SEPSIS WITH PURPURA FULMINANS 
- REPORT OF TWO CASES 

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Abstract

Purpura fulminans is a supracaute hemorrhagic cutaneous syndrome, characterized by massive and rapid extensive ecchymoses, caused by the disseminated intravascular coagulation (DIC) and dermal vascular thrombosis.

The authors present two clinical cases: a girl (M.A.) aged 3 and a boy (P.A.) aged 1 year and 9 months, who were hospitalized and treated in the Intensive Care Clinic Pediatrics of County Hospital Emergency Craiova, then in the Infectious Diseases Clinic, subsequently in Pediatric Surgery Clinic. In both cases, after a brutal start with high fever, petechial and echimotic elements have been expanding rapidly, within few hours, on the abdomen, buttocks, legs, since the first day of admission. Clinical manifestations had included arterial hypotension, convulsions, coma and cutaneous ecchymoses turned into extensive necrosis. Treatment in both cases included hypovolemia correcting and electrolytical rebalancing, blood and plasma transfusions, broad-spectrum antibiotherapy, corticotherapy, catecholamins, immunoglobulins, local treatment of skin lesions.

Evolution of the sepsis was onto healing in about 21 days, but skin lesions required treatment for another 3-6 weeks. The particularity of these cases, compared with other similar cases of medical literature, consists of the evolution towards healing with restitutio ad integrum without requiring surgical interventions.

Keywords: sepsis, purpura fulminans, petechial elements, necrosis.

Introduction

Purpura fulminans is a grave disease, having as pathognomonic sign the purpuric cutaneous syndrome, manifested by massive and rapid extensive ecchymosis (especially at members) which appears at the infant in the context of some infections or having as background hyperimmune reactions.

At an infant with meningococcical sepsis it has the name of Waterhouse-Friderichsen syndrome (meningococcical purpura fulminans).

The sepsis is defined as a systemic inflammatory response syndrome provoked by an infection. Severe sepsis continues to be a major cause of morbidity and mortality.

Presentation of clinical cases

Case 1

Presenting the case of the female patient M.A. (F.O. 18468/06.04.2007), aged 3 years and 3 months, weighting 14 kg, brought as an emergency in the Pediatrics of the Emergency Clinical County Hospital Craiova.

Heredo-collateral antecedents: she was the fourth child of parents aged over 35, respectively 45, has 2 deceased brothers (one at 6 weeks having aspiration pneumonia, and the other at 1 year and 3 months having bronchopneumonia). Personal Antecedents: born on the natural way with 2650 g.

The beginning of the affection was at admission, with fever (41°C), convulsions, then lethargy, coma. She was admission in a critical general state, abolishment of the conscience state with lack of reactivity at pain stimulus, febrile (41°C), lethargic, generalized tonic-clonic seizures. Stethacoustic pulmonary harsh vesicular murmur, heart rate (HR) 130 beats per minute, cold extremities, with filiform pulse and arterial hypotension; capilar refill time (CRT) >3 sec, neck rigidity. After a few hours, the rash with petechial elements disseminated on the teguments appeared, having purple hue and with the tendency to confluence in the placards (Fig. 1).
Paraclinical examination: Hemoleucogram: Hb = 7.3 g%, WBC = 32200 /mm³, leucocitary formula PMN =69%, Lf = 17%, Blood Platelets (BP) = 93000 /mm³, AST = 150 u/l, initial creatinine 1.45 mg%, after a few days, repeated, was 0.31 mg%. Urea = 40 mg%, glycemia = 104,7 mg%, BT = 0.56 mg%, pH = 7.51, PCO₂ = 37mmHg, SvO₂ = 100%, K = 3.1 mEq/l, negative uroculture. Thorax X-ray: prominent basal bilateral pulmonary interstitial. FO: papillae with optical nerve with dull nasal edge, normal retinian vessels. Lombary punction: clear LCS, slightly hypertensive, after lyses 26 elements/mm³, rare cocci G+ in diplo on the smear, negative cultures, albumin 0.33 g%, Pandy (-), glucose 0.55 g%; normal aspect CT. The lombary punction was repeated at the Infectious Diseases Hospital – with normal results, hemoleucograma also indicated anemia and leukocytosis.

