Neonatal ascites is commonly the result of hematologic disorders that lead to hydropsfetalis; less frequently it may be caused by non-immunological disorders. One of the rare causes of non-immunological disorders aremetabolical diseases. We hereby present the case of a 5 month old infant in which 4D ultrasound performed at 24 weeks of gestation revealed increased fetal abdominal circumference by fluid accumulation in peritoneal cavity. The presence of congenital isolated ascites along with the peculiar aspect of the infant - dysmorphic features that included frontal bossing, depressed nasal bridge and broad nasal tip, large low-set ears, long philtrum, macroglossia, broad hands and feet, brachydactyly and joint contractures, coarse skin, hepatosplenomegaly, and inguinal hernia, along with biochemical analysis of β-galactosidase enzyme in leucocytes lead to the diagnosis of GM1 gangliosidosis.

**Key words:** congenital ascites, β-galactosidase, GM1 gangliosidosis.

**Introduction**
Ascites in the neonate is usually a feature of hydropsfetalis, caused by hematologic disorders. Less frequently, isolated ascites is the dominant feature. Various mechanisms have been incriminated in the pathogenesis of ascites, that include abnormal lymphatic drainage, obstruction of venous return, cardiac failure, decreased plasma oncotic pressure, as in fetel anemia, hepatic failure (storage disease) or congenital nephrosis, increased capillary permeability, urinary tract obstruction, or meconial peritonitis [1]. Far less common causes are infections such as congenital syphilis, cytomegalovirus (CMV), varicella, toxoplasmosis, and hepatitis A [2].

We report a case of GM1- gangliosidosis, in which isolated persistent ascites was the dominant clinical feature.

**Case report**
A 5 months old infant girl was referred to the Intensive Care Unit presenting with increasing abdominal girth. The infant was born to a 32 year-old woman after a spontaneous delivery at term. The data gathered revealed that the pregnancy of 35 weeks. The data gathered revealed that the infant was the result of aseond pregnancy (first ended in spontaneous abortion at 6 weeks). Routine prenatal testing revealed positive anti-Toxoplasma IgM between 8 and 20 weeks gestation, leading to oral treatment with Rovamicine. Particular prenatal phenotype detected by ultrasound prompted further evaluation; however the karyotype performed revealed no abnormalities. 4D Ultrasound performed at 24 weeks gestation revealed increased fetal abdominal circumference by fluid accumulation in peritoneal cavity.

Upon admission in our Unit the physical examination revealed an ill appearing malnourished infant with mottled, pale dark-green skin, peri-oral cyanosis during crying, facial dysmorphism with coarse features; (fig.1) low grade fever (37,9C), fed with difficulty, marked psychomotor agitation, discrete palpebral and lower limbs edema; polypnea (60 rpm), discrete intercostal retractions, no pulmonary rales upon auscultation; bradycardia, AV = 86 bpm, systolic murmur; the abdomen was distended and tense, with shifting dullness without visible collateral circulation,(fig.2) liver edge palpable at 3.5 cm below the right costal margin, spleen at 3 cm below the left costal margin; accelerated intestinal transit, with watery stools. Initial laboratory tests revealed sepsis with staphylocooccus epidermidis, moderate metabolic acidosis, hypoglycemia, high levels of alkaline phosphatase, and coagulopathy. Abdominal ultrasound (fig.3) and computed tomography revealed hepatosplenomegaly and moderate amounts of ascitic fluid. Bone marrow aspirate revealedlow cellularityand vaculated lymphocytes. Biochemical analysis of β-galactosidase enzyme in leucocytes revealed very low enzyme levels consistent with a diagnosis of GM1 gangliosidosis.

Fresh frozen plasma, packed red blood cells, platelet transfusions,broad spectrum antibioticotherapy, maintenance fluid with appropriate glucose and electrolytes failed to maintain normal homeostasis of the infant as the patient developed bronchopneumonia requiring mechanical ventilation and an increased requirement for inotropie support. Persistent coagulopathy and poor perfusion resulted ultimately in her demise at one month of hospital day.
Discussion

Although inborn errors of metabolism and other single-gene defects represent merely 1 percent of cases of nonimmune fetal hydrops, their importance resides in the substantial risk of recurrence in subsequent pregnancies [2]. Most of these disorders, such as Hurler’s syndrome, mucolipidosis type I, GM1 gangliosidosis type I, Gaucher’s disease, Niemann–Pick disease, and β-glucuronidase deficiency are lysosomal storage diseases [2-7].

