants during neonatal period. Vegetable oils have also disadvantages: some of them are unstable, degradable by hydrolysis and oxidation, increasing the risk for microbial growth especially in humid and warm environments. (5) Careful attention is warranted with storage of this oils. Also, for neonates, formulations without preservatives may haste degradation (5) while many preservatives are harmful to neonatal skin. (93) Refined oils are free of impurities, have a smooth texture and almost no smell, and longer validity. (94) Refinement destroys proteins binding allergens, therefore refined oils have a decreased risk for allergic reactions (95), experts recommending individual vials of about 50 ml of extremely refined vegetable oil as safe and not toxic for preterm infants. (82,96) Cold pressed oils are not sterile and may contain bacteria and/or fungal spores, increasing the risk for infections. (82) Since oil massage is traditional worldwide, cookery and kitchen vegetable oils

are sometimes used but experts are cautioning that these oils are chemically heterogeneous, sensitive to oxidation and light, and have variable biological activity and thus may have unpredictable effects when topically applied. (88,89)

F. Vegetable oil content - less known aspects

Vegetable oils are refined lipids containing mainly triacylglycerol. (97) Most of the oils are vegetal and, beyond triacylglycerol, they contain other lipid fractions. These lipids may be simple (not saponifiable) - free fatty acids, steroids, carotenoids, monoterpenes, tocopherols - or acyl lipids (saponifiable) - mono-, di-, triacylglycerols, phospholipids, glycolipids, waxes, sterol esters. (97). Other lipids and even nonlipid components are collected together with glycerides from vegetal tissues during the extraction process. These minor fractions are important for the sensorial, chemical, physical, and biological properties of the oil. Some of these fractions are responsible for oils chemical instability and for the specific taste and aroma, and are removed through refinement.

Crude oils are processed to eliminate unwanted components as phospholipids, glycolipids, free fatty acids, waxes, pigments, autooxidation products, phenolic compounds, trace metal ions, and other contaminants. The refining process consists in several steps: lecithin removal through washing with water, degumming (carbohydrates and protein removal) by phosphoric acid addition, free fatty acid removal mainly through alkali addition or distillation (for oils with high content of free fatty acids), bleaching Al-silicates and activated charcoal, and deodorization through vacuum steam distillation. (97,98)

The most important fraction of oil are triacylglycerols, esters of glycerol with fatty acids. Fatty acids are aliphatic carboxylic acids that can be differentiated through their chain length and number, position, and configuration of double bounds. Fatty acids present in oils are responsible for their physical properties (as, for example, viscosity and solid or liquid phase at room temperature), and chemical and biological properties. According to sources, each oil has a different composition in fatty acids. Table no. 1 is presenting the fatty acids composition of the most used vegetable oils. As expected, olive oil has the highest content in oleic acid, around 75%. Other oils have also a high content in oleic acid: rapeseed (canolla) and peanut oil have an oleic acid content higher than 50% while the lowest level of oleic acid is found in sunflower oil.

Table no. 2 is presenting the reported content in oleic and linoleic acid in some other edible vegetable oils. Regular mustard seeds oil (rapeseed, *Brassicacea*) has a high content in erucic acid which is harmful for humans (97,99,100) in proportions higher than 5%. (97) Varieties of rapeseeds with no erucic acid are normally used for producing the edible oils. (101) These oils are containing 68% monounsaturated fatty acids (mainly oleic acid). Other edible vegetable oils with lower oleic acid content are safflower and corn oil. Another oil with low content of oleic acid is extracted from melon seeds (lower than 18.2%). (102) The highest content in oleic acid is observed in Camelia oil (tea) (79.5%). (103) High levels of oleic acid are also seen in hazelnut, avocado, almond, and apricot kernel oils (78, 70.55, 69.9, and respectively 60% oleic acid).

A special attention must be paid to oils obtained from plant varieties genetically modified. Oils with higher oleic acid and lower linoleic acid content are preferred as they are more stable. (97,104,105) The content of oleic acid in oils from genetically modified sunflower reaches 87.4–91.2% while the regular sunflower oleic acid content is 15.0–50.9%. (106) Worldwide, areas cultivated with high oleic acid varieties increased at about 11% of total area cultivated with sunflower. (107) Other plants were genetically modified to increase the oleic acid content of the oil: an oil with 81.8% oleic acid was produced from safflower, another one with 65% oleic acid from corn, while from peanut and soya oils with 80, respectively 85.6% oleic acid were obtained. (100)

Refined oils are indicated for human use, edible or for external use. Crude oils are more flavored and contain many valuable components as carotenoids, sterols, tocopherols, phospholipids but they also contain many harmful components as free fatty acids which are more exposed to oxidation, oxidation compounds, microorganisms, proteins with allergenic potential. Regular rapeseeds are containing glucosinolates which are decomposed in esters of isothiocyanic and other volatile compounds that are hazardous to health and detrimental to oil flavor. (97) Crude oils are refined in order to increase oil stability and shelf life. Natural and synthetic antioxidants are also added. Natural antioxidants added are carotenoids and tocopherols, while butylhydroxytoluene (BHT) and butylhydroxyanisole (BHA) are used synthetic antioxidants. (97)

Conclusions

Available data regarding vegetable oil usage for massaging preterm and term infant, even though abundant, are recently challenged by studies showing that benefits and risks associated with vegetable oil use in the neonatal period are highly dependent on the fatty acid content of the oil. No clear recommendations exists about the use of topical oils for the skin care in neonates, past and recent controversies and the lack of data on long-term complicating the development of such recommendations. Parents are prone to errors in the absence of competent advise, falling often in the trap of the misconception that "what is natural is safe". (87) More studies are needed to establish the biological value of the vegetable oils in neonates, and to more clearly delineate which vegetable oil is the best in terms of efficiency and safety for massaging the preterm and term infants.

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CARDIOVASCULAR INVOLVEMENT OF KAWASAKI DISEASE IN THE WEST PART OF ROMANIA

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Abstract

Introduction: Kawasaki disease is a self-limited vasculitides, that usually affects medium and small vessels, and more often is the affliction of children with ages between 0-5 years. Complications of Kawasaki disease include: coronary artery disease, left ventricle dysfunction, myocarditis, myocardial infarction. Aim: To present the cardiac involvement in patients diagnosed with Kawasaki disease, admitted into our clinic over a period of one year, despite the fact that this diagnosis is very rare in our region. Materials and Methods: Five patients were admitted into our clinic for prolonged fever, for whom clinical examination, lab tests, ECG, Echocardiography and in severe cases, Computer Tomography with Angiography and/or Coronary Angiography were performed. Results: Kawasaki disease was confirmed in all five cases. The majority of patients were females. One single case was a recurrent Kawasaki disease. 60% of our patients were found with cardiac involvement, out of which one was diagnosed with giant aneurysmal dilatation of the right and left coronary artery, of over 8 mm, later complicated with intracoronary thrombus and IIIrd grade mitral regurgitation. One case had mild left coronary artery aneurysmal dilatation with wall thickening and the third just minor aneurysmal dilatation of the left coronary artery. All patients presented thrombocytosis, but the level of the thrombocytes was extremely high in patients associating coronary affliction. Intravenous immunoglobulin (IVIG) and Aspirin was administered in all cases. Anticoagulation therapy was associated in one patient with intracoronary thrombus formation. Conclusions: Kawasaki disease incidence is increasing in the west part of the country. Coronary artery involvement was present in 60% of cases. Giant coronary artery aneurysm with intraluminal thrombus formation was the most severe complication found. High thrombocyte values were associated with coronary artery involvement. Immediate IVIG administration and Aspirin can help in preventing coronary artery complications and in reducing the coronary inflammatory process. Anticoagulant therapy was needed when thrombus was present. A regular follow-up plan is needed in all patients with Kawasaki disease and cardiac involvement, especially in patients with giant aneurysm formation.

Keywords: Kawasaki disease, coronary artery, giant aneurysm, thrombus

Background

Kawasaki disease is a relatively rare disease in our country. It is more frequently diagnosed in Asian countries, with a peak incidence in Japan, where it was for the first time described by Tomisaku Kawasaki. As of late, there are more cases, not only in Japan or China, but they have been diagnosed in the Central part of Europe. Although Kawasaki disease is a self-limiting disease, it can sometimes have severe cardiovascular complications. For a positive diagnosis, which is mainly clinical, a high grade fever for more than 5 days is needed and four or more of the following symptoms: polymorphous rash, extremity modifications with edema of the hands and feet, bilateral conjunctivitis, strawberry tongue, cracked lips, unilateral cervical lymph node enlargement. The complications consist of myocarditis, left ventricle dysfunction, valvular dysfunction, more frequently regurgitations, dilatation of the coronary arteries that can lead to aneurysm formation, intravascular thrombus formation, myocardial infarction and even sudden death. By far, the most common complication is aneurysmal dilatation of the coronary arteries.

Aim

The objective is to present the cardiovascular implications in patients admitted into our clinic for prolonged fever, that were diagnosed with Kawasaki disease, study performed over a one-year period. Proper treatment can reduce vascular inflammation in order to prevent severe cardiac complications or to stop progression of the coronary artery damage, this being the case for some patients.

Material and method

Five patients were admitted into our clinic, over the last year, with symptoms of high grade fever that would not easily respond to antipyretics, peculiar rashes, nonexudative bilateral conjunctivitis, cervical lymph node, strawberry tongue and fissured lips. All of them underwent thorough clinical examination, laboratory tests, Electrocardiograms and Echocardiography, even daily when it was necessary. Whenever Echocardiography results were not sufficient, Computer Tomography with Angiography and/or classic Coronary Angiography were performed in selected cases.

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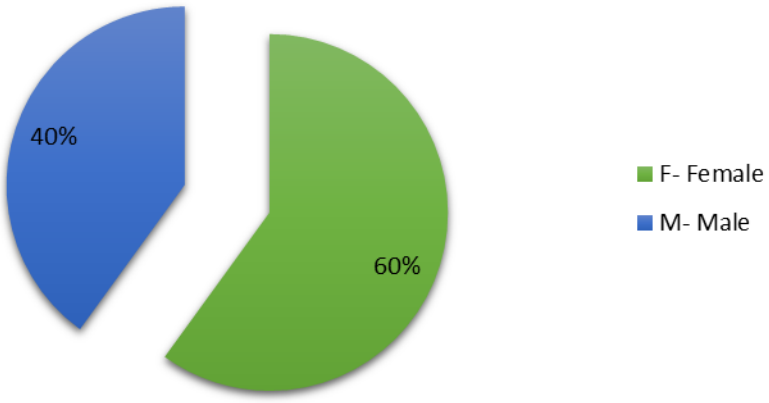

Fig.1. Case repartition according to gender.

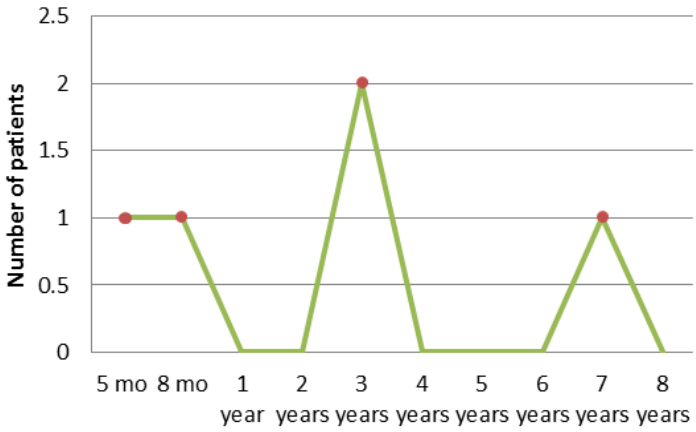

Fig.2. Case repartition by age

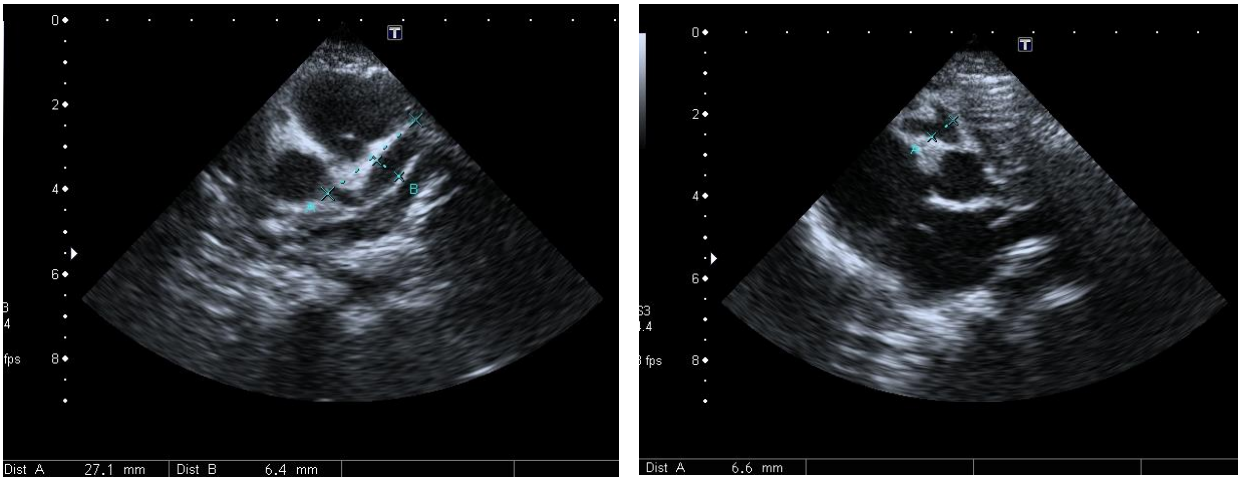

Fig.3. A. Medium dilatation of the left coronary artery (LCA-LAD) of 6.4 mm;
B. Medium dilatation of the right coronary artery (RCA) of 6.6 mm.

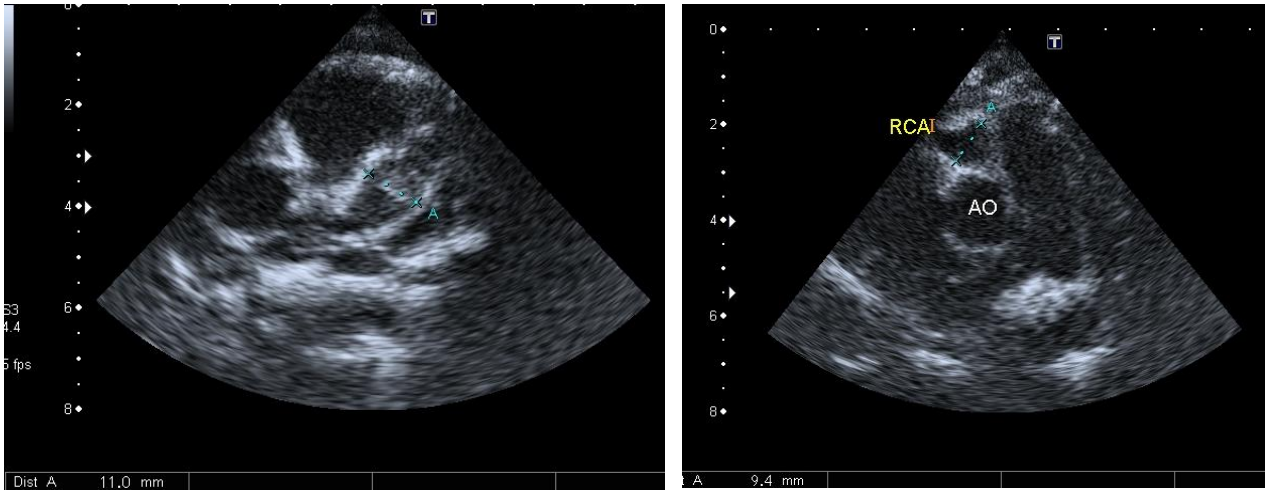

Fig.4. A. Giant aneurismal dilatation of the left coronary artery (LCA-LAD) of 11 mm with thrombus formation inside;

B. Giant aneurismal dilatation of the right coronary artery of 9.4 mm

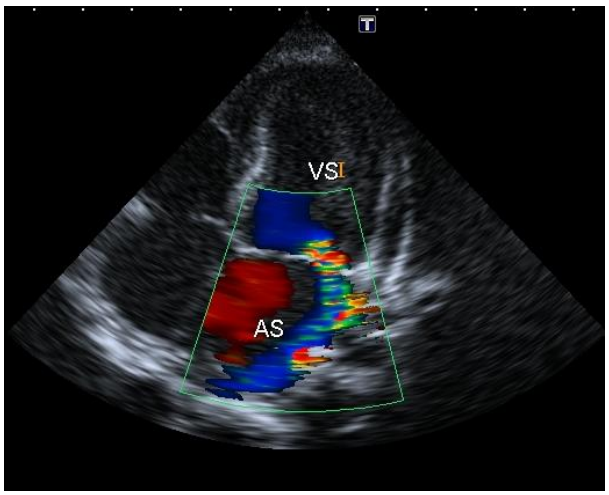

Fig.5. Third grade mitral regurgitation

Results

Over the last year, five children with Kawasaki's disease were diagnosed in our clinic. There was a predilection for the feminine gender, 3 patients, representing 60% of all patients, were females, and only 40% of the total amount of patients, were represented by males, 2 patients (Fig. 1). Regarding the age distribution, two cases were infants with ages of 5 and 8 months, two children of 3 years and one pre-school patient, of 7 years (Fig. 2). The infants were one male and one female. The children were both girls and the preschool patient was a 7-year-old girl.

After the clinical examination we classified the patients according to their clinical manifestations of the disease; if they exhibited the entire pallet of symptoms from the Kawasaki criteria, they were classified as complete Kawasaki disease, 60% of our patients were part of this group, meaning 3 cases. If they only had fever and a couple of symptoms, they were classified as incomplete Kawasaki disease, 20% of patients being repartitioned here, meaning 1 patient. The last group was recurrent Kawasaki disease, also 20% of patients, meaning one case.

Three, out of five patients, meaning 60% were discovered with cardio-vascular complications at the first cardiological examination. All of them presented aneurysmal dilatation of the coronary arteries. We classified them according to severity of aneurysmal dilatation of the coronary artery, into three classes: minor – the caliber of the coronary artery is beneath 5 mm, medium – the coronary artery caliber is between 5-8 mm and severe or giant – the coronary artery caliber is over 8 mm. There were two patients, one with small and one with medium left coronary artery aneurysm and the third patient was found with giant coronary aneurysm.

Even though there is no specific test for Kawasaki's, after the lab examination, we noticed that all patients, representing 100%, presented with thrombocytosis, out of

which 60% of patients had values slightly over the upper limit, but 40% of patients had severe thrombocytosis, with values ranging between 800.000 - 980.000/mm3.

Coronary artery dilatation is a serious complication, which is why we would like to highlight the particular case of Kawasaki disease with giant coronary dilatation. An 8 month old male presented in the emergency room with high-grade fever for almost a week, that would not cease upon administration of antipyretics. He was agitated. At clinical examination, a rash, with the aspect of perianal erythema, conjunctivitis and unilateral cervical lymph-nodes, strawberry tongue and extremity changes with edema were found. On ECG, sinus tachycardia, 153 beats/minute and an incomplete right bundle branch block was present, but with no other modifications. Echocardiography found a medium sized aneurysmal dilatation of the left coronary artery – left anterior descending coronary artery (LCA-LAD) and of the right coronary artery (RCA) and mild mitral regurgitation (Fig. 3 A.B). Laboratory tests showed severe thrombocytosis, 800.000/mm3, which is present in almost all complicated cases of Kawasaki disease.

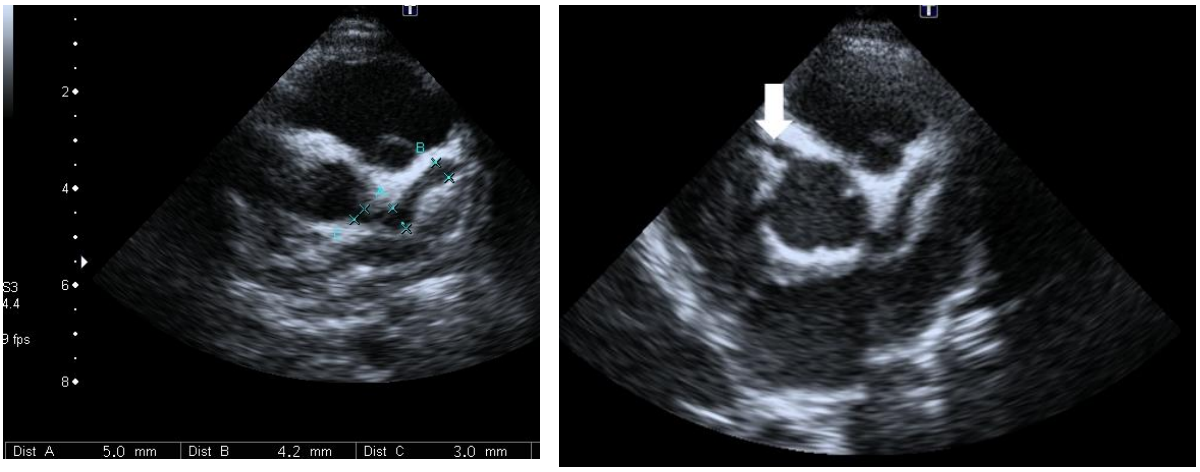

Fig.6. A. Moderate dilatation of LCA of 5 mm and the hyperechogenicity of the walls; B. minor dilatation of the RCA

After consulting the guidelines, we immediately treated the patient with IVIG 2g/kg/day and Aspirin 5 mg/kg/day. He was closely monitored, and the surprise was that, in spite of the proper treatment, he developed giant aneurismal dilatations of 11 mm of the left coronary artery – left anterior descending coronary artery (LCA-LAD) and 9.4 mm of the right coronary artery (RCA) and also associated third grade mitral regurgitation.

