Atypical Course of Hereditary Spherocytic Anemia With Severely Elevated Liver Enzymes

Quality of life of children with hereditary spherocytosis depends on the frequency and severity of hemolytic crises, which impacts the long-term outcome [1]. Follow-up care of these children is aimed at prevention and timely diagnosis of potential complications, such as formation of bilirubin gallstones, cholecystitis, splenic vein thrombosis with subsequent gastrointestinal bleedings and signs of hypersplenism. Recent publications are focused mostly on timing and long-term outcomes of splenectomy in these patients [2,3]. We describe an 8-year-old child with hereditary spherocytosis, and an atypical course of hemolytic crises.

This diagnosis was established four years prior to presentation, and since then the boy experienced two crises at the ages of 7 and 8 years. The patient's father and elder brother were also affected with this disease. At presentation, the boy had complaints of jaundice, nausea, weakness and pain in the umbilical area. There was also a history of dark discoloration of urine. Physical examination was remarkable for a lemon-yellow tint of the skin, and mild hepatosplenomegaly.

Complete blood count showed a red blood cell count of 435×10^9/L with microspherocytosis and reticulocytosis (20.6%), and hemoglobin of 12.8 g/dL; leukocyte count and erythrocyte sedimentation rate were normal. Biochemistry revealed elevated transaminases (alanine aminotransferase (ALT), 678 U/L; aspartate aminotransferase (AST), 445 U/L), elevated total bilirubin level of 231.5 µmoL/L with direct bilirubin of 32.9 µmoL/L. Screening for hepatitis A, B, C and E viruses, and cytomegalovirus, Epstein-Barr virus and autoimmune hepatitis was negative. Patient's medical records revealed that the previous crisis (1 year and 10 months before) was also associated with severely elevated ALT level of 179.5 U/L (**Table I**), and testing for viral hepatitides at that time was also negative. Abdominal ultrasound confirmed the presence of hepatosplenomegaly with preserved parenchymal echogenicity.

The patient was treated with prednisone (30 mg intravenously), and supportive therapy for 5 days. Repeat blood chemistry a day later showed the ALT level of 443 U/L, and 6 days later, 86 U/L. The patient was discharged from the hospital.

Review of literature did not reveal a similar case of hereditary spherocytic anemia. In this disease, hemolytic crises are rare and usually associated with viral syndromes [3]. The presented case is characterized by hepatosplenomegaly with preserved echotexture and severely elevated liver transaminases, thus making the differential diagnosis with hepatitis challenging. The possibility exists that severely elevated liver transaminases may be one of the atypical manifestations of hemolytic crises, so that monitoring liver enzymes may have utility in this regard. It is also possible that such presentation might be associated with α-spectrin gene mutation (*SPTB*), which is identifiable by next-generation sequencing (NGS) [4]. *SPTB* mutations resulting in insufficient spectrin protein synthesis and affecting the integrity and stability of erythrocyte membranes have been linked not only to hereditary spherocytosis, but also to progressive liver failure in neonates [5], and liver dysfunction and cirrhosis in adults [6]. Since NGS is presently not available in our region, we plan to perform NGS in our patient (as per availability), for it may be helpful for assessment of potential genetic risks [6].

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Table I Serial Changes of Transaminases and Bilirubin Levels of the Patient

Indices/date	*Age 7 y; January, 2020*			*Age 8 y; Novemaber, 2021*		
	Day 1	*Day 4*	*Day 8*	*Day 1*	*Day 4*	*Day 8*
Alanine aminotransferase (U/L)	179.7	154.5	48.0	678.0	443	86
Aspartate aminotransferase (U/L)	102.9	106.0	29.1	445	125	30
Bilirubin, total (µmol/L)	196.4	96.9	111.8	231.5	112	72.6
Bilirubin, direct (µmol/L)	53.1	21.9	13.5	32.9	14	12.4

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