Because of the wide-spread necrotic lesions, with necrosis and infection tendencies, it was decided to transfer her in the Pediatric Surgery Clinic where she was hospitalized for 6 weeks. Paraclinical investigations from the Pediatric Surgery Clinic pointed out: Hb 8.30 g%, Ht = 28%, BP = 579000 /mm³, WBC = 32300/mm³, leucocitary formula: PMN = 77%, Lf = 19%, Mo = 4%. After the blood transfusion: Hb = 13.9 g%, WBC = 14000 then 10800 /mm³, BP=254000 /mm³, total proteins = 5.4 g%, culture from the wound’s secretion: 1. Hemolytic Staphylococcus aureus, sensitive at Linezolid, 2. Klebsiella sensitive at Imipenem. Repeated hemocultures were negative (because of the precocious established antibiotherapy).

Sepsis diagnosis was established based on fever, tachycardia, leukocytosis, the evident disseminated intravascular coagulation (petechial rash, thrombocytopenia) and on the infection proved indirectly.

In evolution she became afebrile, after 13 days from admission, her general state improved, she began to receive oral alimentation, but the purple elements evolved into wide-spread cutaneous necrosis.

She received treatment using Penicillin G 2,4 mil units/day and Amikacin 300 mg/day for 3 days, Dexametazone, Diazepam, Fenobarbital, vitamins, continuing the parenteral nutrition and plasma perfusions. Subsequently the before-mentioned antibiotics were replaced with Ceftriaxon and Gentamicine, human immunglobulines iv being added to the treatment of cutaneous lesions.

The evolution was slowly favourable, towards fully healing, without the need of surgery.

**Case 2**

Male patient P.A., aged 1 year and 10 months, was hospitalized in Pediatrics Clinic and Infectious Diseases Hospital, for fever, coughing, alteration of the general state.

From the heredo-collateral antecedents we remember that the mother of the child had TBC, and the parents have a sociocultural and economic level under the medium.

The infant was the first born, coming from a physiological pregnancy and an normal birth with BW = 3400 g, was naturally fed 12 months, diversified at 1 year and had no previous admissions.

The beginning of the affection was 5 days before the admission with fever (39° - 39,7°C), coughing, inappetence and didn’t follow any home treatment.

At admission is noted the critical general state, W = 12 kg, fever (39°C), lips cyanosis, cold cyanotic extremities, petechial purple lesions with a diameter >1 cm at the legs, buttocks, belly and chest, with coughing, pulmonary stetacustic: harshened breathing, BR = 38 /min, HR = 124 b/min, capillary recoloring time >3 seconds, vomiting, meteorized belly, liver with the lower end at 2 cm below the costal rebord, slightly pointy, palpable spline at 1 cm below the rebord, granulous and congested oropharynx, oral candidose, meningeal syndrome, problems when walking because of the lesions from the legs, somnolence alternating with impatience (Fig. 2).
Paraclinic investigations: Ht = 23%; Hb = 6 g%; BP = 220.000 /mm²; WBC = 13.600 /mm²; PMN = 88%; LF = 8%; M = 4%; on the smear: anisocytosis, poikilocytosis, hypochromia. After the blood transfusion: Hb = 8 g%; WBC = 30.000 /mm²; FL: myelocytes = 3%, metamyelocytes = 4%; PMN segm = 56%; pres PMN with toxic granulations; EO = 3%; LF = 20%; Mo = 8%; TQ = 100%; TH = 100 sec; AST = 30 U/l; ALT = 68 U/l; BP = 170.000 /mm²; glycemia = 53 mg%; fibrinogen = 220 mg%; ESR (Eryctrites Sedimentation Rate) = 20/46 mm; urea 46 mg/dl; creatinine = 0,69 mg%. At the Infectious Diseases Hospital, paraclinic examinations: Hb = 11 g/dl; BP = 168.000 /mm²; WBC=20.900/mm²; PMN = 81%; LF = 14%; E = 3%; M = 2%; Er = 4,62 · 10⁶ /mm³; TQ = 13”; ESR= 38/56 mm. Lumbar puncture: LCS with nucleated elements = 95 /mm³, Pandy (+), Cytologic examination : LF = 95%, PMN = 5%, Coproculture: negative. Pulmonary radiography: “Both hiles enlarged, bilateral accentuated interstitial drawing”. Dermatologic examination: “Necrotic crusts on right buttock”. Surgery examination: “Crust on right buttock and multiple small disseminated crusts in the lumbar region and legs”.