Returning to the guidelines, we initiate with double antiplatelet therapy: Aspirin and Clopidogrel (0.2 mg/kg/day). Under this medication, he developed an intraluminal thrombus in the left coronary artery-left anterior descending coronary artery and a third grade mitral regurgitation (Fig. 4, 5). Computed tomography of the coronary artery was performed and a clear visualization and confirmation of the thrombus was obtained. Coming back to the guidelines, anticoagulant treatment with Warfarin was started, with close INR monitoring and a follow-up schedule was established. Upon reevaluation, both coronary arteries had shrunk down, but the thrombus persisted, without obstruction, so we maintained the Warfarin and Aspirin treatment and recommended invasive catheterization with selective cardiac coronary angiography in a specialized clinic, that reconfirmed the giant left coronary artery with the thrombus inside, without obstruction.

On the 6 months' follow-up we found that the coronaries were even smaller than the previous examination and the thrombus was less intense in structure. ECG was normal, without signs of myocardial ischemia. We maintained the same treatment and recommended a second catheterization with selective cardiac coronary angiography a year after the first symptoms, as the guide underlines. The patient is doing well, with complete regression of the mitral regurgitation.

The second important case of Kawasaki disease with cardio-vascular complications was a 3-year-old female, exhibiting all necessary symptoms for a positive diagnosis and severely elevated platelet levels of 980.000/mm3. Echocardiography showed moderate aneurismal dilatation of the LCA and minor dilatation of the RCA. The particular aspect of the case was the association of moderate aneurysmal dilatation of the LCA and mild dilatation of the RCA with LCA walls thickening (Fig. 6 A.B.). Computed tomography of the coronary artery confirmed both the dilatation and the thickened walls (Fig. 7 A.B). IVIG and Aspirin were the therapy of choice.

In evolution, under treatment, the coronary artery dimensions were reduced compared with the first presentation. Platelet level reduced to normal and Aspirin therapy was stopped; now she is only on a follow-up program.

The third case presented slight enlargement of the left coronary artery with a small aneurysm that rapidly regressed under treatment.

Discussions

Although a rare disease in this part of the world, the numbers of cases seem to be growing, from a single case in years, to five cases per year, therefore the infectious hypothesis cannot be infirmed. In accord to all studies we found that the most frequent age of Kawasaki's disease diagnosis is beneath 5 years of age. Our cases were diagnosed in infancy, as usual, two cases, but also in small children, one case. However, one case was diagnosed with recurrent Kawasaki disease, which is mentioned in literature, but is relatively rare and in our female patient it occurred at the age of 7. Four years after the first episode of Kawasaki disease, the patient suddenly developed high grade fever, for more than five days, with a polymorphous rash, conjunctivitis, strawberry tongue, extremity changes and unilateral cervical lymph node enlargement. She had no cardiac involvement, except mild myocarditis with tachycardia, but because the diagnosis was recurrent Kawasaki disease, she was treated accordingly with intravenous immunoglobulin (IVIG), with a good outcome.

From the affected patients with coronary artery implication, two were females and one was male. In infant patients, one was female and one was male. The third affected patient was a three years old girl. Jane Newburger et all stipulate that the number males outnumber females in Kawasaki disease, but in our experience we claim that females are affected, rather than males, but our group was very small.

Of these five children, three had cardiovascular implications at the moment of diagnosis, such as: aneurysmal coronary artery dilatation, the left coronary artery aneurysm being more frequently involved than the right coronary artery and thickening of the coronary artery walls. One of the patients developed a severe complication such as giant coronary artery aneurysm with intraluminal thrombus formation. The rest of the patients had no coronary affliction. Under treatment with IGIV, initiated in the first 10 days of the fever onset, the evolution was good. Guidelines were not clear regarding the treatment of complex giant aneurysms, where is mentioned that "some experts recommend Aspirin and Clopidogrel". The reality was different, because under this medication, a large thrombus formed inside. It was a challenge to treat the intracoronary thrombus at such a small age, in infancy, so we had to review the literature to see the experience of different centers with severe cases of Kawasaki disease, because of the rarity of such severe complications. Finally, the patients with aneurysmal dilatation of the coronary arteries are well, with reduction of the coronary artery size, but are included in a follow up program, with special focus on the patient with thrombus, which has tendencies of reduction. This patient will remain on anticoagulant therapy. All of them have a good clinical evolution.

There are no diagnosis criteria for laboratory test to confirm Kawasaki disease, however we argue the importance of platelet count, whereas we had 100% of patients with thrombocytosis. All patients with coronary involvement presented high levels of platelets. Furthermore the levels of platelets were correlated with the severity of coronary artery affliction. The patient with giant coronary artery aneurysm and intraluminal thrombus and the patient with medium dilated coronary artery but with coronary artery wall thickening presented the highest platelet count, ranging between 800000-1 million/mm3.

IVIG is important to be administered in the first 10 days of illness, to prevent cardiac complications or to stop the progression of the coronary artery damage. One of our cases proved that despite all the effort and properly timed treatment, severe complications can still occur. Therefore, in cases with giant coronary artery aneurysm and intracoronary thrombus, anticoagulant treatment is mandatory. Giant coronary artery aneurysms are discussed in literature as isolated cases with a "single Centre's experience", so it was difficult to choose the best treatment for the case. Each Center has its own experience. Finally we turned to Warfarin and the patient is safe. New Guidelines have to be completed with recommendations for such severe cases with stratification risk of level V.

Regarding the recurrent Kawasaki disease case, it is very rare described in literature, but in our case, the clinical features matched perfectly with the Kawasaki disease criteria, being in the first ten days from the onset of fever, we decided to treat her as Kawasaki disease, with intravenous immunoglobulin (IGIV) in order to prevent cardiac involvement. The evolution was spectacularly good, with rapid fever subsidence, and extremity peeling. The patient is well. There is no indication in literature to follow up patients with Kawasaki disease without cardiac implication, because of the rarity of the recurrence.

Conclusions

Kawasaki disease's incidence has grown over the years, spreading from Japan to America and, as of late, to Europe as well. Despite all studies, we had more females affected than males, maybe a larger cohort is needed in order to sustain this assumption. Early administration of IVIG can help in preventing and reducing cardio-vascular involvement, with rare exceptions, including giant coronary artery aneurysm with intracoronary thrombus formation. Platelet count must be taken into account when the suspicion of Kawasaki disease is raised, because it is associated with cardiac involvement. In our experience, in the West part of Romania, Kawasaki disease produced, more often than not, severe cardio-vascular complications. A thorough follow-up plan is a must in Kawasaki disease with coronary artery involvement, as in the guidelines, but new guideline indications are mandatory in severe complications with risk stratifications level V, such as giant coronary artery aneurysm with thrombus formations.

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INVASIVE ASPERGILLOSIS IN AN ELBW PREMATURE

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Abstract

Invasive aspergillosis represents a severe condition, with extremely rare incidence in the neonatal period, but it is a major cause of morbidity and mortality, especially among patients with compromised immunity: extreme prematurity newborn from a mother with HIV, immune deficiency syndromes. We present the case of a ELBW premature newborn, with gestational age of 26 weeks and weight at birth of 850 grams, from a pregnancy not taken into evidence, with severe intrapartum asphyxia, APGAR index 1 on 1 minute, with severe neonatal respiratory distress and neonatal sepsis, who was transferred into the Prematures Department of the "Louis Turcanu" Emergency Clinical Children's Hospital in Timisoara in the first day of life, from a 1st degree maternity in Romania. The newborn required mechanical respiratory support throughout the entire period of hospitalization and the evolution was fulminant, towards death in the 15th day of life. Necropsy was performed, and the histopathological examination detected Aspergillus at the level of the pulmonary, hepatic, renal and intestinal parenchyma.

Keywords: Aspergillus, invasive aspergillosis, premature, sepsis.

Introduction

Aspergillus sp. continues to be an important cause of life-threatening infections in the immunocompromised patients. Patients with severe and prolonged neutropenia, severe immunodeficiency, prematures, patients with HIV or stem cells transplant have an increased susceptibility to fungal infections.

Aspergillus sp. are conditionally pathogenic fungi present in the air, water, soil or decomposing plants. Outbreaks of disease among immunocompromised persons may appear in renovation or construction works within hospitals or around them [1, 2], through inhalation of spores (conidia) in the air [1]. These colonize the superior and inferior respiratory tract and then hematologically disseminate, later determining the invasive form of disease (invasive pulmonary aspergillosis, Aspergillus sinusitis, disseminate aspergillosis).

There are known approximately 180 species of Aspergillus, of which 34 have been associated with human disease [3]. In the pediatric area most illnesses are caused by Aspergillus fumigatus (90%), followed by A. flavus, A. niger and A. nidulans [1].

Premature neonates, due to cortisone therapy and wide-spectrum antibiotic therapy, of damaging the barrier function of the skin, or the very immaturity of the immune system, may develop primary cutaneous aspergillosis or even invasive aspergillosis, with multiple organs involvement.

Case Report

We present the case of a male newborn, born prematurely at gestational age of 26 weeks, with a weight of 850g. The newborn comes from a pregnancy not taken into evidence, with imminence of abortion at 11 weeks of pregnancy, the mother 32 years old, with intrapartum anemia (Hb=7g/dl), G IX P III (we do not have data on the number of abortions requested versus pregnancies interrupted in evolution). He was born naturally, membranes broken in expulsion and clear amniotic fluid, in a 1st degree maternity in our country. APGAR score was 1 at 1' and 3 at 5'; he was ventilated with positive pressure with 100% O_2 through mask in the delivery room, then CPAP ventilation was instituted nasally, maintaining SaO_2 of 87-92%.

General condition was severe from the first day of live, and the newborn was transferred to our ward with the following diagnoses: Extreme prematurity, Neonatal respiratory distress, severe asphyxia.

On admission he presents an influenced general condition, erythematous thin skin, white-pearly umbilical stump, purulent conjunctival secretions in both eyes, cold extremities, anterior fontanelle of 2/1.5cm normotensive; functional respiratory syndrome – Silverman score=7; SaO_2=86-92% with oxygen therapy 8 l/min under cephalic tent; AV=122b/min; BP=49/31mmHg; meconium stool; diuresis present.

Cardiopulmonary X-ray was performed: discrete alveolar opacities at the base of the left lung, enhanced right infrahilar interstitial tissue, normal heart.

Laboratory tests on admission indicate: leukocytosis (Le =44.370/mm^3 on admission, increasing up to 72.680/mm^3 in evolution), reactive C protein positive, elevated Procalcitonin (1,3ng/ml) (Figure 1.), hypoglycemia, hypoproteinemia, dyselectrolytemias, mixed acidosis.

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3 hours after admission, the general condition of the premature aggravates, the respiratory functional syndrome enhances (Silverman score = 8), ASTRUP indicates severe respiratory acidosis and requires orotracheal intubation (OTI) and mechanical ventilation (MV) SIMV mode (subsequently IPPV). At 15 hours of life Surfactant was administered. Wide spectrum antibiotic therapy was also instituted, from admission into our Clinic, plus hydration and hydroelectrolytic and acid-alkaline balancing perfusion, inotropic support, gastric protector, antihemorrhagic drugs. (table 1).

General condition remained severe all throughout the admission in our Clinic (table 1). He required continuous mechanical respiratory support, transfusion of erythrocyte mass isogroup isoRh, repeated transfusions of freshly frozen plasma, Cryoprecipitate, he also received human albumin and immunoglobulin. He develops multiorgan failure, digestive hemorrhage, subsequently also pulmonary hemorrhage and death occurs in the 15th day of life.

Necropsy was performed and the macroscopic morphopathological diagnosis was: thrombosis of choroid plexuses, bronchopneumonia, hepatic and renal abscesses, suprarenal hemorrhage.

Organ fragments were also taken for the histopathological exam. On microscopic examination of samples taken specific modifications were observed, of a chronic inflammatory type, specific for *the Aspergillus type* at the level of the pulmonary parenchyma, renal parenchyma, of the liver and the intestine (Fig. 2-11).

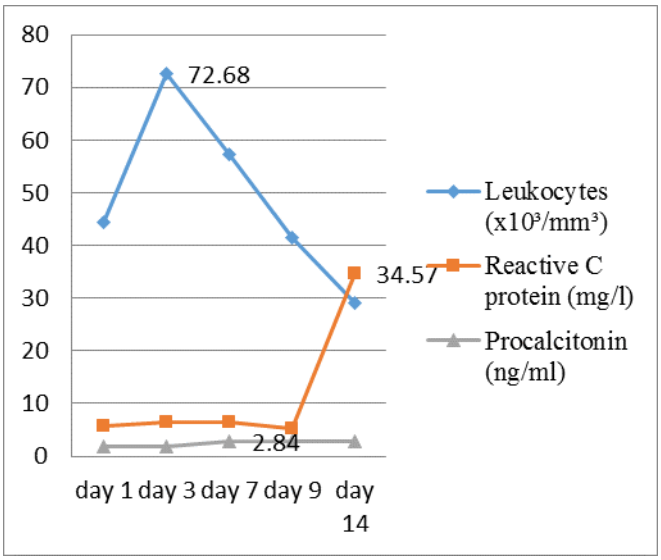

Fig. 1. Evolution of inflammatory markers

Medical problems	***Day's onset (no. of days of life)***	***Treatment***
Extreme prematurity (GA=26 weeks, WB=850g)		
Neonatal sepsis with Enterobacter aerogenes	d1	Wide spectrum antibiotic therapy, human Immunoglobulin
Neonatal respiratory distress. Acute respiratory failure, severe form	d1	Surfactant, mechanical ventilation
Arterial hypotension	d1	Dopamine, boluses with saline solution
Metabolic conditions (hypo/hyperglycemia, hyproteinemia, hyperkalemia, hypocalcemia)	d1	Hydroelectrolytic & acid-alkaline rebalancing, human albumin
Acute renal failure	d2	Dopamine, Furosemide
Thrombocytopenia	d4	Plasma
Mixed anemia (of prematurity, intrainfectious)		Transfusion of erythrocyte mass isogroup isoRh in d14
Hemorrhagic syndrome (digestive, pulmonary hemorrhage)	d12-14	Plasma, Cryoprecipitate, Etamsylate, Fitomenadione

Table 1. Medical problems and consecutive treatment.

Discussion

Early detection of infection with Aspergillus is extremely important in the premature newborn, due to the immaturity of their defense system, immune system, due to the complex and severe pathology of prematures, of complications that may occur and that are associated with high neonatal morbidity and mortality. Early diagnosis may be easier in cutaneous forms, when biopsy performed from a skin lesion with initial aspect of erythematous or purple papula, which progresses rapidly (24 hrs) towards ulceration and bedsores [4], uncovers the fungal infection and it is difficult in the invasive forms, when many times the diagnosis is established post-mortem. Diagnosis is based on a combination of clinical risks, symptoms and signs, culture, histopathology, and detection of the fungal components such as the antigen galactomannan [3].

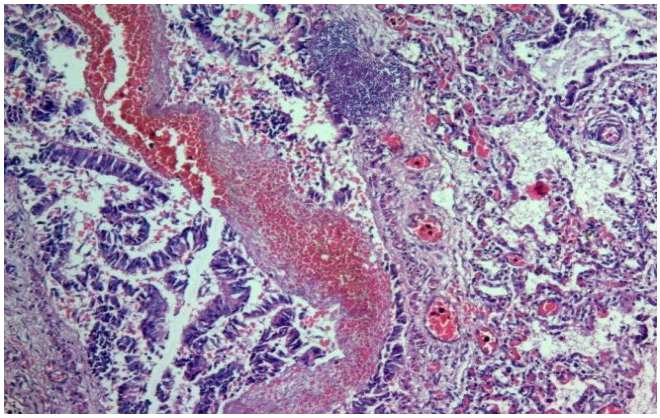

Fig. 2. Pulmonary parenchyma with specific chronic granulomatous inflammation of Aspergillosis type – hematoxylin-eosin stain

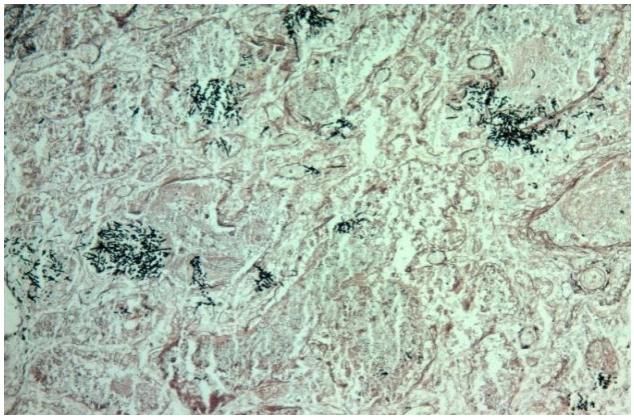

Fig. 3. Pulmonary Aspergillosis – Grocott stain

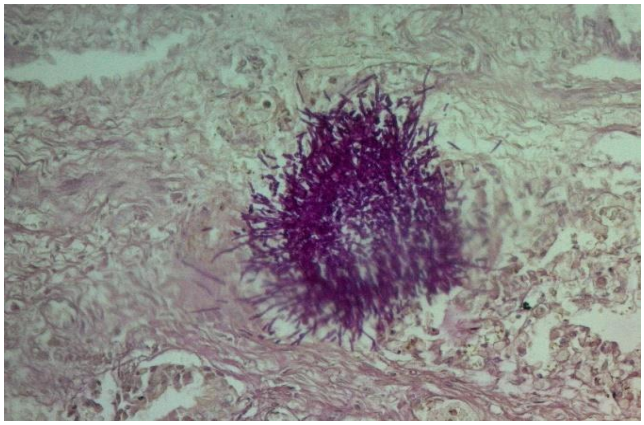

Fig. 4. Pulmonary Aspergillosis – PAS stain

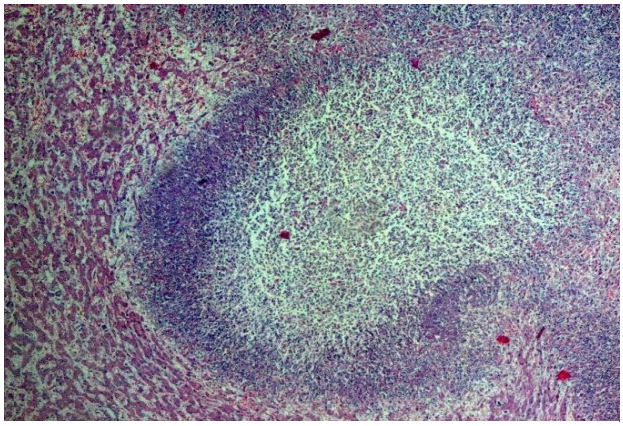

Fig. 5. Hepatic parenchyma with chronic granulomatous inflammation of Aspergillosis type – hematoxylin-eosin stain

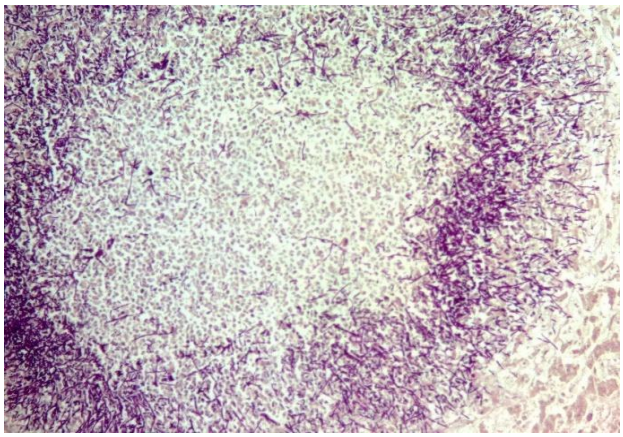

Fig. 6. Aspergillus sp. in the liver parenchyma – PAS stain

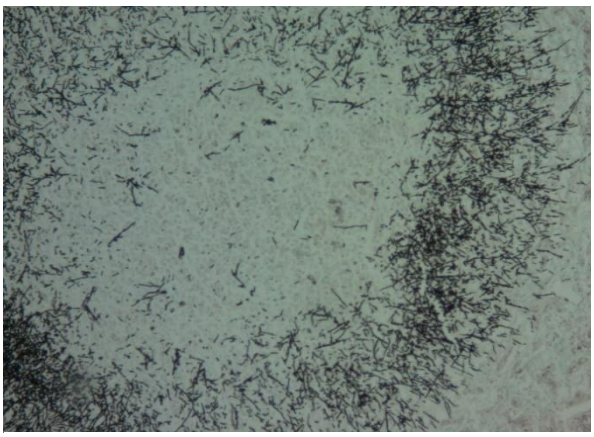

Fig. 7. Aspergillus sp. in the liver parenchyma – Grocott stain

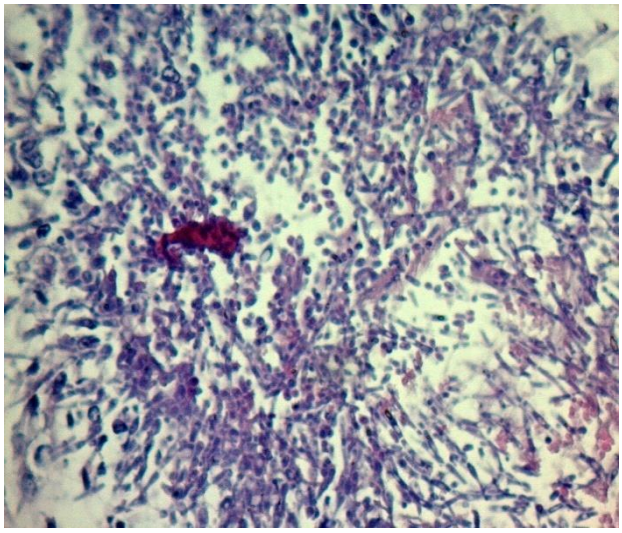

Fig. 8. Renal parenchyma with chronic granulomatous inflammation of Aspergillosis type (hematoxylin-eosin)

