CASE REPORT

Familial case study: a recurrent metabolic disease in a Tunisian family

Nadia Ben Jamaa1, Tanya Kitova2, Moez Ben Amara3, Denis Milkov2, Dorra Zghal4, Sami Jabnoun5, Mohamed Yacoubi5, Mahdi Khila1, Imen Kessibi2, Samia Kacem4, Faouzia Zouari6, Soumeya Siala-Gaigi1, Aida Masmoudi1

1Department of Embryo-fetopathology, Center of Maternity and Neonatology of Tunis, Tunisia
2Medical University of Plovdiv, Bulgaria
3Department of Neonatology, Center of Maternity and Neonatology of Tunis, Tunisia
4Department of Gynecology and Obstetrics C, Center of Maternity and Neonatology of Tunis, Tunisia
5Department of Pathology, University Hospital Farhat Hached of Sousse, Tunisia

Abstract

We report a recurrent case of Sly syndrome in a Tunisian family. The mother was a 32-year old, parity three, five gestations, from a first-degree consanguineous marriage. Her first pregnancy ended in a miscarriage; the second pregnancy ended with the birth of a healthy child. The other three pregnancies were interrupted through medical intervention due to hydrops fetalis.

The histological placental examination of the first two fetuses found cytoplasmic vacuolization affecting the trophoblast and Hofbauer cells (Hale coloration). The prenatal diagnosis by amniocentesis of the third pregnancy revealed a high level of glycosaminoglycans with a predominance of chondroitin sulfates in electrophoresis, confirming the diagnosis of Sly disease.

In conclusion, the histological examination of the placenta is essential for the biological and genetic examination, as a basis for the diagnosis of Sly disease and for a further genetic counseling.

Key words

Hofbauer cells, hydrops fetalis, mucopolysaccharidosis VII, placenta, Sly syndrome.

Introduction

Lysosomal storage diseases are a group of 50 inherited monogenic diseases that are characterized by malfunctioning lysosomes and an accumulation of unprocessed biopolymers in various tissues and organs. The clinical symptoms progressively develop with a coarsening of facial features, bone, skin, and eye changes, organomegaly and a severe retardation in the neuropsychological development. Lysosomal storage diseases belong to the group of rare diseases. As separate diseases, they are extremely rare, but the incidence of the group as a whole is 1 in 5000-7000. The most common classification of lysosomal storage diseases is according to the type of metabolite accumulating in lysosomes mucopolysaccharidoses, glycoproteinoses, sphingolipidoses and glycogenoses [1].

Mucopolysaccharidoses are a large heterogenous group caused by a deficit of any of the eleven enzymes involved in the metabolism of these biopolymers [2, 3]. They are characterized by an intracellular accumulation and increased excretion of mucopolysaccharides (glycosaminoglycans, GAGs) [2, 3]. Mucopolysaccharidosis type VII (MPS VII), or Sly syndrome, is a rare lysosomal storage disorder first described by Sly et al. in 1973 [4]. MPS VII occurs in less than 1 out of 250,000 births. It is an autosomal recessive disease caused by a deficiency of the enzyme β-glucuronidase, leading to a lysosomal accumulation of heparan, dermatan and chondroitin sulphate [5, 6]. The gene for β-glucuronidase is mapped to be at 7q 21.2-22.

According to the clinical symptoms, MPS can be divided into four phenotypes: MPS which predominantly affects the skeleton and soft tissues; MPS which only affects the skeleton and soft tissues; MPS which affects the skeleton; MPS which predominantly affects the central nervous system [8]. The diagnosis of lysosomal storage diseases and, in particular, of MPS VII is based on the histopathologic discovery of an accumulation of metabolites and a confirmation of an enzyme deficiency by electrophoresis.

The clinical diagnosis is always difficult due to the polymorphism of clinical symp-
The karyotypes of these three fetuses were normal. A fetal examination was performed in all three cases. The three fetuses all had facial dismorphism – pericephalical edema in the first two fetuses and a thickened nuchal fold in the third fetus, hypertelorism and prominent infra-orbital folds, long philtrum, low-set and malformed ears (Figure 1A). All three fetuses had very short necks (Figure 1A).

In the three fetuses there were symptoms of multiple dysostosis, which in the first two fetuses was represented by a rhizomelic dwarfism (Figure 1A). The radiography of the third fetus shows multiple symptoms of dysostosis – shortened and thick proximal and distal ends of long bones, pes equinovarus and abnormalities of the vertebral bodies and arches. The epiphyses had a rugged contour (Figure 1D).

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The three fetuses had hydrops, hepatosplenomegaly and bilateral pulmonary hypoplasia (Figure 1B). The brain examination found no neuropathological signs. The histological examination showed no abnormalities of the visceral organs in all autopsies. The macroscopic study found an edema of the placenta (Figure 1C). The microscopic

toms [7]. The genetic heterogeneity of lysosomal storage diseases limits the diagnostic and prognostic capabilities of a genomic analysis. The first ultrasound symptoms are always anasarca and a thickened nuchal fold in the first trimester, progressive ascites in the second trimester, and a pericephalical edema or a generalized edema of the body, often accompanied by ventriculomegaly. Facial dismorphism with an indentation of the middle level of the face was observed. There were also multiple hypertrophic epiphysal disostoses, fetal immobilization, vacuolated lymphocytes and anemia or thrombocytopenia.

**Case presentation**

We report a recurrent case of Sly syndrome in a Tunisian family and the treatment of this condition.

A 32-year old woman, parity three, five gestations, 0+ blood group from a first-degree consanguineous union. Her first pregnancy ended in a miscarriage; the second pregnancy ended with the birth of a healthy child (now a 6-year old daughter). The other three pregnancies were interrupted through medical intervention due to hydrops fetalis. The karyotypes of these three fetuses were normal. A fetal examination was performed in all three cases.

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The three fetuses had hydrops, hepatosplenomegaly and bilateral pulmonary hypoplasia (Figure 1B). The brain examination found no neuropathological signs. The histological examination showed no abnormalities of the visceral organs in all autopsies. The macroscopic study found an edema of the placenta (Figure 1C). The microscopic
The prenatal diagnosis by amniocentesis has been done for the third pregnancy. It revealed a high level of glycosaminoglycans with a predominance of chondroitin sulfates during the electrophoresis, confirming the diagnosis of Sly syndrome.

**Conclusion**

The association of hydrops fetalis, hepatosplenomegaly and multiple dysostosis with consanguinity is suggestive of a metabolic disease. The histological examination of the placenta is essential to diagnose Sly syndrome. The biological and genetic examinations confirm the diagnosis and may be used as a basis for counseling.

**References**


The examination of the placenta of the fetuses found evidence of accumulation-vacuolization of the Hofbauer cells.

The placenta of the second fetus had reproduced the same lesions and the Hale coloration showed cytoplasmic vacuolization affecting the trophoblast and Hofbauer cells-suggesting Sly syndrome (Figure 2).