In evolution, the fever diminished after three days from admission and the petechial elements (with an aspect of “geographical map”: some small, others with plaques with a diameter greater than 1 cm) evolved into necrosis with elimination of the saceled tissues, with the persistency of atonous scars similar to the deep crusts. Treatment Pediatrics Clinic and Infectious Diseases Hospital: O₂ therapy, transfusion of erythrocytary mass, fresh plasma, Penicillin G 1 mil/6 hours, then Sulperazone, Aciclovir, Hydrocortisone, symptomatics.

In the Pediatric Surgery Clinic he needed surveillance for another 3 weeks and treatment with Penicillin G, then Ceftriaxon and Cotrimoxazol.

The infant was cured without the need of a segment graft, in the absence of a wide-spread necrosis which would need amputations.

Discussions

Purpura fulminans (PF) is a life-threatening affection characterized by cutaneous bleedings and necrosis produced by Disseminated Intravascular Coagulation (DIC) and dermal vascular thrombosis.

There were identified three distinct categories: PF produced by congenital or contracted anomalies of the protein C or of other proteins involved in coagulation (without infectious context); Acute infectious PF – the cases described fit into this category; Idiopathic PF.

The most common affection associated with PF is the meningococcic sepsis. Varicella is also a common context for the installment of PF (but without the shock state). Rarely, it was signaled in association with pneumococcic sepsis and with measles (15). In the neonatal period, PF can be triggered by infections with streptococcus group B in most of the cases, but also with stafilococcus, Escherichia coli, Enterobacter and so on. Infectious purpura fulminans provokes a lose in the equilibrium of the procoagulant and anticoagulant balance activities of the endothelial cells (9).

The endotoxines of the germs causing PF are a trigger factor for the production of citokine-proinflammation: IL-12, IL-1, TNFα interferon which lead to the consumption of protein C (PC) and protein S (PS). Protein C is a glicoprotein vitamin-K-dependent with anticoagulant and anti-inflammation properties, contributing to survival. In meningococcemia there exists a direct correlation between the severity of the contracted deficiency of protein C and mortality (18). That’s why the perfusion with fresh plasma, administered in both cases described, was salvatory.

In the USA there has been a study (which results were published in 2006) about the effects of the treatment with activated Drotrecogin ALFA (Drot A A) in pediatric sepsis. Drot A A is even a recombind form of human activated protein C (4). Protein C and protein S are vitamin-K-dependent factors, which are synthesized in the liver. Protein C is controlled by chromosome 2, and protein S by chromosome 3. Deficiency in these proteins is recessive autosomal transmitted, having frequently associated deficits of other factors of coagulation. The state of heterozygote of the anomalies of protein C and S causes hypercoagulability. In rare situations, homozygotes with deficiency of protein C or protein S can present a purpura fulminans which endangers life even from the age of newborn (18).

*Positve diagnosis* must be established very close to the beginning bearing in mind that the evolution of PF is very fast, between a few hours and 12-24 hours. It will be established on: a) toxic infectious syndrome (fever, altered geeral state), b) purple syndrome (petechial ehimotic elements which become in evolution necrotic and quickly extensive) and c) shock state: tahicardia, cold, cyanotic extremities, capilar refill time > 3 seconds, polypnea, agitation or somnolence, hypotension. All these diagnostic criterias were present at the two studied patients. As a proof of Disseminated Intravascular Coagulation (DIC), at the female patient could be observed the swering from thrombocytopenia to thrombocytosis.

The antibiotic treatment with ceftalosporines and/or Penicillin G in large doses must be early instituted, after the apparition of purple fever (some ehimotic elements are enough) even if it reduces the proportion of positive hemocultures from 50% to 5%. The detection of soluble antigenes and especially of meningococcic DNA using Polymerase Chain Reaction (PCR) allowed the proof of the meningococcic disease in 50-85% of the cases, but these investigations were not accessible in our clinics.

Besides shock-state treatment with corticotherapy, vasoactive drugs, O₂-therapy, it is always recommended the perfusion with fresh plasma for the correction of the deficit of protein S and C.

Conclusions

The evolution of the sepsis at the two cases was onto healing in about 21 days, but the cutaneous lesions needed treatment for another 3-6 weeks, the girl M.A. presenting complicated sepsis and suprainfection of the postnecrotic lesions.
The presented patients, even if they were in a very grave state at admission, healed without deep scars, without the necessity of graft of teguments and without going to phalanx amputations like in some cases described in the medical literature (9,18).

References


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