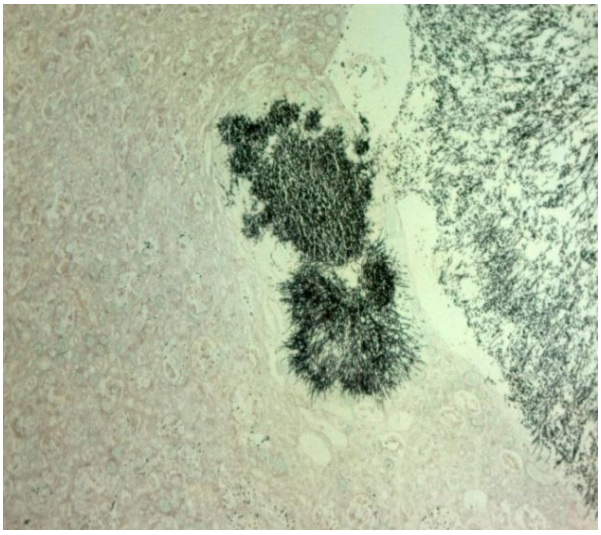

Fig. 9. Renal Aspergillosis (Grocott stain)

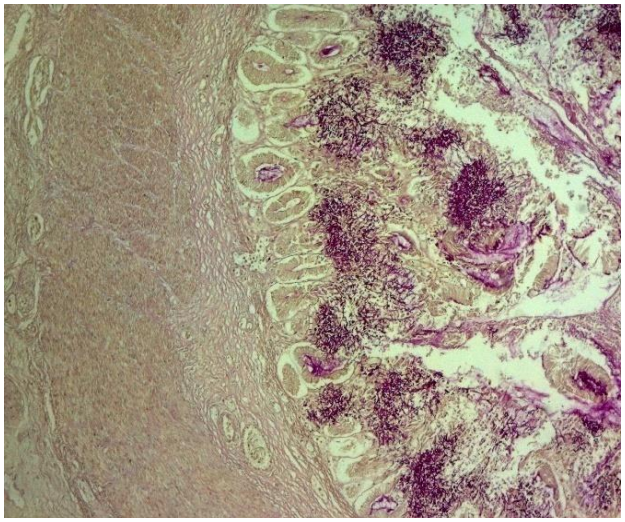

Fig. 10. Intestinal aspergillosis – PAS stain

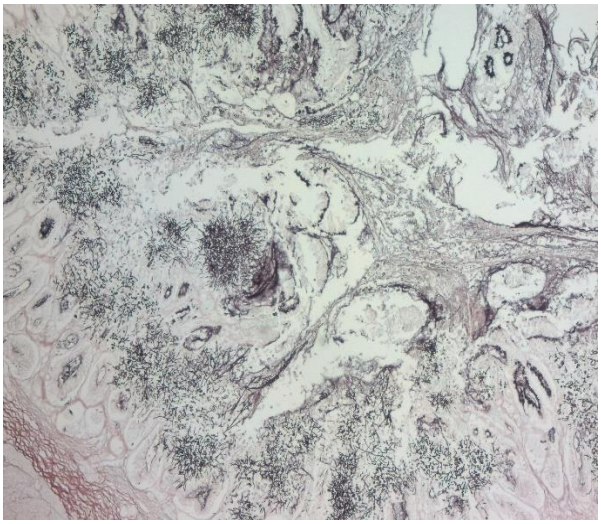

Fig. 11. Intestinal aspergillosis (Grocott stain)

The certainty diagnosis of aspergillosis is given by the histopathological or cytological exam and cultures from biopsy material (skin, lung), from secretions and blood.

In the case of suspicion of fungal infections (persistent fever in an immunocompromised patient, in spite of wide spectrum antibiotic treatment, acute pneumopathy with respiratory failure, radiologic modifications, neutropenia), detection of Aspergillus antigen through the galactomannan method is preferred to the PCR (polymerase chain reaction) technique for detecting the Aspergillus DNA, the latter not being routinely recommended anymore in medical practice. Serum and bronchoalveolar lavage galactomannan is recommended as an accurate marker for the diagnosis of invasive aspergillosis in pediatric patient [5].

In regard to the radiological diagnosis, it is difficult, the changes being non-specific (from focal or peripheral nodular lesions, to diffuse consolidations or cavities). Pulmonary computer tomography can be of greater help [6].

Isolating the Aspergillus from the sputum is a precise indicator of the invasive infection; however, according to specialty studies, only 25% of patients who were diagnosed tardy with aspergillosis had a positive sputum culture ante-mortem [7].

Bronchoalveolar lavage is also of great help in diagnosis, and nasal culture may be predictive for nosocomial aspergillosis from the renovation works.

In the case of our patient, several samples of tracheobronchial aspiration were taken, which did not detect Aspergillus or other germs at that level. Also, nasal culture was sterile. Cardiopulmonary X-ray performed on admission presents discrete alveolar opacities at the base of the left lung and enhanced right infrahilar interstitial tissue,

modifications that have been interpreted as being within the neonatal respiratory distress syndrome.

Hemoculture performed on admission detected Enterobacter aerogenes at 48 hours, the patient receiving treatment in accordance with the antibiogram. The culture from the tip of the endotracheal intubation tube (performed post-mortem) indicated Candida albicans.

The diagnosis of invasive aspergillosis was established following the necropsy and the microscopic exam (HE, PAS and Grocot stain). Chronic inflammatory modifications specific for the Aspergillus type were observed in the pulmonary, hepatic, renal and intestinal tissue. The distinction between the infection with Aspergillus discovered post-mortem and the severe pathology of the neonate – the sepsis, respiratory distress syndrome, complicated with pulmonary hemorrhage, multiorgan failure – is extremely difficult to make without identifying the specific pathogenic agent and the favoring factors that trigger the disease.

Conclusions

Pathology of the ELBW premature remains a challenge for the clinician, in the conditions in which the results of cultures taken are received late and many times are negative or sterile. Wide spectrum antibiotic therapy is initiated early, but the antifungal treatment begins only in the moment of a positive culture or in the case of a clinical suspicion of fungal infection.

A critical factor that influences the rate of infection with Aspergillus is the level of contamination of the environment. Specialty literature quotes the increase in incidence in units with ongoing adjacent building work, or whose systems of air filtration are defective [1,2]. During that period, in our unit or immediately close to the hospital no renovation works have been performed and no other cases of infections with Aspergillus were reported.

The septic state of the premature, the severe respiratory distress that required mechanical ventilation throughout the entire period of hospitalization, the necessity of administering wide spectrum antibiotic therapy and cortisone therapy, have created an ideal environment for the development of Aspergillus, whose source has not been detected. It is possible that the initial infection was on a respiratory or pulmonary level, with invasion of vascular structures and dissemination on the hepatic, renal and intestinal level.

It is very difficult to distinguish between the severe pathology of the newborns and the fungal infections that they may develop, while not being able to discover the specific pathogenic agent or certain trigger factors for the disease.

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THE USE OF ABDOMINAL ULTRASOUND AS A SCREENING METHOD IN THE NEONATAL AND INFANT PERIOD – IS IT USEFUL?

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Abstract

Introduction: In recent years' abdominal ultrasound has become a very useful and accessible method for exploring the pediatric gastrointestinal pathology. Study objective: Assessing the need to perform an abdominal ultrasound in the neonate and infant, as a screening procedure, in order to find evidence of malformative or tumoral pathology. Methods: Abdominal ultrasounds were performed on 769 patients hospitalized in our clinic during July 2013 - March 2015. The patients were aged between 0-1 years, with an average of 3 ± 2.5 months. Of these, 450 patients (58.51%) received a routine abdominal ultrasound without any clinical evidence to justify this investigation. Results: The most common pathology was that of the reno-urinary tract: renal malformations – 1 case (cystic renal dysplasia), Ist and IInd degree hydronephrosis – 75 cases (16.67%), IIIrd and IVth degree hydronephrosis – 18 cases (4%); other findings consisted in ovary cysts – 39 patients (8.6%), vascular portal malformations – 5 cases (1.1%), digestive malformations (midgut cyst) – 2 cases (0.04%), tumoral pathology – 10 cases (2.2%), congenital spleen cyst – 1 case. Discussions: The relatively high prevalence of abdominal pathology (75 cases, 28%) detected accidentally by performing routine abdominal echography in these patients has not changed the therapeutical approach in 92% of cases. 6 cases were subject to surgical referrals. 2 cases required immediate surgery (neuroblastoma and nephroblastoma), while other 2 cases would undergo surgery at a later stage. Conclusions: Abdominal ultrasound during the neonatal period and infancy is important in order to establish a complete diagnosis and subsequent monitoring of these cases.

Keywords: abdominal ultrasound, screening, newborn, infant

Introduction –

The purpose of the paper The most common pathology was that of the reno-urinary tract: renal malformations – 1 case (cystic renal dysplasia) (Figure 1), Ist and IInd degree hydronephrosis – 75 cases (16.67%), IIIrd and IVth degree hydronephrosis – 18 cases (4%); other findings consisted in ovary cysts – 39 patients (8.6%) (Figure 2), vascular portal malformations – 5 cases (1.1%), digestive malformations (midgut cyst) – 2 cases (0.04%) (Figure 3), tumoral pathology – 10 cases (2.2%), congenital spleen cyst – 1 case (Table 1).

Infection diseases represent a matter of highest Ultrasound scanning is a painless, safe, radiation and side-effect free examination. It is the most commonly used diagnostic imaging method. Abdominal ultrasound is increasingly used as part of the initial patient evaluation, without a specific indication. However, such an indiscriminate use of abdominal ultrasound is still controversial. The primary screening examination of asymptomatic persons leads to clinically relevant findings in less than 0.5% of cases (1).

The aim of the present study is to evaluate the benefit of routinely performing abdominal scans on newborns and infants with a view to detecting possible abnormalities. The scans applied to children who had not beneficiated of antenatal ultrasounds, but also to patients monitored during pregnancy, to find malformations which may have been missed ante-natally.

Material and method

Abdominal ultrasounds were performed on 769 patients hospitalized in our clinic during July 2013 - March 2015. The patients were aged between 0-1 years, with an average of 3 ± 2.5 months. Of these, 450 patients (58.51%) received a routine abdominal ultrasound without any clinical evidence to justify this investigation.

The scans were performed using a portable ultrasound scan (USS) (General Electrics – Logique e) machine with Doppler facilities. Multiple views of the abdomen were acquired to visualize all the abdominal organs. If neonatal hydronephrosis was present, the Society for Fetal Urology, America (SFU) grading was used. Neonates with abnormal USS findings had follow-up scans (2).

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Table 1. Abnormal USS findings at initial scans.

Total	Normal USS	HNI/II	HN III/IV	Ovary cysts	Tumors	Vascular abnormalities	Digestive malformation	Spleen cyst
450	299(66.4%)	75 (16.67%)	18 (4%)	39 (8.7%)	10 (2.2%)	5 (1.1%)	2 (0.4%)	1 (0.2%)

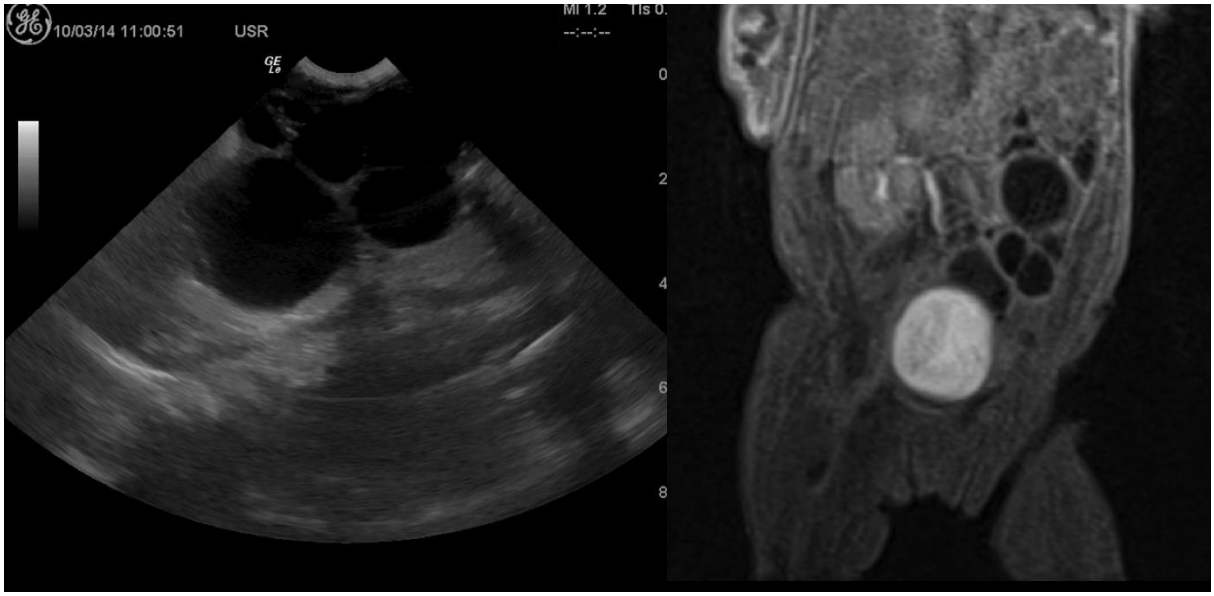
HN-hydronephrosis, USS-ultrasound scan

Results

The most common pathology was that of the reno-urinary tract: renal malformations – 1 case (cystic renal dysplasia) (Figure 1), Ist and IInd degree hydronephrosis – 75 cases (16.67%), IIIrd and IVth degree hydronephrosis – 18 cases (4%); other findings consisted in ovary cysts – 39 patients (8.6%) (Figure 2), vascular portal malformations – 5 cases (1.1%), digestive malformations (midgut cyst) – 2 cases (0.04%) (Figure 3), tumoral pathology – 10 cases (2.2%), congenital spleen cyst – 1 case (Table 1).

The tumoral pathologies detected were: one hemangioendothelioma, one intrahepatic calcification without any evident clinical or biological sign of an infectious disease (Figure 4), one neuroblastoma in an 8 month old infant addmited for fever, one 3 mm nephroblastoma in a 10 month old infant addmited for bronchiolitis (Figure 5), one pancreatic lesion in a 10 month old girl with a suspicion of tuberous sclerosis (Figure 6), 4 cases of hemangiomas, one ectopic intraabdominal testicle.

The vascular abnormalities found were 3 cases of portal cavernoma, one case in an 7 month old boy with hydronephrosis grade III on the restant kidney after nephrectomy who developed 2 months later portal cavernoma (Figure 7 a, b). Another vascular abnormality (heterotaxic syndrome) was discover in a 1 month old girl with polisplenia (Figure 8 a, b).



a. USS examination b. MRI examination

Fig. 1. Cystic renal dysplasia in a 20 day old girl

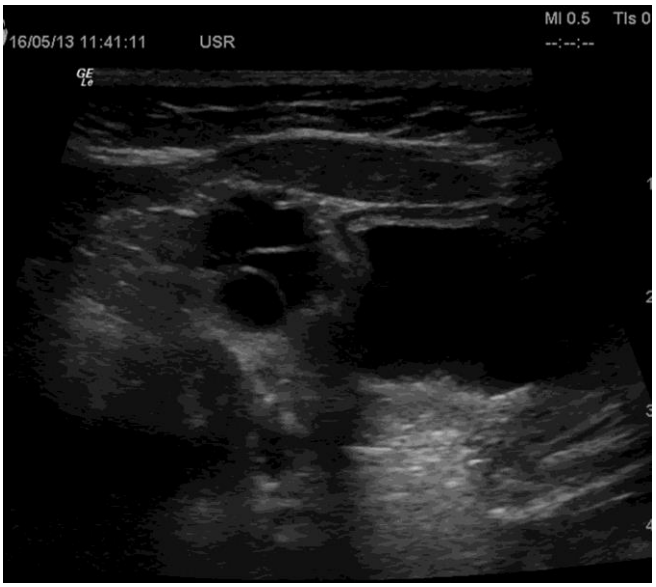


Fig. 2. Ovary cyst

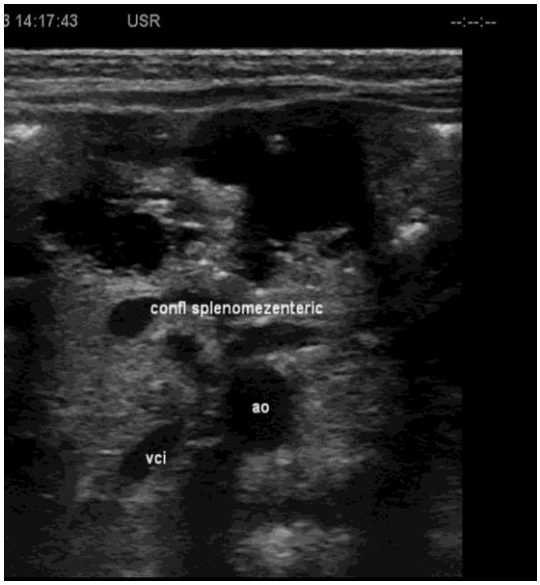


Fig. 3. Midgut cyst in a 7 day old boy

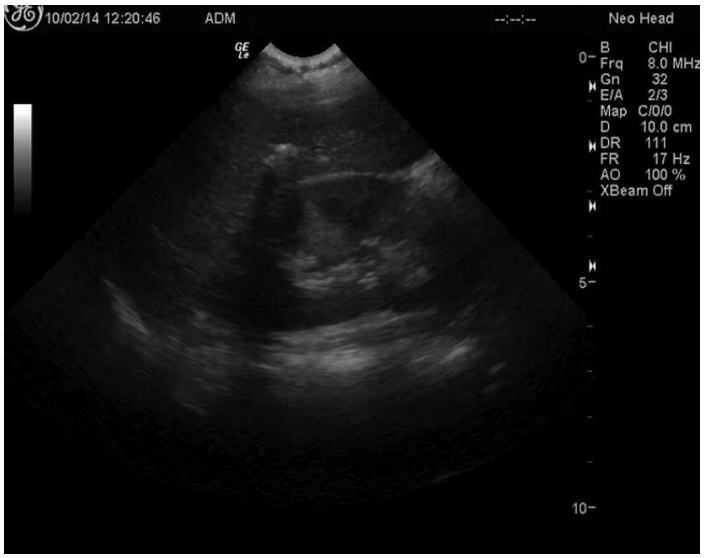


Fig. 4. Intrahepatic calcification of unkown ethiology

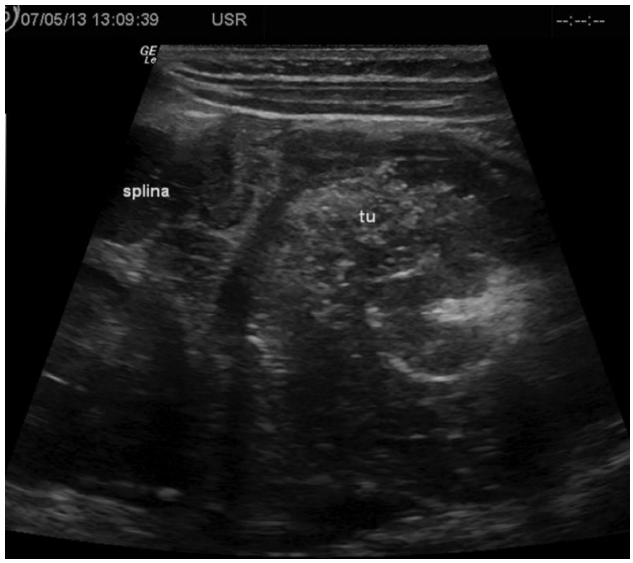


Fig. 5. Nephroblastoma

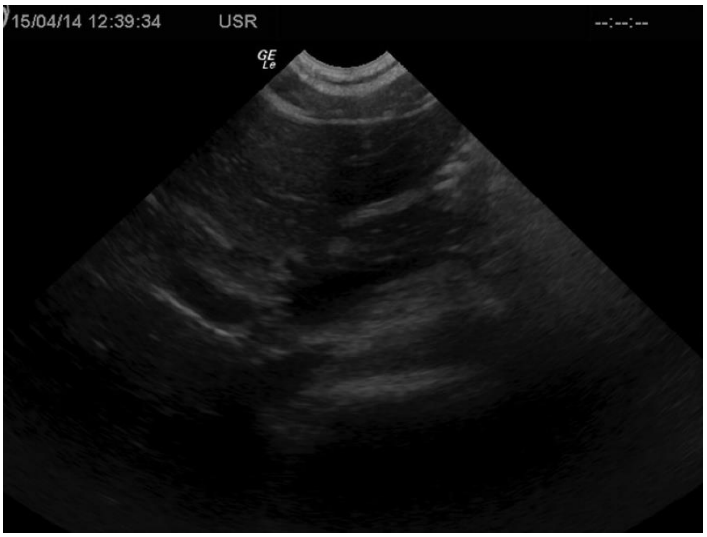
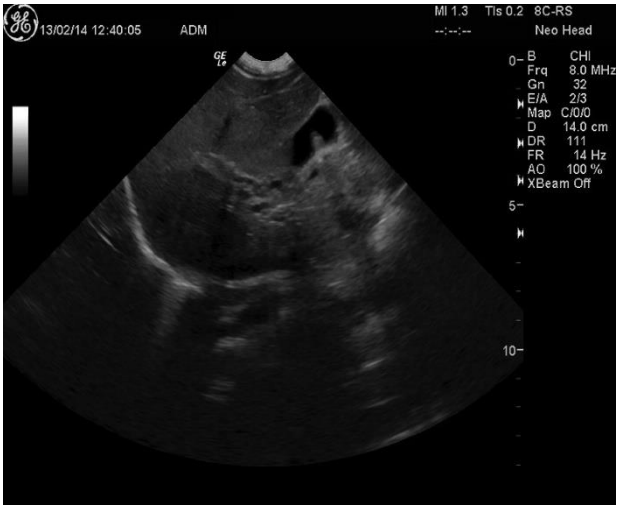
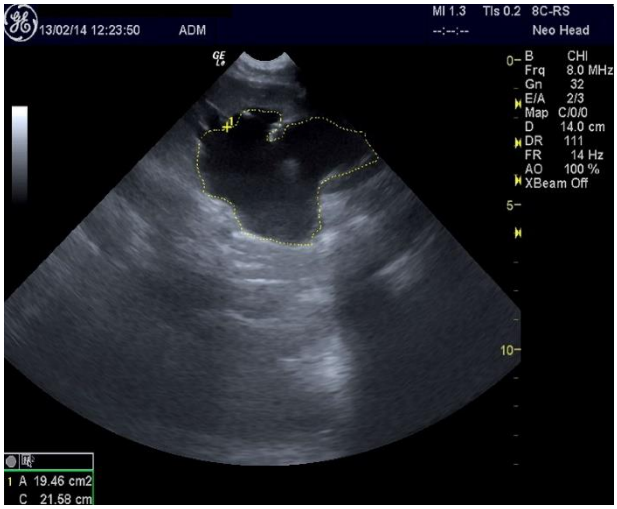