GM1 gangliosidosis is a rare lysosomal storage disorder characterized biochemically by deficient beta-galactosidase activity [8] and clinically by dysmorphic features, visceromegaly, dysostosis multiplex and neurological alteration [9].

Prevalence at birth is estimated to be approximately 1:100,000 to 200,000 live births [10].

Based on the age of onset there are three types of GM1 gangliosidosis: type I (infantile), type II (late infantile/juvenile), and type III (adult) [11]. The severe infantile phenotype (type I) is characterized by psychomotor regression by the age of 6 months, visceromegaly, cherry red spot, and facial and skeletal abnormalities [11]. Disease severity seems to be related to the level of beta-galactosidase activity [12].

It is interesting to note our patients’ extremely early onset of symptoms (24 wk of gestation). GM1 gangliosidosis does not usually have a prenatal presentation, but when it happens, the most common finding is, as in our case, fetal or neonatal ascites, for reasons that remain yet unclear. Storage material in Kupffer cells, sinusoidal obstruction and subsequent portal hypertension, or hypoproteinemia due to hepatocellular dysfunction, have been hypothesized as possible explanations [13]. However, in our case, liver ultrasound and hepatic function were normal.

The clinical manifestations are the result of the accumulation of ganglioside in the lysosomes. Clinical suspicion is based on signs such as facial coarsening, hypertrophic gums, cherry-red macula, visceromegaly, dysostosis and psychomotor delay [11]. Bony deformities include stubby hands, broad wrists, anterior beaking of the lumbar vertebrae, thickening of the midshaft of the humerus, and spatulate ribs [14]. There is usually rapid progression of symptoms with the development of spasticity, seizures and general neurologic deterioration with death typically occurring by age 2 [11]. In our case, the infant exhibited dysmorphic that included frontal bossing, depressed nasal bridge and broad nasal tip, large low-set ears, long philtrum, macroglossia. Additional anomalies were broad hands and feet, brachydactyly and joint contractures, coarse skin, hepatosplenomegaly, ascites and inguinal hernia. The infant exhibited no macular cherry red spot, however this feature is seldom present under the age of 6 months [15]. There was no ultrasonographic evidence of dilated and/or hypertrophic cardiomyopathy or valvulopathy. The infant developed seizures during the course of his stay in Intensive Care.

Peripheral blood smear (testing vacuolated lymphocytes) and urine oligosaccharides represent orientation tests [16]. Gaucher-like foam cells have been
reported on bone marrow examination [16]. Diagnosis is confirmed by biochemical assay of beta-galactosidase activity in peripheral blood leukocytes and/or by molecular genetic testing [17]. Patients with the infantile form have almost no enzyme activity, whereas patients with the adult form may have residual activity of 5-10% of reference values [11]. In our case enzyme testing for beta-galactosidase activity revealed significantly diminished activity 0.06%, consistent with classical GM1-gangliosidosis.

Differential diagnosis includes mucopolysaccharidoses, sphingolipidoses and oligosaccharidoses, but the disease resembles mostly with Mucopolysaccharidosis type IVB (Morquio B). Infantile GM1 gangliosidosis shows features of mucopolysaccharidosis at birth [10]. GM1 gangliosidosis and Morquio B are autosomal recessive storage disorders caused by the deficiency of β-galactosidase (GLB1), a problematic partition between Morquio B and juvenile GM1 gangliosidosis phenotypes being long discussed in literature [18]. There are currently no effective therapies for GM1 gangliosidosis, only symptomatic and supportive treatment. A main obstacle is the blood–brain barrier, which prevents the passage of therapeutic enzymes and proteins into the brain. Substrate reduction therapy is a potential approach for clinical trials in late-onset forms [19].

Conclusions

Gangliosidosis does not usually have a prenatal presentation, but, at our patient, it is interesting to note the extremely early onset of symptoms (24 wk of gestation). Even the neonatal ascites may have as a possible explanation the storage material in Kupffer cells, sinusoidal obstruction and subsequent portal hypertension, or hypoproteinemia due to hepatocellular dysfunction, in our case liver ultrasound and hepatic function were normal. There are currently no effective therapies for GM1 gangliosidosis, only symptomatic and supportive treatment, as it has an extremely poor prognosis in the severe infantile form.

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