Fig. 6. Pancreatic lesion

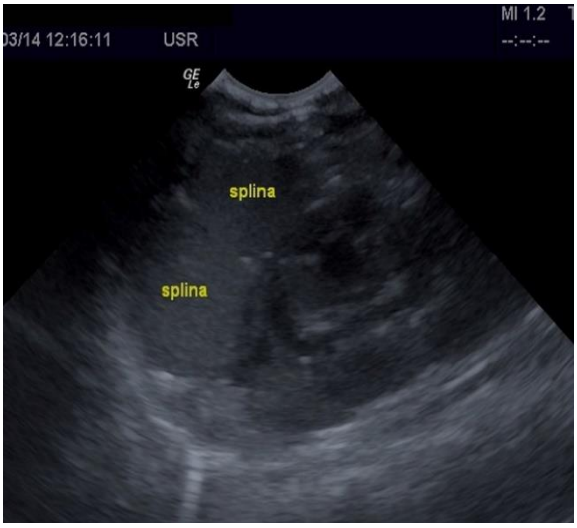


a. Portal cavernoma in an 9 month old boy

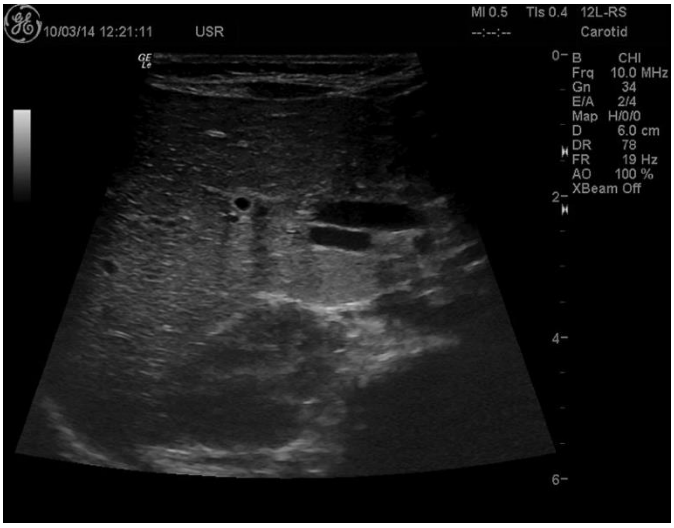


b. Grade III hydronephrosis on the restant kidney in the same 9 month old boy

Fig. 7.



a. Polisplenia



b. Visualisation of azygos vein posterior to portal vein, anterior and on right side of the aorta

Fig. 8. Heterotaxic syndrome

Discussion

The relatively high prevalence of abdominal pathologies (151 cases, 33.5%) detected accidentally by performing routine abdominal echographies in these patients has not changed the therapeutical approach in 92% of cases; they remained on a follow-up schedule.

In a study performed by Tato and Zoller (1) approximately 50% of the persons examined had abnormal findings without clinical relevance. The authors of this study concluded that this high frequency of abnormal findings may cause high costs due to unnecessary follow-up examinations.

Ovarian cysts are seen more frequently than expected in the neonatal period. In our study, they were incidentally discovered in 8.8% of cases. Ovarian cysts are the rule, not the exception in newborn infants. Nowadays, the routine use of ultrasound allows the detection of ovary cysts during the neonatal period. Ovary cysts with a diameter exceeding 4 cm are considered pathological. The incidence of ovarian cysts has been estimated at more than 30% (this estimate is based on an investigation of stillborns or infants who died within 28 days of birth) (2). The correlation of the diameter with the clinical symptoms and ultrasound appearance allows an optimal therapeutic approach (3). Their presence is attributed to immaturity of the hypothalamic–pituitary–ovarian axis (“gonadostat”) (4).

On prenatal ultrasound, the fetal abnormalities most frequently detected are those of the urinary system. Of these, hydronephrosis is the most common, seen in about 50% of such cases (5), and it most often occurs in males (6). For cases of hydronephrosis not diagnosed in utero, the role of postnatal abdominal ultrasound will be to determine the cases due to obstruction, which can lead to renal damage and therefore require surgical intervention or long term follow-up of renal function. Up to 60% of antenatally detected cases of hydronephrosis resolve spontaneously (7, 8) and the threshold for spontaneous resolution of fetal or neonatal hydronephrosis has been established at renal pelvis diameter between 5 - 20 mm and SFU grade I to II by several authors (9, 10). This corroborates with findings in this study where persistent hydronephrosis was only seen in cases with SFU grades III and IV up to four months of age. It is however generally agreed that conservative management options should initially be considered for most patients. In our study hydronephrosis was the most frequent abnormality detected on USS. Grade I and II were detected in 16.67% of cases, with a good outcome on follow up.

Out of the 450 patients screened, only 6 (1.3%) were subject to surgical referrals. Two cases required immediate surgery (one case of neuroblastoma with poor outcome and one case of nephroblastoma discovered in stage 1 with very good prognosis). Other two cases would undergo surgery at a later stage (one case of renal dysplasia and one case of grade III hydronephrosis associated with portal cavernoma). The two cases of midgut cyst without any digestive symptomatology required USS follow up.

Conclusions

Abdominal ultrasound in the neonatal period and infancy is important in order to establish a complete diagnosis and subsequent monitoring. It can be extremely useful in the detection of serious birth defects or tumoral pathology in a subclinical phase, is non-invasive, affordable, with a low cost/efficiency ratio. However, it is time consuming, therefore its use remains at the discretion of each physician. A sonographic screening of asymptomatic patients may nonetheless be useful for specific indications in preselected individuals.

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GIANT DOUBLE ILEAL DUPLICATION CYST - A CASE REPORT -

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Abstract

Alimentary tract duplication cysts are malformations that occur during the embryologic development of the organs that form the digestive system. These malformations can appear at any level of the alimentary tract. The incidence at which these malformations occur is estimated at 1 every 4500 newborns. We present a case of a new-born suffering from intestinal duplication, with two ileal duplication cysts, a giant tubular shaped one and a spherical one. Although the vast majority of intestinal duplications develop in the small intestine, they are solitary and small. Multiple intestinal duplications in the same patient are a rarity, as well as the giant ones.

Keywords: giant intestinal duplication, echography, alimentary tract malformation

Introduction

Alimentary tract duplication cysts are malformations that occur during the embryologic development of the organs that form the digestive system. These malformations can appear at any level of the tract, beginning from the oropharynx and leading towards the anus (1, 2).

Calder in 1733 first mention this condition, but the modern term of alimentary tract duplication cysts has been introduced by Dr. William E. Ladd in 1937, in the attempt to better organize the individual pathologies that affect the alimentary tract system (3).

The incidence at which these malformations occur is estimated at 1 every 4500 newborns[2]. It has been observed that 80% of the tumors can be found in the abdominal cavity, 20% can be found in the thorax, neck and head regions (Fig.1). Within the group found in the abdomen, 75-80% are formed along the length of the jejunum and ileum, always on the mesenteric side (4).

From a morphological point of view, we cam distinguish two types of tumors, cystic and tubular. The cystic ones are rather round shaped and have no lumenal connections with the intestines, whereas the tubular one do communicate with their respective segment. Histologically the insides of these tumors can present heterotopic gastric mucosa that has acidic secretion capacity, which can lead to complications.

Clinical manifestations depend on the size, location, intimacy with surrounding structures and whether or not the tumor presents gastric mucosa. Frequently the symptoms can falsely lead the examiner to think of an acute abdominal pain syndrome, but most of these embryological defects are detected incidentally either ante-partum or after birth. The presence of other associated malformations is very common, most of them regarding the pancreas or the vertebral column.

Pain, regurgitation and a palpable abdominal tumor, are signs and symptoms associated with the presence of these malformations. Nevertheless, this condition is an exclusion diagnosis in any physical exam, given the rarity of its occurrence. Pain is felt when the affected intestinal segment gets infected and expands. In the case that gastric mucosa is present, signs of superior digestive hemorrhage can appear, like hematemesis or melena, and haematochezia if the tumor appears in the distal part of the digestive system (5).

The treatment is exclusively surgical, and the way it is performed depends on the site duplication, blood supply, and the relationship with surrounding structures. It is considered that small cysts can be enucleated without the need to perform intestinal resection, if the tumor and the healthy intestine segment do not share a common blood supply. In most cases, enteric resection is performed with end-to-end or end-to-lateral anastomosis of the remaining segments, and the tumor is removed alongside the healthy intestinal segment which is stripped of blood supply after the operation (6).

Case presentation

We present a case of a new-born suffering from intestinal duplication, with two ileal duplication cysts, a giant tubular shaped one and a spherical one.

The patient, coming form unmonitored pregnancy, born at 38 weeks of gestation with a weight of 2200 grams, 47 centimetres in size, 32,5 centimetres of head circumference, was admitted in Neonatology Department, ICU Unit of our Hospital at the age of 9 days presenting vomiting, abdominal distension and a palpable abdominal mass.

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No significant family history was found.

Surgical consultation at admission detect a large abdominal mass from the epigastric region to the right iliac fossa. Plain abdominal radiography discloses hypo-aeration in the lower abdominal quadrants, with no airfluid levels or pneumoperitoneum, also a T6-T8 vertebral block is observed incidentally. Abdominal echography shows a tubular mass with thin but well delimited walls, with no peristalsis, low echogenicity content and a calibre of 4 centimetres. The mass expands from the liver to vicinity of urinary bladder (Fig. 2).

Medical treatment and preoperative preparation with double antibiotherapy with Meropenem and Amikacin, Etamsylate, Calcium gluconate, Pantoprazole, Metoclopramide, Dopamine, as well as parenteral nutritional support and electrolytes were established. Blood tests shows hyperbilirubinemia with mild hepatocytolysis, slightly rise of creatinine levels, hypoglycemia, low total serum protein level and monocytosis.

Transfonatanellar ultrasound detect grade II intraventricular haemorrhage.

Cardiac evaluation shows a Patent Foramen Ovale (PFO), which is normal at this age.

Thoracic, abdominal and pelvic computed tomography (CT) reveal a cystic giant formation that occupies the entire anterior abdominal cavity as follows: it has its own wall and liquid content, with debris deposits. It has a sinuous tract, it is predominantly developed in the anterior abdominopelvic compartment, exerting a displacing compressive effect on intestine and parenchymal organs. Behind the transverse colon is a similar but smaller image (3.6 cm long). T6-T8 spinal vertebral anomalies and T5 hemi-vertebra are revealed (Fig. 3).

The patient is transfered to Surgery Department for surgical treatment and after proper preparation radical treatment is applied. Surgical treatment consist of medial laparotomy that reaveal a tubular ileal duplication cyst that starts upward from about 5 cm from the ileocecal valve, in intimate contact with the mesenteric face of about 8-10 cm of the ileum to subsequently lose intimate contact with the ileum. The described formation continues through an atretic portion with another spherical duplication cyst that is not intimate with the normal intestinal segment. The block resection of the two duplication cysts is performed with the loss of approximately 10 cm of the terminal ileum that shares common blood supply with the cyst segment being in intimate contact with it. The excised piece is taken for histopathological examination. Reconstruction of the digestive tract is accomplished by end-to-end anastomosis in double layer and "cut-back" on the distal portion due to the large incongruence between the two ends of the intestinal anastomosis segments (Fig. 4). Appendectomy, peritoneal drainage and incision closure is performed, as well as CVC into the right subclavian vein.

First Author	Institution	No. D (No. Pts)	Oral	Esophagus	Thoracoabdominal	Stomach	Duodenum	Jejunum/ileum	Colon	Rectum	Other
Gross, 1952[2]	Children's, Boston	68 (67)	1	13	3	2	4	32	10	3	0
Basu, 1960[21]	A. H. Children's, Liverpool	33 (28)	0	7	0	1	3	16	4	2	0
Grosfeld, 1970[22]	Children's, Columbus	23 (23)	0	4	2	1	0	9	7	0	0
Favara, 1971[12]	Children's, Denver	39 (37)	1	6	0	3	4	20	4	0	1
Bower, 1978[23]	Children's, Pittsburgh	78 (64)	0	15	1	6	6	34	12	2	2
Hocking, 1981[24]	RHSC, Glasgow	60 (53)		8	2	8	1	32	4	5	0
Ildstad, 1988[25]	Children's, Cincinnati	20 (17)	0	6	0	1	0	5	8	0	0
Bissler, 1988[26]	Children's, Akron	11 (11)	0	1	0	1	2	4	2	1	0
Holcomb, 1989[14]	Children's, Philadelphia	101 (96)	0	21	3	8	2	47	15	5	0
Pinter, 1992[27]	Hungary	30 (28)		6	2	4	3	9	3	3	0
Bajpai, 1994[28]	IIMS, New Delhi, India	15 (14)	0	8	1	0	1	1	3	1	0
Stringer, 1995[13]	Hospital for Sick Children, London	77 (72)	2	15	6	10	3	21	10	6	4
Iyer, 1995[29]	Children's, Los Angeles	29 (27)	2	0	0	3	1	9	8	6	0
Yang, 1996[30]	NTUH, Taipei, China	20 (17)	0	2	0	1	0	14	3	0	0
Karnak, 2000[31]	Ankara, Turkey	42 (38)	1	7	2	1	3	17	9	2	0
Puligandla, 2003[32]	Montreal Children's	73 (73)			0	6	7	51	5	4	0
TOTALS		719 (665)	7 (1%)	119 (17%)	22 (3%)	56 (8%)	40 (6%)	321 (45%)	107 (15%)	34 (6%)	7 (1%)

Fig. 1. Alimentary Tract Duplications by Location as Described in Literature Reports (George W. Holcomb III et al. Ashcraft's Pediatric Surgery 6th Edition, Ed. Saunders Elsevier, 2014, eBook ISBN: 978-0-323-18736-7, p. 539-547)

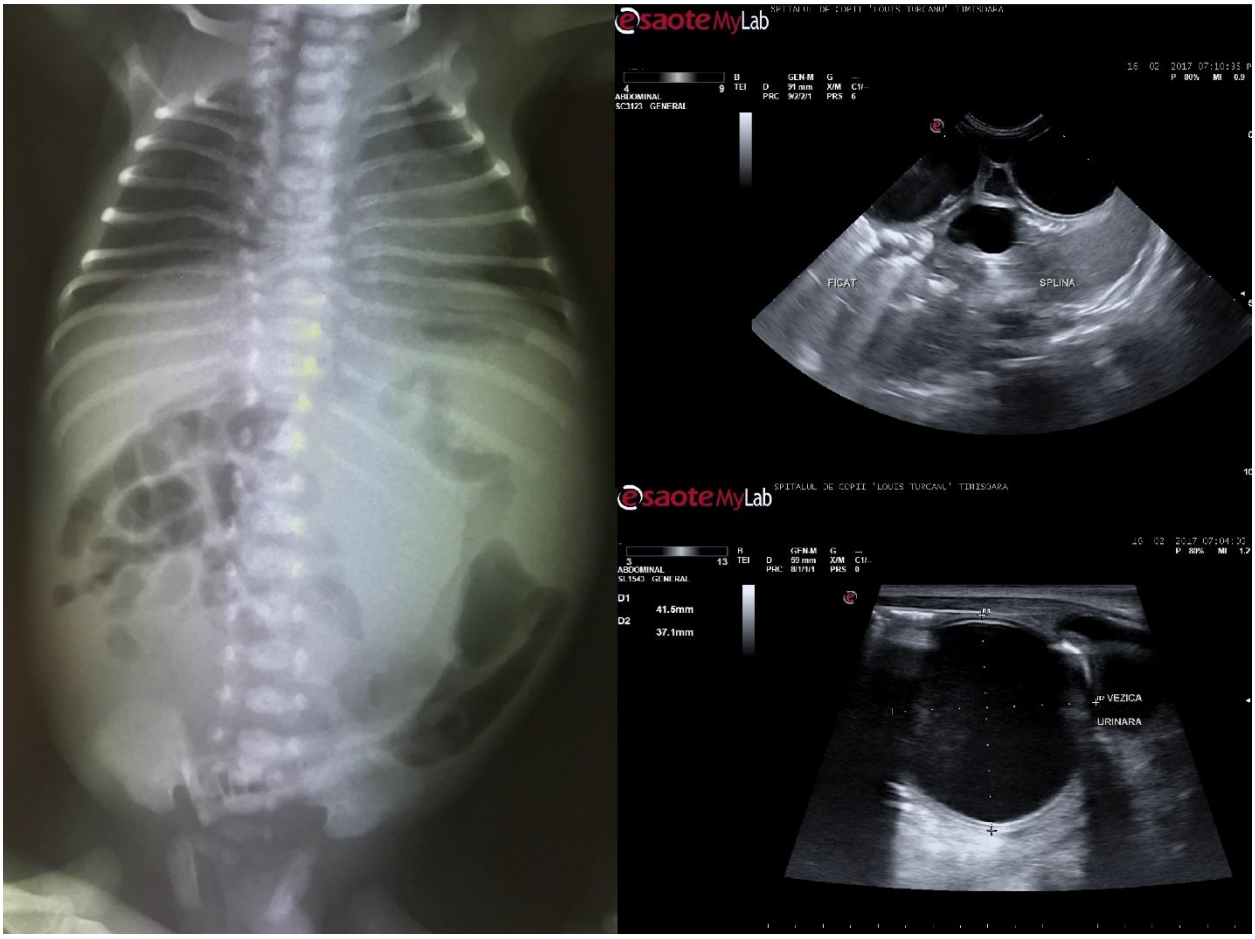

Fig. 2. Plain Thoracic and Abdominal Radiography and Ultrasound images showing the characteristics of abdominal duplication cyst.

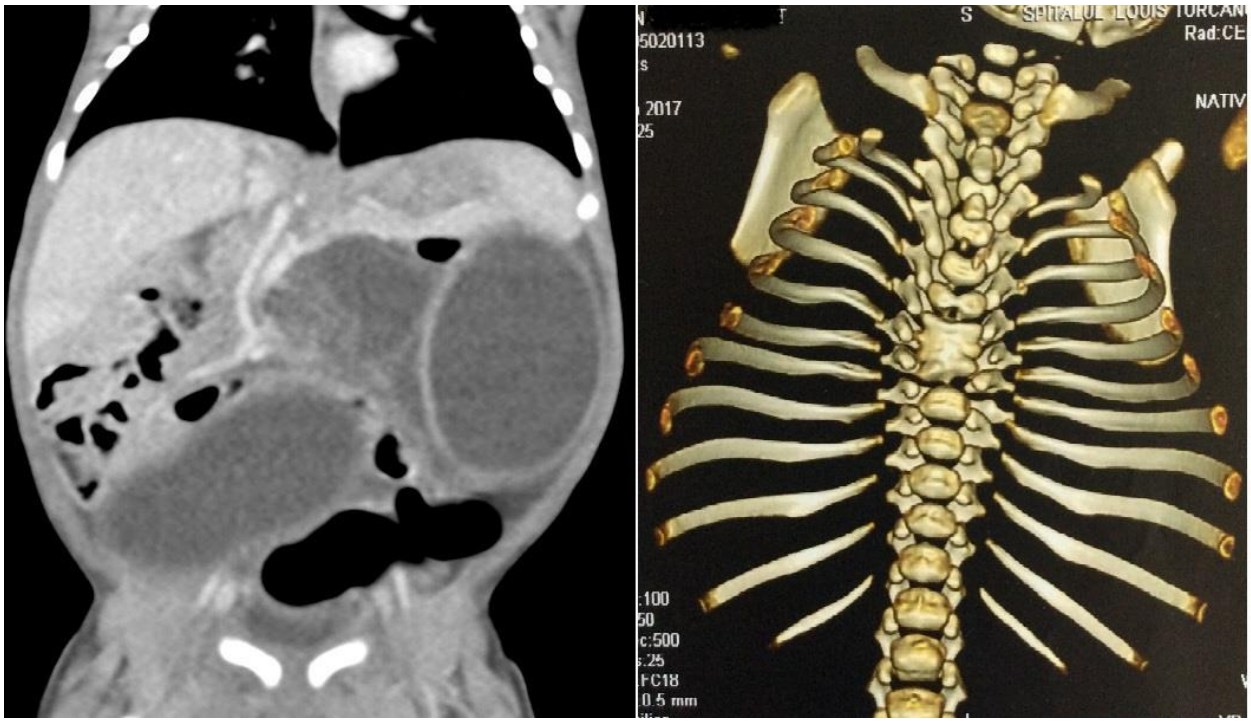

Fig. 3. Computed Tomography Image of the Duplication and 3D Reconstruction to better highlight the vertebral malformation.

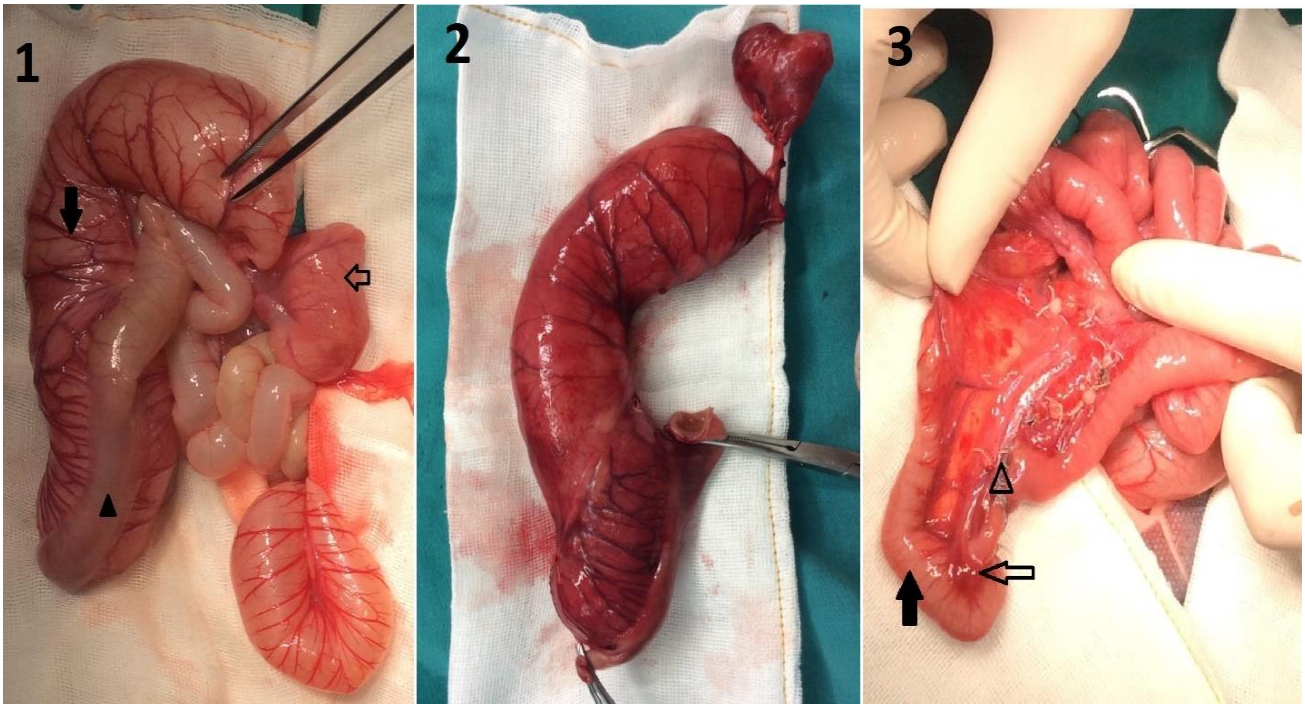

Fig. 4. First image show intraoperative aspect of the duplication. Full arrow marks the tubular duplication cyst; empty arrow marks the smaller duplication cyst; Triangle marks the terminal ileal segment of intestine where cyst is in intimate contact. In second image resection specimen includes both cysts and a segment of the small intestine which shared common blood supply. Third image showing the intestines after resection of the duplication and end-to-end anastomosis. Full arrow marks ascending colon which can be observed to be of abnormally small caliber; empty arrow marks ileocecal valve; triangle marks the end-to-end anastomosis.

The histopathological examination reveals the following aspects: the macroscopic examination - intestinal fragment of 8.5 centimeters length, presents a cystic formation of 21.5 / 3 / 3.5 centimeters attached to it. The cyst has liquid content, gray color, elastic consistency, wall thickness 0.1 - 0.2 centimeters. Microscopic examination - a small intestine duplication cyst with a wall consisting of muscle layer, submucosa and mucosa that is thinned in patches, sometimes denuded. Fibro-connective tissue that includes lymphoid structures with reactive modifications and lymphoid tissue with intestinal glandular structures, secreted by secretory cylindrical epithelium, including Paneth cells (ectopic gut) (Fig. 6).

Postoperatively major complications occurred.

Immediately postoperative evolution was good but the patient's condition progressively began to deteriorate despite proper medical management and two weeks postoperatively developed digestive intolerance with progressive increase in inflammatory markers and septic status (Fig. 5) and 18 days postoperatively, surgical reintervention is decided, intraoperatively, revealing complete disunion of anastomosis with generalized peritonitis and multiple peritoneal adhesions.

Resection of the ileocecal valve together with the cecum, closure of the ascending colon and cutaneous ileostomy is performed. The postoperative progression was favorable with slight weight gain, correction of electrolyte deficiencies. One month later, reconstruction of the digestive tract was performed by take down of ileostomy. Subsequently, the patient's evolution was to complete recovery and healing and was discharged from Surgery Department the 10th postoperative.

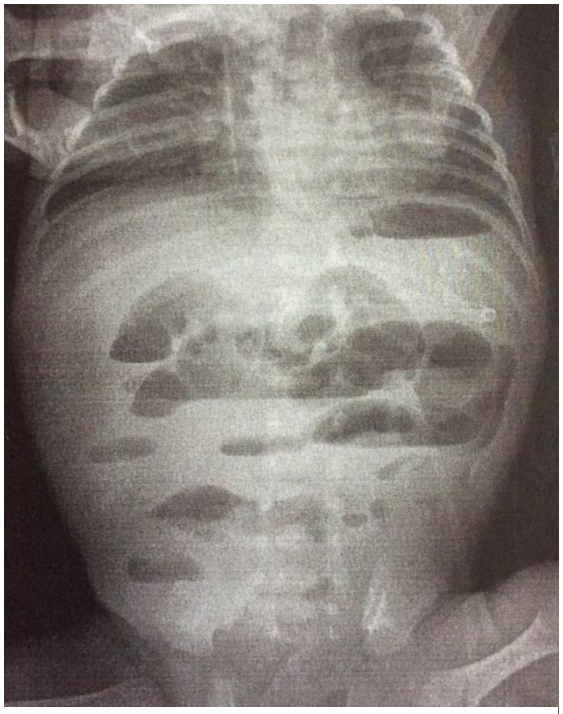

Fig. 5. Plain Abdominal Radiography showing multiple hydroaeric levels due to small-bowl occlusion.

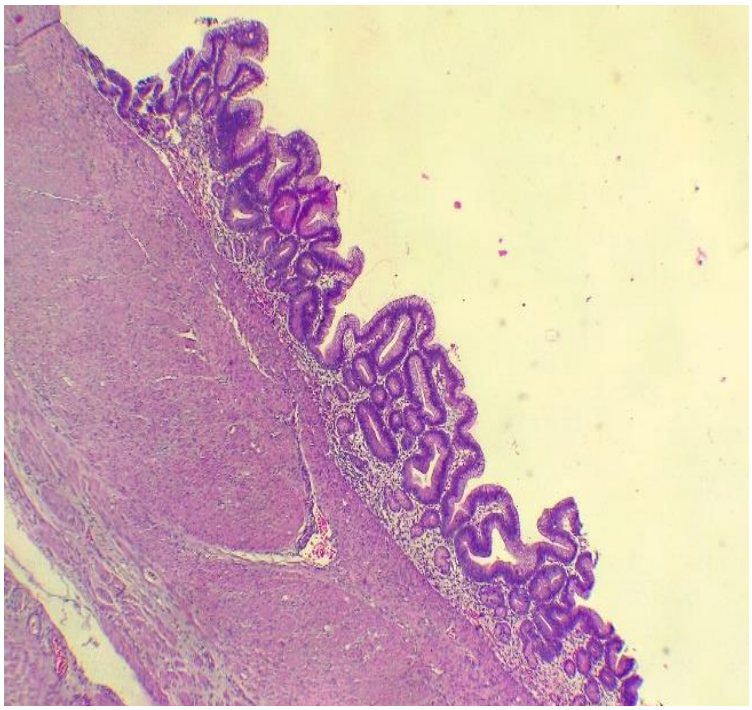

Fig. 6. Microscopic aspects of the duplication

Disscusions

Differential diagnosis was primarily made corroborating ultrasound aspects, CT and biological parameters and consisted mainly of the following pathologies without ultrasound flow:

- omental cyst;
- mesenteric cyst;
- meconium pseudocyst;
- urachal cyst;
- urinoma;
- renal congenital cyst;
- ureterohydronephrosis;
- hepatic cyst;
- choledochal cyst;

We consider echography has the highest diagnostic value in this pathology.

The cost of hospitalization for this patient was over 7,000 euros for a 64-days hospital stay. These calculations only refer to the period of hospitalization at the Surgery Department. When the patient was surgically healed, he was transferred back to the Neonatology Department and then to the Chronic Patients Care Department for nutritional and weight recovery, where he is at this time.

Although the vast majority of intestinal duplications develop in the small intestine, they are solitary and small. Multiple intestinal duplications in the same patient are a rarity, as well as the giant ones. Confrontation with this case has created the opportunity to treat a rare pathology, and its documentation represents a benefit for ourselves as well as for the medical community.

Conclusion

At the occurrence of complications (disunion of primary anastomosis), we consider contributed the poor quality of tissues due to pre-existing low serum proteins levels, but also the quality of the vascularization left after the resection of duplication cysts. Knowing that this type of cysts always develops on the mesenteric side of the healthy intestine can not be excised without resection in block with a healthy portion of the intestine, and in our case it has been preferred to excise the cysts with the resection of only a small segment of the adjacent intestine - the one with which the cyst was in intimate contact. The reasoning behind the decision was, on one hand, the fear of not cutting a large part of the gut (more than 20 centimeters) that could end up with Short Bowel Syndrome, and on the other hand that more than half of the cyst did not have intimate contact with the adiacetic intestine which allowed its dissection. But this seems to have resulted in a compromise of good vascularization necessary for proper healing of anastomosis and the occurrence of complications with the need for surgical reintervention and increasing the healing time of the patient as well as hospitalization.

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INFLUENCE OF MATERNAL PREGNANCY-INDUCED HYPERTENSIVE DISORDERS ON FETAL DEVELOPMENT AND GESTATIONAL AGE

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Abstract

Pregnancy-induced hypertensive disorders (PIH) complicate up to 10% of all pregnancies and represent one of the leading causes of both maternal and fetal morbidity and mortality. Decreased blood flow to the placenta translates into chronic fetal hypoxia and fetal malnutrition, resulting in intrauterine growth restriction (IUGR), small for gestational age (SGA) newborns, prematurity, and even death. Aim of the study: The aim of the study was to determine the impact of maternal PIH on fetal growth and development by determining the prevalence of maternal PIH among newborns and identifying the incidence of preterm birth and SGA neonates born to mothers with PIH. Materials and methods: A retrospective observational study was conducted over a 3-year period (January 2014 -December 2016), at the Clinic of Obstetrics, Gynecology and Neonatology of the Emergency County Hospital Timisoara. Results and discussions: A total of 6108 newborns were included in the study. Patients were divided in 8 subgroups according to the presence or absence of maternal PIH (2 groups), term or premature birth (4 groups) and birth weight for gestational age (8 subgroups). From the total 6108 included newborns, 58 were born to mothers with PIH, representing an incidence of 0.94%. SGA criteria were met by 170 (2.7%) of the total patients and 289 (4.7%) patients were born preterm. The incidence of preterm birth was significantly higher among newborns with maternal PIH than mothers without PIH (62.1% and 4.2, respectively). SGA was more frequent in the preterm study groups compared to the term neonates [41.6% (preterm-PIH) and 24.5% (preterm) compared to 13.6% (term-PIH) and 1.5% (term)], and there was also a significantly higher prevalence of SGA in the term PIH group compared to term newborns without maternal PIH (13.6% compared to 1.5%). Conclusions: The prevalence of both premature birth and SGA was significantly higher in newborns with maternal PIH. Therefore, it can be concluded that maternal PIH exerts a negative effect on fetal growth and development. Intrauterine fetal monitoring of women with PIH and individual therapeutic managementof both mother and newborn are of paramount importance in improving the short and long-term outcome.

Keywords: abdominal ultrasound, screening, newborn, infant

Introduction

Pregnancy-induced hypertensive disorders (PIH), including preeclampsia and eclampsia, complicate up to 10% of all pregnancies and represent one of the leading causes of both maternal and fetal morbidity and mortality[1, 2].There are various risk factors predisposing women to PIH, including maternal age under 20 or over 35 years, nulliparity or multiple pregnancies, preexisting renal pathology, obesity, diabetes or immunological disorders, previous history of PIH, history of chronic hypertension, tobacco smoking, and alcohol and drug abuse[3-5]. A genetic substrate is shown by an increased incidence of PIH among patients with a positive family history [6]. PIH seems to be triggerd by an abnormal invasion of the cytotrophoblast by the spiral arteries, leading to reduced utero-placental perfusion [7-10]. Decreased blood flow to the placenta translates into chronic fetal hypoxia and fetal malnutrition, resulting in intrauterine growth restriction (IUGR), small for gestational age (SGA) newborns, prematurity, and even death [11-14]. The incidence of preterm birth and IUGR increases significantly due to maternal PIH [15].

Aim of the study

The aim of the study was to determine the impact of maternal PIH on fetal growth and development by determining the prevalence of maternal PIH among newborns and identifying the incidence of preterm birth and SGA neonates born to mothers with PIH.

Material and method

A retrospective observational study was conducted over a 3-year period (January 2014 -December 2016), at the Clinic of Obstetrics, Gynecology and Neonatology of the Emergency County Hospital Timisoara.

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The definition used for SGA was length and/or height less than two standard deviations (< -2SD) or third percentile (< Perc. 3%) below the mean for gestational age [16, 17]. Preterm birth is defined as alive birth that occurs prior to 37 weeks of gestation [18]. The cases of maternal PIH were determined from case-mix records using the RO DRG v1. classification system: code O13 (pregnancy induced hypertension), code O14 (preeclampsia), code O15.0 (eclampsia)[19].

An electronic registry composed of anonymized patient data was created by searching individual patient records. Inclusion criteria: inborn patients, age of 0-28 days. Exclusion criteria: women with pre-existing (chronic) hypertension, chronic renal disease, diabetes, cardiovascular disease, placenta previa, premature rupture of membranes and infections as well as newborns with documented infections, congenital malformations, and perinatal asphyxia.

A total of 6108 newborns were included in the study. Patients were divided in 8 subgroups according to the presence or absence of maternal PIH (2 groups), term or premature birth (4 groups) and birth weight for gestational age (8 subgroups).

Results

The mean and standard deviation for anthropometric parameters and APGAR score of the studied groups are shown in Table 1. Three of the four SGA neonate groups show difficulty of early neonatal adaptation, the most affected of which is that of Preterm SGA neonates with maternal PIH.

From the total 6108 included newborns, 58 were born to mothers with PIH, representing an incidence of 0.94% (Figure1). SGA criteria were met by 170 (2.7%) of the total patients (Figure 2), and 289 (4.7%) patients were born preterm (Figure 3).

As shown in Figure 4, the incidence of preterm birth was significantly higher among newborns with maternal PIH than mothers without PIH (62.1% and 4.2, respectively).

SGA was more frequent in the preterm study groups compared to the term neonates [41.6% (preterm-PIH) and 24.5% (preterm) compared to 13.6% (term-PIH) and 1.5% (term)], and there was also a significantly higher prevalence of SGA in the term PIH group compared to term newborns without maternal PIH (13.6% compared to 1.5%).

Group			n	Gestational Age	Birth Weight	Birth Length	Head Circumference at birth	APGAR score
No maternal PIH	Term	AGA	5707	38.9 ± 2	3342 ± 674	50.1 ± 3	34.1 ± 1.2	9.2 ± 1.7
		SGA	90	38.7 ± 1	2409 ± 146	47.9 ± 2	33 ± 1.25	8.85 ± 0.6
	Preterm	AGA	191	33.4 ± 3	2021 ± 567	45.5 ± 4	30.83 ± 2.69	7.12 ± 2.11
		SGA	62	34.2 ± 2.5	1878 ± 315.8	43 ± 4.75	30.1 ± 1.79	7.2 ± 1.20
maternal PIH	Term	AGA	19	38.4 ± 1.02	3326 ± 332	50.9 ± 1.73	34.7 ± 1.38	8.58 ± 0.84
		SGA	3	38.33 ± 0.57	2353 ± 66.5	47.67 ± 0.57	32.33 ± 0.57	7.66 ± 0.57
	Preterm	AGA	21	35.8 ± 1.3	2660 ± 517	48.2 ± 2	33.5 ± 1.4	8.1 ± 0.9
		SGA	15	34.27 ± 2.49	1785 ± 580	41.93 ± 3.35	30.36 ± 2.53	6.9 ± 1.16

AGA – appropriate for gestational age; SGA-small for gestational age; PIH-pregnancy induced hypertension

Table 1. Anthropometric characteristics and parameters of early neonatal adaptation of the studied groups

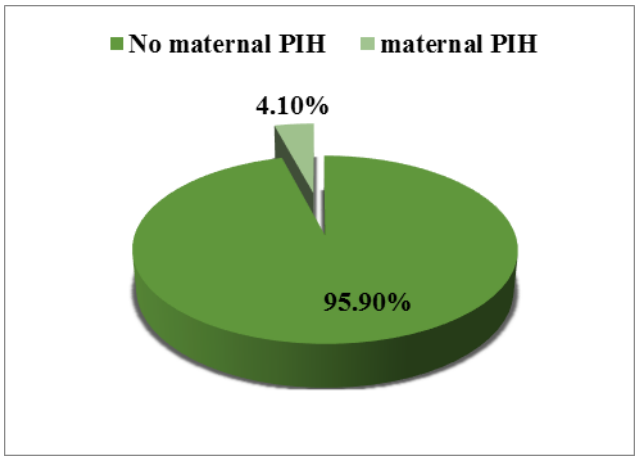

Fig.1. Incidence of maternal PIH among studied neonates

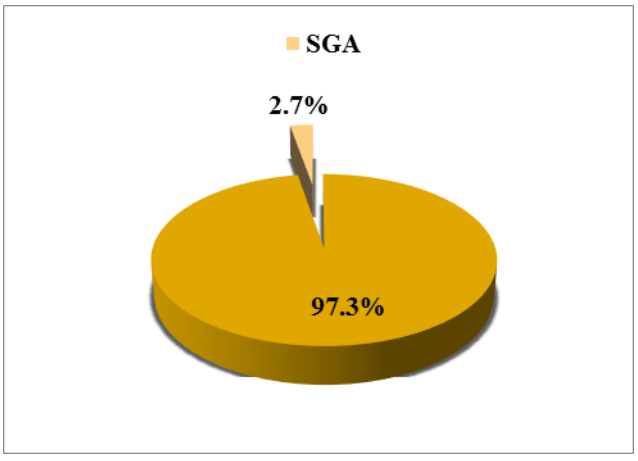

Fig. 2. Prevalence of SGA amid neonates included in the study

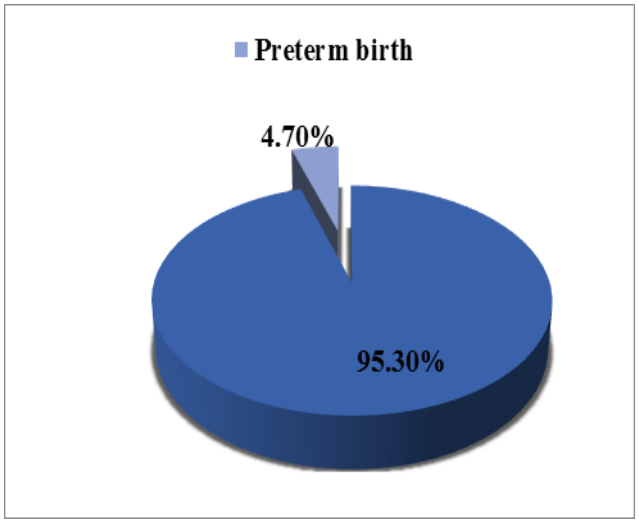

Fig.3. Prevalence of preterm birth from the total number of newborns

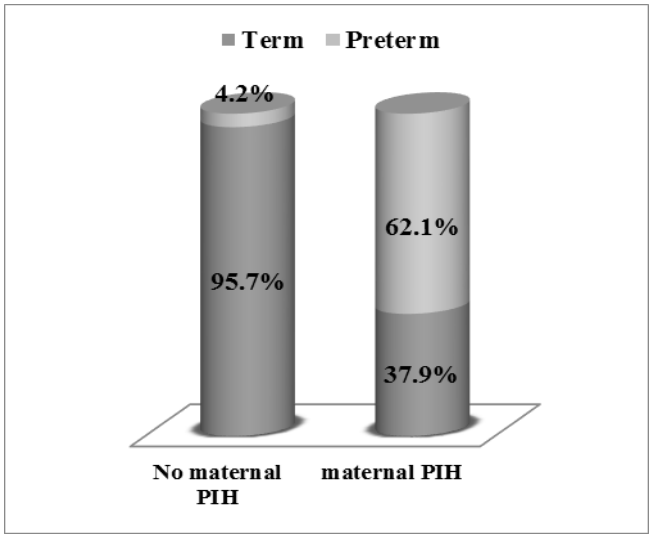

Fig.4. Percentage distribution of newborns by gestational age

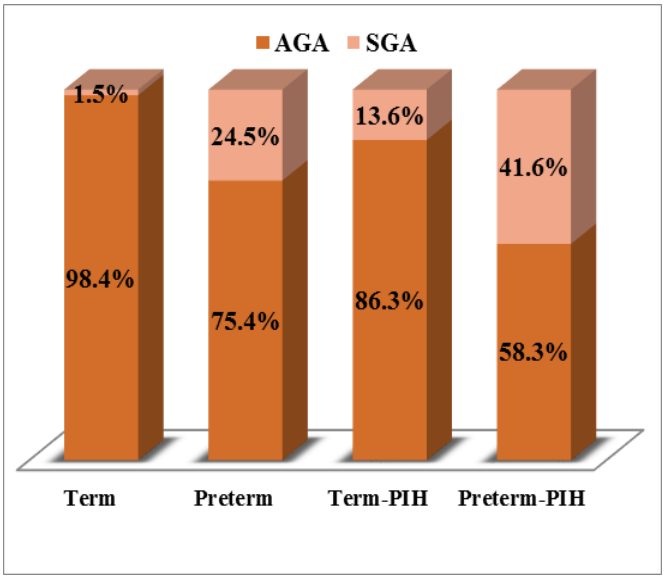

Fig.5. Percentage distribution of AGA and SGA newborns by gestational age and maternal PIH

Discussion

The incidence of PIH in this study was 0.94%, significantly lower than that quoted by literature. Various worldwide incidences have been reported for PIH. A study conducted by Muti, M., et al. shows an incidence as high as 19.4 % [20] whereas a report from the American College of Obstetricians and Gynecologists mentions a lower incidence of 10%[2], along with a study published by Sajith, M., et al. whose measured incidence is 7.8%[21].

Early neonatal adaptation was significantly more difficult for SGA neonates with maternal PIH. The increase of the mean APGAR score is correlated with a concurrent increase of gestational age and birth weight means. However, low APGAR scores can be noted in all of the studied groups of newborns with maternal PIH.

The prevalence of preterm birth was higher among newborns with maternal PIH and SGA was more frequent in all newborns with maternal PIH, which is consistent with previous literature [22, 23].

Conclusions

Abdominal ultrasound in the neonatal period and infancy is important in order to establish a complete diagnosis and subsequent monitoring. It can be extremely useful in the detection of serious birth defects or tumoral pathology in a subclinical phase, is non-invasive, affordable, with a low cost/efficiency ratio. However, it is time consuming, therefore its use remains at the discretion of each physician. A sonographic screening of asymptomatic patients may nonetheless be useful for specific indications in preselected individuals.

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THE POTENTIAL SEVERE COMPLICATIONS OF GASTROESOPHAGEAL REFLUX – A CASE REPORT AND A REVIEW OF THE LITERATURE

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Abstract

Gastroesophageal reflux (GER) represents the involuntary passage of the gastric contents into the esophagus and is one of the most common symptoms in both children and adults. The symptoms vary very much and the severe complications are rather uncommon in children nowadays due to a widely available treatment. We present the case a 12-year-old male patient, admitted in our clinic for morning vomiting after meals, with abundant mucus, dysphagia for solid food, epigastric pain, food refusal, nocturnal agitation associated with sleep disorders for approximately 1 month, and weight loss (2-3 kg in the last 6 months), whose personal history revealed multiple acute upper airways infections during the first year of life and gastroesophageal reflux diagnosed approximately at the age of 1 year, which improved without treatment until the age of 3 years. The esophagogastroduodenoscopy and barium transit exam established the diagnosis of esophageal stenosis and gastroesophageal reflux with favorable evolution after a prolonged treatment with proton pump inhibitors. The particularity of the case consists in diagnosing a peptic esophageal stenosis in a 12-year-old child, with onset of symptoms approximately 1 month ago, whose personal history revealed multiple acute upper airways infections during the first year of life and gastroesophageal reflux at 1 year of age which apparently solved without treatment until the age of 3 years.

Keywords: gastroesophageal reflux, child, esophageal stenosis

Abbreviations: cm – centimeters, GER – gastroesophageal reflux, H – height, kg – kilograms, W -weight

Introduction

Gastroesophageal reflux (GER) represents the involuntary passage of the gastric contents into the esophagus, and it can be either a physiological or a pathological phenomenon, but in any case it is one of the most frequent occurring symptom in both children and adults (1). The so called 'physiological' GER occurs in the first months of life or when it has no associated symptoms, and it has a protective role during meals or early after meals, while the pathological GER occurs with an increased frequency and it is associated with symptoms and complications (1). If GER causes mucosal damage or impairs the quality of life it will lead to gastroesophageal reflux disease (GERD) (2,3). Daily regurgitation occurs in approximately 50% of infants under the age of 3 months reaching a percentage up to 66% at the age of 4 months, and decreasing to only 5% at 1 year of age (4,5). Reflux esophagitis is one of the most common, but severe complications of GER that can lead in time to esophageal stenosis requiring even surgical management. Reflux esophagitis is encountered in up to 62% of children that undergo evaluation for GER symptoms, while Barrett's esophagus in up to 3%, and GERD that requires surgical management in up to 13% of the cases (1). The factor that influence the development and outcome of GER are multiple and interconnected. Thus, among the factors that were proved to contribute to this pathology were reported: genetic susceptibility, alcohol, smoking, drugs, food habits, overweight and obesity, posture, mastication and swallowing, sphincter incompetence, Helicobacter pylori infection, race, etc. (1).

The clinical manifestation of GER is very complex and variate, and depends on the age. The most frequently described symptoms include: regurgitation, excessive crying and irritability, vomiting, food refusal, persistent hiccups, failure to thrive, persistent cough, aspiration pneumonia, wheezing, laryngitis, ear problems, sleeping disturbances, anemia, melena, hematemesis, apnea, heartburn, hoarseness, chronic asthma, and sinusitis, while esophageal stricture, Barrett's esophagus, and esophageal adenocarcinoma are symptoms that prove a prolonged untreated GER that appear with a more decreased frequency in children (1). GERD may lead to severe complications like esophagitis, Barrett's esophagus, strictures or esophageal adenocarcinoma (1). Nowadays, due to a widely available therapeutic options for GER, esophageal stenosis and ulceration are uncommon in children (6).

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The most frequently used diagnostic tools for GER are radiologic contrast studies (e.g. barium transit exam), ultrasonography, 24-h esophageal pH monitoring and esophagogastroduodenoscopy that can reveal different anatomic malformations and esophagitis, not reflux (1).

The management of GER cases is complex and can include: non-pharmacological measures such as dietary treatments, posture, pharmacological treatment or surgical one in carefully selected cases.

Case report

We present the case of a 12-year-old male patient, admitted in our clinic for morning vomiting after meals, with abundant mucus, dysphagia for solid food, epigastric pain, food refusal, nocturnal agitation associated with sleep disorders for approximately 1 month, and weight loss (2-3 kg in the last 6 months). The personal history revealed the following pathological elements: multiple acute upper airways infections during the first year of life and gastroesophageal reflux diagnosed approximately at the age of 1 year, which improved without treatment until the age of 3 years.

The clinical exam performed at the moment of admission revealed the following pathological elements: influenced general status, ailing face, pallor, poorly represented adipose tissue, tenderness at palpation in the epigastric area; W: 29 kg, H: 130 cm. The CBC count, the inflammatory biomarkers and the biochemistry test were all within normal ranges. We also excluded a celiac disease and a food allergy based on the negative values of the anti-transglutaminase and anti-endomysial antibodies, and the total level of immunoglobulin E, respectively, which was normal. We performed an esophagogastroduodenoscopy which revealed intense hyperemia of the mucosa in the inferior third of the esophagus with erosions associated with esophageal stenosis and esophageal spasm that do not allow the exploration of the stomach. We also took biopsy specimens from the esophageal mucosa, and the histopathological exam revealed inflammatory infiltrate with neutrophils.

Therefore we performed an esogastroduodenal barium study which pointed out thin walls of the esophagus with an esophageal stenosis of approximately 2 cm length in the inferior part of the esophagus, gastric dilation with obvious gastroesophageal reflux in Trendelenburg position.

Thus, our diagnosis was esophageal stenosis as a result of gastroesophageal reflux. The dietetic management consisted in semiliquid semisolid food, frequent meals in small amount. We also initiated treatment with proton pump inhibitors (Esomeprazole), domperidonum and spasmolytic drugs (Papaverin) for 8 weeks.

The follow-up exam revealed a favorable clinical evolution after 8 weeks of treatment was favorable, without vomiting, he is able to consume semisolid food and intermittently even solid, and he also gained 2 kg. The esogastroduodenal barium study revealed major improvements of the esophageal stenosis, without esophageal spasm or obvious gastroesophageal reflux. We also repeated the esophagogastroduodenoscopy and we were able to explore also the stomach, which presented a normal aspect. Therefore, we recommended the continuation of diet and proton pump inhibitor treatment for another 4 weeks. After this period, the patient no longer presented symptoms and he continued to gain weight.

Discussions

GERD is probably one of the most frequent gastrointestinal conditions worldwide affecting all human beings independently by the age that can lead to severe complications impairing the patients' life quality. In the past, when reflux treatment was not available, approximately 40 years ago, esophageal strictures were encountered in up to 5% of children who presented with reflux symptoms (7). This condition is diagnosed in more than 10% of adult population, and even though most of the patients present a favorable outcome after an adequate acid-suppression therapy, approximately 10% are refractory to treatment and can develop serious complications (8). Nevertheless, it has been proven that certain complications of GER, such as Barrett's esophagus can present a positive influence of patient's symptoms. This fact has been explained by the increased resistance of metaplastic epithelium present in Barrett's esophagus to gastric acid, leading therefore to the significant improvement of symptoms (8). Similarly, in our case the lack of symptoms can be due to the presence of Barrett's esophagus taking into account that the patient was diagnosed with GER at 1 year of age which apparently solved without treatment until the age of 3 years. Most likely the condition did not solve, but the patient developed a Barrett's esophagus which improved his symptoms until he developed the symptoms of esophageal stenosis.

In certain countries this condition might be considered a major public health problem, such as Russia, where according to a study performed on 34 903 upper endoscopies on patients with symptoms of gastric dyspepsia, the prevalence of erosive esophagitis was of 4.9% and peptic esophageal strictures were encountered in 0.2% of the patients (9). Peptic esophageal strictures are frequently encountered in children from developing countries due to the lack of appropriate medical centers (10), but it is also encountered in developed countries. The chronic effect of GER on the esophageal mucosa will lead in time to the development of fibrotic tissue and as a consequence to peptic esophageal strictures. The main symptom of this disorder is dysphagia and the most appropriate diagnostic tools are barium transit exam and upper endoscopy (11). In our case, the diagnosis was also established by the previously mentioned diagnostic approaches. Up to 23% of patients diagnosed with reflux esophagitis will develop strictures (12) that are usually located at the squamo-columnar junction and have a length which ranges from 1 to 4 cm (13). Similarly, our patient presented an esophageal stenosis with a length of approximately 2 cm in the lower

part of the esophagus. According to the data reported in the literature, the incidence of GERD is higher in male children (13,14). Our patient was also a male.

Fig. 1. Aspect of the esophageal stenosis at esophagogastroduodenoscopy

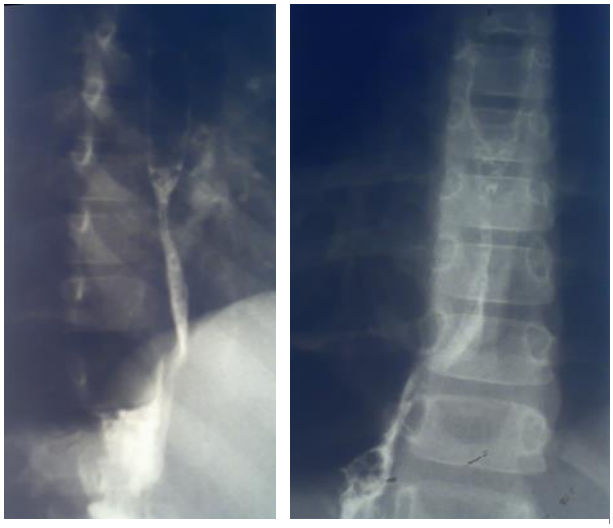

Fig. 2. 3. Aspect of the esophageal stenosis at esogastroduodenal barium study

Even though the cardinal signs of peptic esophageal strictures is dysphagia with an insidious or sudden onset, it has been proven that up to 25% of the patients present no history of heartburn or other suggestive symptoms for GER (13). In the case described by us, similarly to the data mentioned in the literature, the patient did not present any history of suggestive symptoms for GER, but he was diagnosed during his early childhood with GER. On the other hand, it has been stated that GER it is also physiological in infants, in the lack of symptoms or shortly after meals as a defensive mechanism. Despite the fact that GER was defined as physiological in infants, it must be taken into account that it can also become pathological in these age group if it associates symptoms, such as daily vomiting in great amounts, failure to thrive, food refusal, hematemesis, irritability, etc. Therefore, Crankson et al described a case of 7-year-old male infant, with a history of vomiting since birth, who was diagnosed with circumferential thickening of the lower esophagus after a computed tomography exam (15).

Management of peptic esophageal stenosis in children is complex and it often requires a multidisciplinary approach with the involvement of different specialists, such as: pediatrician, gastroenterologist, surgeon, and general practitioner. The management protocols include medical therapy, bouginage, fundoplication, stricture resection or interposition grafting (16). It is well-documented that endoscopic dilation of peptic esophageal strictures is safe in children, but some authors sustain the fact that the outcome will be significantly better if pharmacological treatment is administered before the endoscopic dilation, antireflux surgery or post-operative dilation (16-19). Fortunately, in our case prolonged pharmacological therapy presented a very favorable effect and the patient did not need a surgical approach.

Early diagnosis and management of GER in children is essential in order to prevent severe complications, such as esophageal stenosis or even esophageal adenocarcinoma.

Conclusions

Even though GER is very common in both children and adults and it can be physiological under certain circumstances, it can also lead to very severe complications such as esophageal stenosis and even esophageal adenocarcinoma. Nevertheless, these two complications are rarely encountered in children, it is of major importance to take into account that they can develop even in the absence of suggestive symptoms.

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DIAGNOSTIC DILEMMA IN LARGE CAVITY PLEURISY

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Abstract

A variety of conditions can cause pleurisy in children. The most frequent is a results of infection, secondary to a pneumonia or a tuberculosis. In most of the cases the diagnostic is easy, by biochimical and bacteriological examination of the pleural fluid. We know from the literature that empyema is a sign of bacterial pleurisy, but in some cases there is dificult to obtaining the diagnosis of certainty. We present a case of pleural effusion whose unexpected diagnosis followed a long line of intermediate diagnoses. This all have been suggested by clinical evolution, but also by laboratory data. The final diagnosis resulted after the occurrence of laterocervical lymph mass and was confirmed by immunohistochemical studies on ganglion biopsy.

Keywords: pleural effusion, empyema, tuberculosis, Non Hodgkin Lymphoma, children

Introduction

Large cavity pleurisy appers in children in a various causes. Most commonly results secondary to an infection, but may be a primary or a secondary manifestation of many disorders. Pleuresy develops because of excessive filtration or defective absorption of fluid (1). Tiukhtin shows a dominance of tuberculous etiology in over 85% of cases, follow by parapneumonic pleurisy in 10%, tumoral pleurisy in 1%, posttraumatic pleurisy in 0,5% cases (2). Other possible aetiologies are nephrotic syndrome, heart failure, metabolic diseases. The most common form of extra pulmonary tuberculosis is, in children, massive pleural effusion, about Merino and Kim (3). This form of Mycobacterium tuberculosis infection appear most commonly in adolescents and young adults (following a recent infection), rarely in the elderly (by reactivation). Not all the time the diagnosis is very easy in a case of pleural effusion. We may encounter difficulties in obtaining the diagnosis of certainty, because the cultures or the serological diagnosis for mycobacterium, but also for the other infectious etiologies (adenovirus, Mycoplasma) being laborious.

Case presentation

We present a case of 6 years old boy, from rural area, who came in our clinic in october 2016, presenting dyspnoea, fever, asthenia, sweating, dry cough. The boy has a rich history of respiratory infections, and no BCG scars. Clinical presentation showed a overweight boy (W 34kg, T 124cm, BMI more then percentil 97% for age and gender), without palpable lymf nods. Respiratory system showed maquity at percussion to inferior two thirds of the right side, mixed dyspnea, with orthopnee and polypnea (50 breath/min), SaO2 87%. Vesicular breath sound was abolished on the right and we found pleural rub present in both phases of respiration pleural.

After one week of antibiotherapy the child was admitted in the Pediatric Intensive Care Unit (PICU) due to respiratory distress (Fig. 1). Chest X-ray revealed a opacity of medium intensity that occupies the right pleural space and is projected, on profile, on the shadow of the heart (Fig. 2).

Because of respiratory distress pleural drainage has been established an emergency, (drain approximately 200-300ml purulent liquid, daily). Biological dates suggested a bacterial infection, but all the cultures from the blood and pleural efussion was negative.

Biological data: HBG = 12,9 g/dl, HTC = 38,7%, WBC = 20 000/mm3, NEU = 65,1%, L = 22,5%, M = 10,8%, E = 1,9%, B = 1%, TGP=19 UI/l, TGO=33 UI/l, LDH=1210 UI/l, urea=0,13 g/l, creatinine=0,46 mg/l, uric acid=1 mg%, TOTAL PROTEIN=55,3 g/l , albumin=25,8 g/l, alfa 1=5 g/l, alfa 2=11 g/l3, beta=5,8 g/l, gamma=7,4 g/l, A/G=0,88. An important inflammatory syndrome was determined: Fibrinogen = 9,64 g/l , ERS = 65 mm/h, PCR 124mg/dl. We start treatment for 10 days with: Lynezolid (Zyvox) and Ciprinol, for purulent pleurisy.

The unfavorable progression of disease (continued to fever, dyspnea, respiratory distress, with continous oxigenotherapy, pleural fluid quickly recovered) forced reconsideration of the diagnosis. The new exam of pleural fluid showed: ph = 7,5; RIVALTA +; protein = 4,5 g/l; glucose = 0,37 g/dl; cellularity: lymphocites 98%; LDH = 2567 UI/l. Chest X-ray: Radiological evaluation showed the same opacity, without mediastinal adenopathy (Fig. 3).

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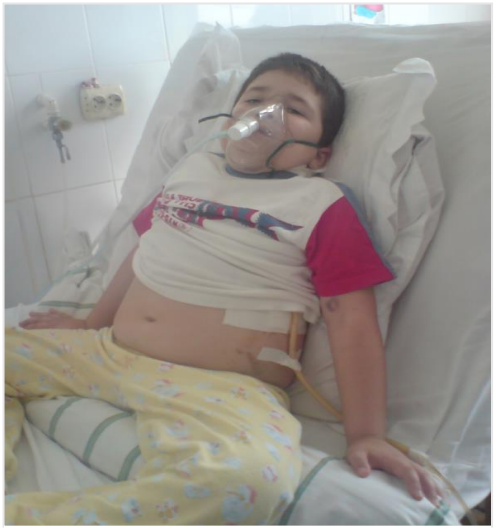

Fig. 1. The child in the Pediatric Intensive Care Unit

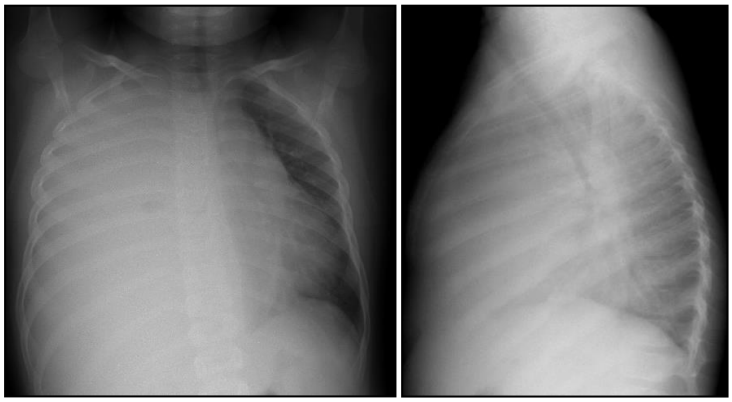

Fig. 2. Chest X-ray

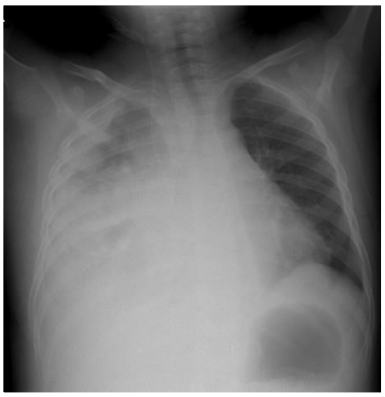

Fig. 3. Second Chest X-ray

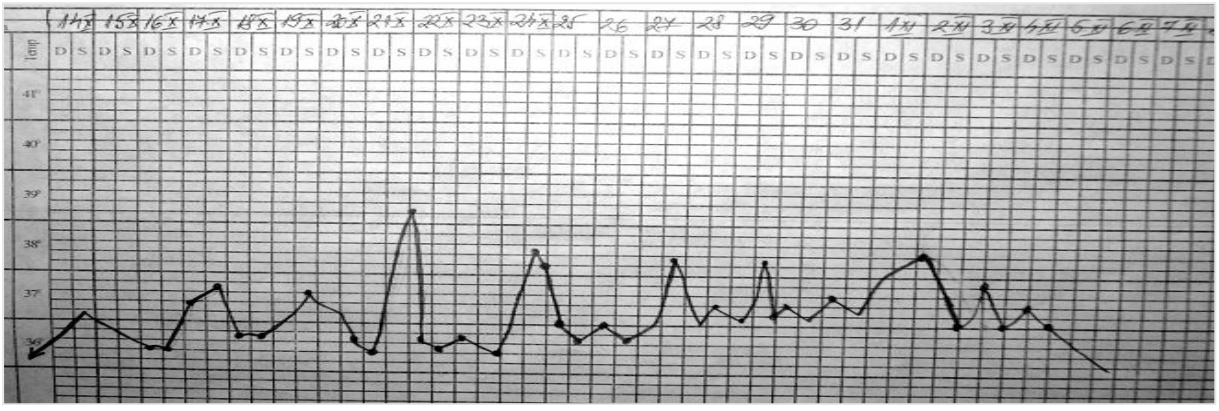

Fig. 4. Fever curve

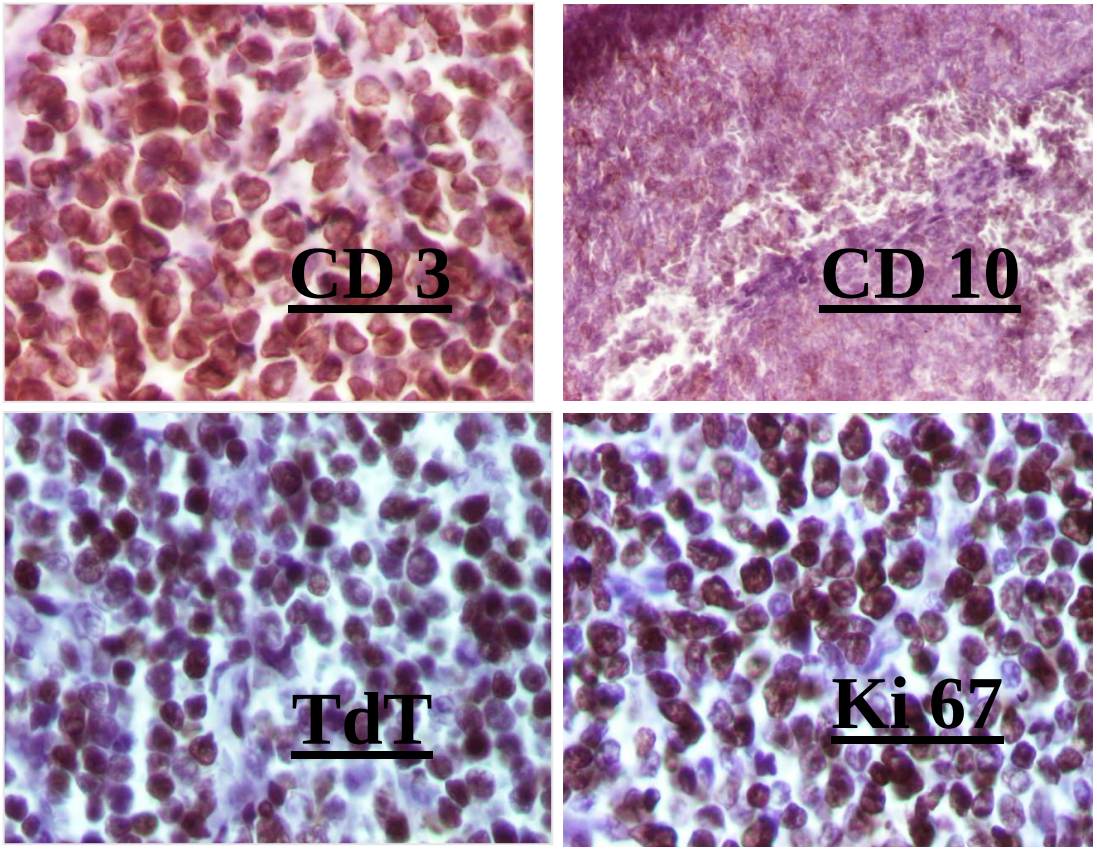

Fig. 6. Immunohistochemical analysis revealed intense positivity of markers CD3, CD 10, TdT

The suspicion of tuberculosis was when the result of test ADA was positive in the pleural fluid (30 U/l), even the IDR 5 u PPD was negative at 72 h. The cultures from Koch bacilli was also collected. The pneumologist considered the diagnosis of Tuberculous pleurisy and has opted for initiating specific therapy with 4 tuberculostatic agents, for 2 months (hydrazide + rifampicin + ethambutol + pyrazinamide), then 2 for another 4 months (hydrazide + rifampicin).

After one week of therapy evolution continued to be unfavorable, the child showed fever (Fig.4), with predominantly in the evening. In the same time appeared a bilateral laterocervical and supraclavicular adenopathic block, with a 2 cm diameter, mobile, painless, local pressing, and oppressive.

On 22 octobre 2016 was performed a ganglionar biopsy. The tuberculostatic treatment was continuing to the 31 X 2016, when the result of biopsy showed non hodgkin lymphoma, atypical mitosis, medium - sized cell proliferation, with homogeneous nuclei, without nucleoli (Fig. 5).

Immunohistochemical analysis was performed with a panel of antibodies effective in paraffin sections, for determining the type of lymphoma. HLA patterns were revealed intense positivity of markers CD3, CD 10, TdT, alog with negative CD20 and Pax 5, suggestive for T-cell phenotype. The antigen Ki 67 was intens positive too, suggesting a lymphoma with a high degree of proliferation (Fig. 6).

To determine the stage of lymphoma we practiced:

- Bone marrow aspiration – no infiltration
- Abdominal ultrasound – no abdominal lymphnods or tumor masses, without hepatic – splenic infiltration
- Lombar puncture – without brain touch

About Lugano classification, which is based on the older Ann Arbor system we diagnosed a III-th stage T – Non Hodgkin Lymphoma (NHL – T).

The tuberculostatic therapy was stopped and was initiated specific therapy for NHL – T. In evolution the fever has quickly disappeared, general condition improved clearly, the child was able to walk and feed. The pleural drain was stopped also (Fig. 6).

Patient parameters, tumor parameters and biological data had led to the development of a prognostic index. The fact that the patient can self-handle in a limited way (more than 50% of the time spent in bed) and the prognostic factors: low age, elevated LDH, adenopathy involving multiple lymph nodes, III-th stage lymphoma, fall into a high risk group, with limited prognosis. For the present the patient are a good response to chimiotherapy.

Discussion

The dilemma of diagnostic started from the fact that the patient had an appearance of pleural empyema, most commonly with bacterial etiology (staphylococcus),

supported by the presence of leukocytosis with polynucleosis and inflammatory syndrome. The unfavorable clinical outcome under large antibiotic therapy, and the positive ADA test reorientated the diagnosis to Tuberculous pleurisy. The diagnosis was cut off by the appearance of the adenopathic block and the anatomo-pathological result of lymphoblastic T lymphoblastic. Reverse, the purulent appearance of the pleural fluid we explain it by the increased number of white blood cells in the fluid. Véronique Minard-Colin shows in his review that T cell lymphoma is the second most common subtype of non-Hodgkin lymphoma (NHL) in children and adolescents. The annual incidence per million inhabitants ranges from 10 in children between 5 and 14 years old, like our child (6). Chaignaud and co established sience 1998 that there is a significantly greater association of T-cell lymphoma and pleural effusions than with Hodgkin's disease (7). The author discusses pleurisy associated with mediastinal T-cell lymphoma. In our case the firs manifestation was pleural effusion, the adenopathic block appearing after 3 weeks of evolution. No mediastinal tumor mass was decent in time.

Conclusions

The particular evolution of our case was at the base of tardiv diagnosis. Maybe a immunohistochemical analysis performed from pleural liquid would have passed the diagnosis earlier. Rapid recognation of the malignant pathology is essential to the vital prognosis of any patient.

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EPIDEMIOLOGY AND CLINICAL EVOLUTION OF CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT

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Abstract

Congenital anomalies of the kidney and urinary tract (CAKUT) are characterized by structural and functional abnormalities of kidney, collecting system, bladder, and urethra. These anomalies are the most commonly diagnosed malformations in the prenatal and postnatal period and constitute the leading cause of Chronic Kidney Disease (CKD) in children, worldwide. CAKUT can be identified as single malformation or it can be part of a complex malformation. Classification of CAKUT on embryological basis consists of: abnormalities in the renal parenchymal development, aberrant embryonic migration and abnormalities of the collecting system. We analyzed 20,326 children admitted in Children Emergency Hospital Timisoara between January 2015 and March 2016 for different pathologies in a cross-sectional study. The prevalence of children with CAKUT was high in our study 5.3‰, with an incidence of 1.5‰ per year. CAKUT is difficult to detect since there is no significant clinical manifestations in early ages. Clinically, CAKUT are silent most of the time, UTI is the most frequent initial distress clue as it was present in 54.12% of cases by the time of diagnosis. Abdominal ultrasound is the preferred method of screening for CAKUT and it should be recommended as a routine of children`s physical examination.

Keywords: CAKUT, Pelviureteric junction obstruction, Hydronephrosis, renal agenesis, multi cystic dysplastic kidney, vesico-ureteric reflux

Introduction

Congenital anomalies of the kidney and urinary tract (CAKUT) represent an important cause of morbidity in children and at the same time they are the most common cause of Chronic Kidney Disease (CKD) in children1,2. The prevalence of CAKUT reaches 3-6 per 1000 live births 3, can appear as solo malformation or in association with other organ involvement.

Barakat and Douglas analyzed 13775 autopsies in 1991 and 636 patients were found with reno-ureteral malformations (4,61%). Higher incidence was found in pediatric population4.

Antenatal ultrasonography after 28 weeks' gestation can identify renal tract abnormalities with an incidence of 1% to 5% of all pregnancies and 14.3 per 1000 births, permitting early treatment of the asymptomatic newborn and reducing later renal damage5,6.

Embryologic development of kidneys and urinary tract take place during the third and fourth week of gestation7. At birth each kidney contains about 1million nephrons7. Structural development of these nephrons completed by the end of the 34th gestation week, anyhow maturation of kidney function will continue until completion 6 months after birth. Most of prenatal diagnosed hydronephrosis are transient or physiological up to 74%5, resolution occurring within the first three years; therefore most patients will not need surgical intervention8. Overall, children with any degree of antenatal hydronephrosis are at greater risk of postnatal pathology as compared with the normal population6.

CAKUT can be identified as single malformation or it can be part of a complex malformation including muscular abdominal wall defect (Prune-Belly Syndrome), abdominal mass (50% of neonates with abdominal mass have a urinary malformation underneath9), undescended testicle, minor genital alterations, limbs alterations or ear malformations10. Regarding clinical manifestations, most CAKUT are asymptomatic, in other cases though, repeated or recurrent Urinary Tract Infections (UTIs) can be a leading sign. Clinical features vary widely depending on the type, severity and laterality of renal anomaly11. Kidney hypoplasia, ectopic kidneys, and anomalies in shape are mainly asymptomatic, detected by ultrasound, accidentally. Renal agenesis, multi cystic dysplastic kidneys (MCDK), bilateral Pelvi-ureteric junction obstruction (PUJO) and cystic renal diseases can present early either antenatally with oligohydramnios or in newborn with UTI, hypertension, proteinuria, renal impairment, abdominal mass, hematuria or stones12.

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	Cases	Bilateral	Right
Total	**109**		
Renal abnormalities	**27**		
- Unilateral Renal agenesis	9	-	7
- Kidney hypoplasia	7	-	3
- Kidney dysplasia	9	3	2
Aberrant embryonic migration			
- Pelvic kidney	4		
- Fused pelvic kidney	1		
Collecting system abnormalities	**92**		
- Double collecting system	9	4	3
- Hydronephrosys	86	26	23
o Grade I	5	-	-
o Grade II	32	-	-
o Grade III	20	-	-
o Grade IV	22	-	-
o Grade V	4	-	-
- Pelvi-ureteric junction obstruction (PUJO)	36	6	9
- Hydroureter	13	7	2
Urethral malformation	**3**		
- Posterior urethral valves	**0**	NA	NA
- Cloaca	**2**	NA	NA
- Vezical diverticulum	**1**	NA	NA

Table 1: Overview of CAKUT classification with patient group information

Despite recent improvements in prenatal diagnosis and early surgical intervention, these anomalies still remain the primary cause of kidney failure in infants13. Ultrasonography evaluation has enhanced early diagnosis of CAKUT14 and is considered to be "gold standard" of identification of these malformations. CT urography can confirm the ultrasound detected abnormality, complex malformations, demonstration of collecting system and vascular anatomy and also can bring supplemental images and 3D reconstruction of the urinary tract and can be used for CAKUT evaluation both before surgery and post-surgery11. Voiding cystourethrography is needed to evaluate vesico-ureteric reflux (VUR)15.

CAKUT can be classified on embryological basis, in: abnormalities in the renal parenchymal development (MCDK, renal hypoplasia, agenesis or supernumerary kidney, and cystic renal diseases), aberrant embryonic migration (ectopic kidney, fusion anomalies - horse shoe kidney) and abnormalities of the collecting system (double collecting system or PUJO)11.

CAKUT are one of the leading causes of CKD in children13.

Purpose

To describe CAKUT in a cohort of children in the west part of Romania, presented in Children Emergency Hospital Timisoara, aged between 2 weeks and 18 years of age admitted in our hospital, and to compare prevalence with literature data. To highlight about the easy and usefulness of performing abdominal ultrasound in children which should be recommended as part of physical examination.

Material and method

We analyzed 20,326 children admitted in Children Emergency Hospital Timisoara between January 2015 and March 2016 for different pathologies in a cross-sectional study. We included patients having Hydronephrosis grade I to V, renal anomalies regarding number, position of kidneys or structural defects, hypoplastic kidney or renal agenesis and MCDK. Children with urinary tract dilatation due to lithiasis were excluded from the group. We analyzed data about family, sex, living environment, age, type of CAKUT, presence/absence of UTI, number of UTIs, Antibioprophylaxis for UTI, age at the time of diagnosis, presence/absence of surgery treatment and renal impairment.

Data was analyzed using Microsoft Excel, SPSS 2.0 for statistical analysis.

Results

The prevalence of CAKUT was 5.3‰ (109 cases out of 20.326) and the male: female ratio was 1.36:1. Prenatal diagnosis of CAKUT (hydronephrosis in particular) was established only in 9.2% by ultrasound. Incidence of CAKUT was 1.5‰ per year (2015), while the most part of patients were diagnosed before January 2015 and presented in hospital for an acutization or for control.

The prevalence of UTI was 54.12%, meaning more than half of patients presented at least one UTI by the time of diagnosis, while more than half presented for other reasons or CAKUT diagnosis was accidental. Sex distribution of patients with CAKUT and UTI shows a ratio male: female of 1.36:1. Age and sex analysis of patients with CAKUT and UTI reveal that patients at risk for UTI are female toddlers (0 to 12 months) and boys over 6 years. Higher frequency of UTI events was reported in children with neurogenic bladder, collecting system anomalies or associated VUR. About 5.1% of children had over 5 episodes of UTI by the time of diagnosis, even though; almost 70% of children had no more than one UTI. Escherichia Coli and Klebsiella pneumoniae were the commonest isolated bacteria (63%).

Prophylactic antibiotic was used in patients with CAKUT and VUR that presented at least three episodes of UTI.

Trying to establish a classification of CAKUT and the prevalence in our study, we took into consideration dividing CAKUT in: renal abnormalities (kidney agenesis, kidney hypoplasia, kidney dysplasia, position or structural anomalies), collecting system abnormalities (duplicated collecting system, hydronephrosis, congenital PUJO, obstructive megaureter) and urethral malformations. Table 1 shows a list of encountered CAKUT.

Incidence of UTI was reduced with the use of pediatric surgery, consequently it led to reduction in the number of UTIs after surgery also. Corrective surgery was performed in 41 cases (37,6%) mostly in those with severe malformations or recurrent and aggressive UTIs. Prophylactic antibiotics were given to 9 patients (8.3%) in other to reduce the frequency of UTIs.

Discussion

Renal parenchymal abnormalities include renal agenesis, renal hypoplasia, MCDK, , and cystic renal disease. Unilateral renal agenesis is not uncommon; its prevalence is 0.7‰12, often asymptomatic and associating compensatory hypertrophy of the existing kidney. In our study unilateral renal agenesis was found in 9 patients representing 0.44‰ of all patients and 8.25% of patients with CAKUT, 2 of them having also CKD due to abnormalities on the remaining kidney (renal dysplasia or hydronephrosis).

Renal hypoplasia refers to small congenital kidneys due to incomplete renal development. Children with renal dysplasia (MCDK) have renal parenchyma replaced by non-communicating cysts of various sizes with very little functional renal parenchyma12. Incidence is in general population about 0.23‰16, slightly more frequent in males and on the left side. In our study incidence was 0.44‰ (9 patients), with the same slightly increased incidence in males having the left side predominantly affected (male: female ratio 5:4, left: right ratio 4:2). More than half of them (5 patients) had impaired renal function at the time of diagnosis and must be kept under close surveillance.

Abnormal migration anomalies include ectopic kidneys (abnormal location of kidneys) and fusion anomalies (horse-shoe kidney). Both types of malformation are inoffensive unless associated with other CAKUT13.

CAKUT referring to abnormal collecting system will actually talk about duplex collecting system and PUJO. Duplex collecting system is characterized by incomplete fusion of upper and lower pole moieties resulting in a variety of complete or incomplete duplication of the collected system. Based on the degree of fusion, it can present as bifid renal pelvis, partial ureteric duplication (Y-shaped ureter), incomplete ureteric duplication with ureters joining near or in bladder wall (V-shaped ureter) and complete ureteric duplication with separate ureteric orifices11. This is often asymptomatic and incidentally detected. We have found 9 cases of different variants.

PUJO is definitely one of the most common types of CAKUT with the highest prevalence of 2‰ in general population11. In our study, hydronephrosis was at a high prevalence 4.2‰, while PUJO was encountered in 1.77‰ of the cohort group with left: right ratio of 18:9. PUJO represented 33% of CAKUT.

VUR is a common finding in pediatric practice that occurs in about 1% of children and is often familial15. In our group VUR prevalence was 0.73‰, representing 13% of CAKUT patients, with a left: right ratio of 8:2. The majority of low-grade cases have a tendency to resolve spontaneously during childhood. However, VUR has been identified as a risk factor for the development of urinary tract infections (UTI). In addition, some children with high-grade VUR have already renal lesions before the advent of any UTI15.

Conclusions

The proportion of children with CAKUT was high. CAKUT is difficult to detect since there is no significant clinical manifestations in early ages, anyhow abdominal ultrasound is the preferred method of screening, as it should be recommended as a routine of children`s physical examination.

Abbreviations:

CAKUT – Congenital Anomalies of the Kidney and urinary tract
UTI – Urinary Tract Infection
PUJO – Pelvi-ureteric junction obstruction
VUR – Vesico-ureteric reflux
CKD- Chronic Kidney Disease
MCKD – Multi cystic dysplastic kidne

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INTRAUTERINE GROWTH RESTRICTION - STILL A GREAT CHALLENGE FOR THE NEONATOLOGIST - A REVIEW ARTICLE

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Abstract

This article makes a review of literature data on an extremely special category of infants – premature neonates with intrauterine growth restriction (IUGR). The antenatal recognition of a true fetal growth restriction helps prevent or decrease the mortality rate and neonatal morbidity. Prenatal and postnatal Doppler velocimetry has a great contribute to the differentiation of healthy SGA and real IUGR but also a challenge to predict which of the fetuses are at high risk for negative outcomes, and there are currently few understandable things about monitoring and treatment strategies most appropriate for preterm infants with RCIU. An international initiative to address these issues would be of great importance to improve the care of the group with IUGR.

Key words: premature neonates, intrauterine growth restriction

Introduction

IUGR remains an important health problem in developing countries around the world, being one of the "major obstetrical syndromes" associated with placental defects, but also one of the topical issues of neonatology, and in particular the association between IUGR and prematurity under 32 weeks of gestation. Neonatal morbidity and mortality remain significant and has an important economic impact. The need for more stringent diagnostic criteria remains a problem.

Intrauterine growth restriction (IUGR) was defined as the fetal growth rate that is below normal related to the growth potential of a child, specific for race and sex. (4) This was also described as a deviation or reduction from the expected growth pattern and is usually the result of a reduced hereditary growth potential or multiple adverse effects on the fetus. The "normal" newborn is the one whose birth weight is between the 10th and 90th percentiles for gestational age, sex, and race without any malnutrition and growth restriction characteristics. The terms "IUGR" and "SGA" have been used as synonyms in medical literature, although there are differences between the two. The definition of SGA is based on cross-sectional evaluation (either prenatal or postnatal) and this term has been used for those newborns whose birth weight is less than the 10th percentile for gestational age or two standard deviations below the population norms represented on the growth charts, and the definition only considers birth weight without any specification of intrauterine growth or other physical characteristics at birth (1-4).

SGA refers to a weight below the 10th percentile for gestational agerepresented on the population growth graphs. It can still be classified as (1-5):

- mild: birth weight between 3 and 10th percentile
- severe: birth weight lower than percentile 3

IUGR classification:

There are 3 types of IUGR:

- Asymmetrical IUGRs (undernourished children)
- Symmetrical IUGRs (hypoplasic small for date)
- Mixed IUGRs.

In mixed IUGR newborns have smaller numbers and smaller cell sizes as well as clinical characteristics of both types of IUGR at birth (symmetrical and asymmetrical)(Table 1). This type of IUGR results when early IUGR is affected during the pregnancy by placental cause (1-5).

Causes of IUGR

IUGR is the common end result of maternal, placental, fetal or genetic factors.

Antenatal diagnosis of IUGR

The purpose of antenatal monitoring is early detection of IUGR so that antenatal management is optimized in order to obtain better neonatal outcomes. Unfortunately, despite these initiatives, the generalized result of these IUGRs has not changed much over time. Careful monitoring will lead to changes regarding the time of birth or management of birth, but there is still controversy over the appropriate type and timing of monitoring.

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Table 1. Characteristics of symmetrical and asymmetrical types of IUGR.

Characteristics	Symmetrical IUGR	Asymmetrical IUGR
Injury period	First part of pregnancy	Late period of pregnancy
Incidence of IUGR	20 – 30%	70 – 80%
Etiology	Genetic diseases or fetal intrauterine infections	Utero-placental insufficiency
Prenatal ultrasound: head circumference, abdominal circumference, biparietal diameter, femur length	All are reduced proportionally	Abdominal circumference-low; biparietaldiam, head circumf; normal femoral length
Number of cells	Low	Normal
Cells dimension	Normal	low
IP	Normal (>2)	low (<2)
Postnatal anthropometric indices:weight, lenght, head circumf.	Low	Low weight; length and head circumf.– normal (brain sparing)
Difference between cranial and thoracic circumference in term IUGR	< 3 cm	➢ 3 cm
Characteristics of malnutrition	Less pronounced	More obvious
Prognosis	Poor	Good

(1-5)

The necessary investigation for mothers at high risk of having fetuses with IUGR includes assessment of risk factors in maternal and family history, maternal anthropometry with pre-pregnancy weight and height, maternal nutrition status, exact gestational dating, palpation of uterine height, cardiotocography, Doppler ultrasound, and precise measurement of fetal weight using biometric measures (abdominal circumference [AC], head circumference [HC], biparietal diameter and femur length [FL]). The HC / AC ratio was used for diagnosed fetuses with asymmetric growth restriction (FGR) (5-9).

The appropriate gestational age should be calculated using both the date of the last menstrual period and the length of the fetus in the first trimester of pregnancy. The specific weight gains charts (depending on race and ethnical origin) can be used to diagnose IUGR. To accurately highlight IUGR using echocardiography, serial examinations should be made (at least every three weeks to reduce false-positivity rates in diagnosing asymmetrical restriction).

Once identified maternal and IUGR risk factors, further investigations are needed: fetal karyotype for chromosomal abnormalities, TORCH profile, syphilis serology, malaria - especially in the endemic areas. A detailed anatomical fetal study, TIFFA (target imaging for fetal abnormalities) and Doppler on the uterine arteries should be performed by a fetus specialist if severe SGA is identified at the 18-20 week evaluation.

Extensive antenatal Doppler ultrasound allows assessment of well-fetal status and detection of IUGR and Doppler on uterine arteries, umbilical arteries, and on middle cerebral arteries. Although almost all veins and large arteries have been studied through Doppler in the case of IUGR neonates, however, in practical management is used Doppler velocytometry on the umbilical arteries and middle cerebral artery. Umbilical arteries were the first Dopplerevaluated. Doppler waves at their level have a characteristic appearance of "saw teeth". In the case of fetuses suspected of having IUGR, if the Doppler waves in the umbilical arteries look normal and the intrauterine growth curve ascends over a period of two weeks, the fetus may be considered to be healthy, small constitutional. The abnormal appearance of Doppler wavelengths of the umbilical arteries is an early sign of fetal suffering. The average time interval between the absence of enddiastolic flow in the umbilical arteries and the onset of delayed deceleration was estimated at about 12 days (0-49 days). Also, studies have demonstrated a progressive increase in velocimetric flow velocity in the umbilical arteries to extreme cases of inverted enddiastolic flow (Fig. 1). Increasing diastole at the MCA level is a fetal compensatory mechanism that is reactive to uteroplacentral failure ("brainstorming" mechanism). If compensatory mechanisms are overcome, fetal damage occurs rapidly. Therefore, the serial Doppler ultrasounds will estimate the duration of use of fetal compensatory mechanisms, the abnormal venous Doppler appearance indicating fetal deterioration and the need for emergency cesarean section (Fig. 2). (5-9)

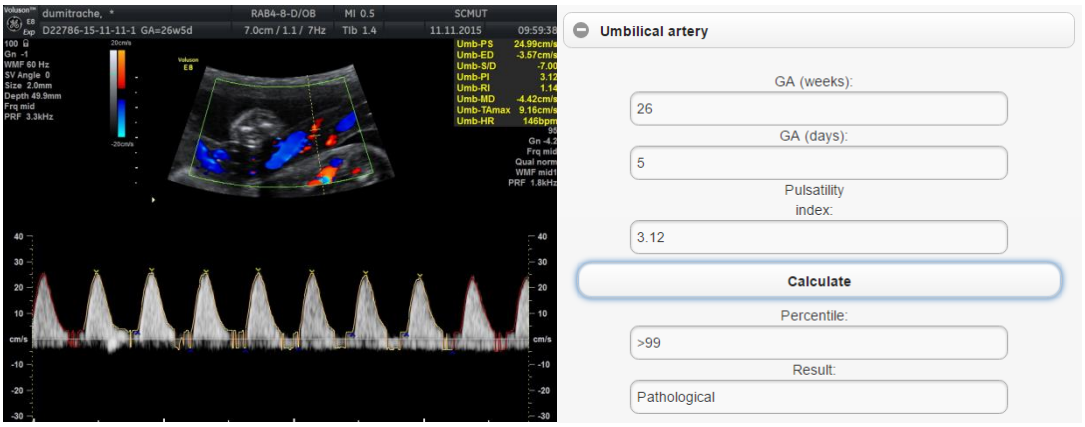

Fig. 1. Example of pulse rate index / umbilical artery resistivity index in a pregnancy 26 weeks of gestation with early RCIU http://medicinafetalbarcelona.org/calc/

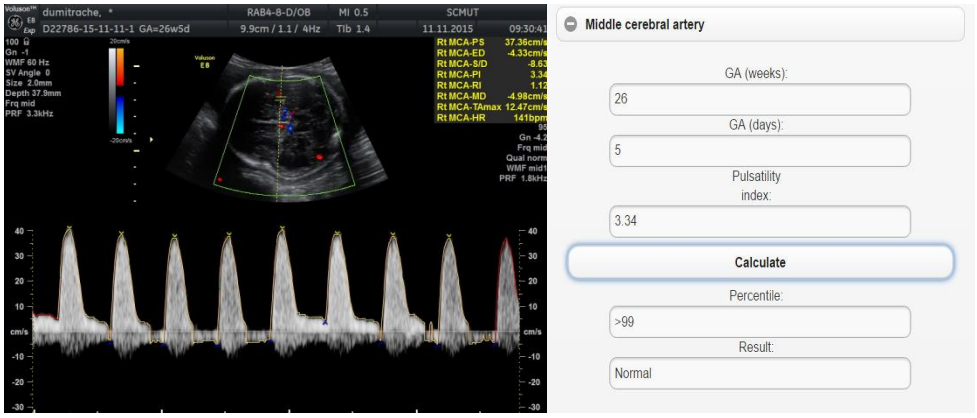

Fig. 2. Example of index pulsatility index / middle cerebral artery resistivity index and cerebro-placental index in a26 weeks of gestationpregnancy with early IUGR http://medicinafetalbarcelona.org/calc/

Postnatal diagnosis of IUGR

1. The postnatal diagnosis of IUGR includes clinical examination, anthropometry, weight index, clinical evaluation of nutrition score (CAN), cephalic index, middle arm circumference and ratio of middle arm / head circumference.(1-9)

Early and late neonatal development in a IUGR prematureis influenced by fetal hypoxia that activates a series of biophysical, cardiovascular, endocrinological and metabolic responses. Fetal cardiovascular response to hypoxia, include changes in heart rate, increase in blood pressure, and redistribution of cardiac output to vital organs are probably the most important adaptation responses to maintaining homeostasis. Redistribution of blood flow to the fetal brain is known as the "brain-sparing effect". Despite numerous attempts to manage the fetal growth restriction, there are no effective treatments to improve fetal growth. The tested methods include maternal nutritional supplements, plasma volume expanders, amino acid and medicines given to the mother- such as aspirin in low doses. moreover, maternal hyperoxygenation found in fetal pO2 reaching or nearing normal value. Even fetal glucose supplements have been tried and have proven to be of no benefit, and can exacerbate acidosis. (10-13) However, the available universal therapeutic outlook for outcome improvements includes antenatal steroid administration in preterm pregnancies and birth in an institution with a neonatal care unit that is able to cope with the complexity of neonatal growth restriction management. Antenatal corticosteroids should be administered to each affected growth-restricted fetus whose birth is expected before 34 weeks of gestation. Although there is a tendency to consider corticosteroids to be beneficial after 34 weeks of gestation (especially in certain cesarean surgeries), the reduction in respiratory distress syndrome in infants over 34 weeks has not reached statistical significance. The gestational age of the fetus is a critical component in the decision process of birth. Unfortunately, there are no randomized group studies in the total clinical spectrum of the fetal growth restriction to assess the optimal moment of birth. In principle, the moment of birth in term newborns is directly correlated with the time when fetal lung maturity was documented, if fetal distress is present or maternal causes determine birth. The management is more complicated in pregnancies between

25-32 weeks of gestation, where every day gained in the uterus can improve survival by 1-2%..(1-9) Early births in neonates with IUGR with abnormal wave on the umbilical artery (after corticosteroid treatment completed antenatally) offers the benefit of an increased rate of live birth fetuses and the disadvantage of increased neonatal mortality.(1-3)) Birth delay until fetal distress is evident may be associated with the increase in fetus mortality by about 5 times higher and neonatal death prior to discharge decreased by more than a third, although total mortality was unchanged. (1-3) It seems that there was insufficient evidence to convince those enthusiastic about this idea that it is wrong both for immediate and delayed birth. When timing is selected, assessment of fetal status should be correct to avoid predictable adverse effects. As a result, the final effect of the antenatal management protocols on the results would probably be very good if the critical results were predicted correctly prenatally. Such results include the risk of fetal death and moderate to severe peripartum acidosis, which has been associated with poor neurological development. (9-13)

Conclusions

Fetal growth restriction (FGR) is associated not only with increased perinatal mortality and morbidity but also with a long-term increased risk for complications such as poor neurological development, type II diabetes and hypertension. Obstetricians should identify fetuses at risk of developing fetal growth restriction, and develop a complet monitoring plan and carefully choose the time and the way of birth.

Main ideas

• Intrauterine growth restriction associated with prematurity under 32 weeks remains a major challenge for neonatologist and obstetrician

• Other causes of small gestational age (SGA) fetuses, such as chromosomal abnormalities and intrauterine infections, should be considered before making the diagnosis of IUGR.

• SGAnewborn is a different condition with a good prognosis and result.

• Fetal Doppler ultrasound is the most accurate and non-invasive method of evaluating placental function.

• Combined Doppler analysis performed on the umbilical artery, medium cerebral artery may show the degree of placental damage, the redistribution level and the degree of cardiac damage.

• The management of a prematur restricted fetus should include a balance between the risks of intrauterine chronic hypoxia with preterm birth and its associated risks.

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ON - AND OFF - SITE NEWBORN MONITORING - A LITERATURE REVIEW

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Abstract:

The newborn admitted to the Neonatal Intensive Care Unit is subjected to various types of treatment from invasive means of correcting deficits to more apparently harmless means. Most of the treatment courses are prone to a keen analysis of hemodynamic and sensory parameters that mainly describe the quality of systemic blood flow, but also give information regarding the neurological and sensorial status of the newborn. One of the most common means of patient monitoring is the pulse oximeter that returns valuable information regarding both peripheral oxygen saturation and heart rate. However, all the monitors from in the NICU bring a harmful sound intensity that may affect both patients and medical personnel, therefore an off-site neonate monitoring system is needed.

Key words: NICU**,** pulse oximetry, newborn/neonate monitoring,

Introduction

The Neonatal Intensive Care Unit (NICU) is supposed to provide an environment that replaces the uterus, providing a place of optimal growth and health recovery for the ill neonate (1). However, medical personnel is incomparable to human alerting and treatment systems, therefore the NICU is overcrowded by means of monitoring the newborn and alerting systems.

This paper considers the various means of newborn monitoring in the NICU and aims to define the needs of clinicians and nurses concerning alerts that regard the patients' clinical status.

Material and Methods

A detailed literature research was conducted using the PubMed online database. We used as key words "pulse oximetry" (1834), "newborn/neonatal monitoring" (32974), "newborn heart rate variability" (7028) and "oxygen saturation" (4368), "wireless pulse oximetry" (51), "NICU monitor alert" (8). The search returned a total of 40 relevant papers. As to the paucity of relevant publications we decided not to define a specific time-frame.

Results and discussions

1. NICU clinical monitoring: hemodynamic and sensory parameters

Monitoring the neonate is usually done by interpreting direct and indirect parameters of systemic blood flow, but also by brain and other sensory monitoring as described below:

1.1 Blood pressure

Blood pressure measurement is the most common used method to assess the neonatal hemodynamic status (2).

1.2 Heart rate

Hemodynamic monitoring, concerning heart rate involves the ventricular output which is determined by stroke volume. In neonates, the circulatory status is mainly evaluated by heart rate, as the only modifiable variable is the heart rate, the stroke volume is considered to be fixed (2).

1.3 Urine output

Dependent on fluid intake, after stabilization, urine output is a poor marker of circulatory failure in the absence of a direct relationship with systemic blood flow (2).

1.4 Brain activity

Most neonates in the NICU are at risk for brain injury, so brain activity monitoring is indicated. The electroencephalogram (EEG), a non-invasive monitoring method should be considered in neonates with seizures, hypoxic-ischaemic encephalopathy, intraventricular haemorrhage, periventricular leukomalacia and stroke (3).

1.5 Pain assessment

Assessment of pain in the newborn is very difficult, because neonates cannot express verbally their discomfort. However, various pain scales have been created. These scales consist of multifactorial observations including physiological parameters (4). To mention physiological parameters, as the autonomous nervous system: CF increase, AP decrease, O_2 saturation decrease, etc. (5).

2. Pulse oximetry

Considering the above mentioned NICU monitoring parameters, we focus our review on pulse oximetry.

Pulse oximetry is one of the most common means of patient monitoring as it returns valuable data concerning the patient's both hemodynamic and sensory status.

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2.1. History

In 1760, Johann Heinrich Lambert, was the first to describe the relationship between light absorption, strength of light and light path length, that was further investigated by August Beer, and published as the Beer-Lambert Law in 1852 (6).

Based on the Beer-Lambert Law, the first to measure the rate of spectral changes of light penetrating tissue when circulation was interrupted, was Karl von Vierordt in 1876. But only in 1931 Ludwig Nicolai measured red light transmission through a hand. In 1940, after great research, JR Squire realized that there was a difference in red light transmission before and after blood expelling from the hand with a pressure cuff. This difference was a function of saturation.

Further, during the World War II, Glen Millikan in 1942, developed a lightweight red and infrared ear clip, that he named "oximeter". And, Wood in 1949, mathematically extended the "oximeter" resulting into a unique function of saturation.

Moreover, Takuo Aoyagi, after obtaining Wood's work in Japanese, reproduced an oximeter earpiece that he used to measure "dye dilution curve, but required calibration with a blood sample". Continuing his study, Aoyagi tested various wavelengths and methods of implementing pulse oximetry (7). His device was first commercialized in 1981, and for the monitoring of oxygen saturation in the newborn it was used starting with 1986 (6).

2.2. Basic principles of pulse oximetry

Pulse oximetry measures peripheral oxygen saturation (SpO2) and heart rate (HR) continuously and noninvasively. It is based on the Beer-Lambert law that relates the light intensity to the properties of the materials through which the light is travelling; and photoplethysmography a method used to detect blood volume changes in the microvascular bed of the tissue (6, 8).

The oximeter consist of a "light emitter" and a "light sensor", which are aligned on opposite sides of a narrow part of body, such as palm, forefoot, finger. The "emitter" sends equal intensities of red and infrared light of wavelengths of 660 nm and 940 nm into the tissue. The "sensor" detects the ratio of red to infrared that emerges and returns the percentage saturation of haemoglobin with oxygen is calculated and displayed (9).

2.3 Pulse oximetry uses

In the NICU a real help was granted regarding the signal of significant change in oxygen saturation in the neonate (10). Thus, by setting alarm limits a great oxygenation control can be achieved. Even more, heart rate can be also monitored by a pulse oximeter as it returns a pulsatile wave signal in concordance with the discontinuous light absorption in the arteries.

3. Alerts and sounds in the NICU

The Neonatal Intensive Care Unit (NICU) is a very busy department and it involves neonates with various conditions that need a close monitoring and a rather highly specialized treatment related to the condition they are in.

The noise in the NICU is higher than advised. The typical average sound intensity in the NICU is of about 54dBA (11), that exceeds the value of 45 dB at which there is cause for concern (1). Thus both the neonates and the care-givers are prone to stress given by alarms going on and off in the NICU, that is why nurses prefer selecting a longer oxygen saturation averaging time that will reduce the number of alarms going on but may also mask serious fluctuations in oxygenation (12).

4. Off -site monitoring

We defined as "off-site monitoring" of the newborn, the means in which a neonate admitted to the NICU may be monitored by using a remote system. For this, literature returned few published papers in which means of monitoring are scares and imply some external changes.

Conclusions

Serious advances have been made in patient monitoring both on-site (next to the patient, within the department) and off-site (at a distance) by using modern information transmitting devices. However regarding the NICU, literature research gives little to no information regarding the off-site patient monitoring systems. Thus research is needed to create solutions in off-site patient monitoring and why not, at least partly, bring noise reduction solutions to the NICU.

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The manuscript must be in English, typed single space, one column on A4 paper, with margins: top – 3 cm, bottom – 2,26 cm, left – 1,5 cm, right – 1,7cm. A 10-point font Times New Roman is required.

The article should be organized in the following format: Title, Names of all authors (first name initial, surname), Names of institutions in which work was done (use the Arabic numerals, superscript), Abstract, Keywords, Text (Introduction, Purpose, Materials and Methods, Results, Discussions and/or Conclusions), References, and first author's correspondence address.