Case report

A case report of a homozygous form of Beta-thalassemia

Presentación de un caso de beta-talasemia homocigótica

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ABSTRACT

Introduction: Beta-thalassemia is a hereditary hemoglobinopathy, which is based on the suppression of beta chains of globin.

Objective: To report a severe case of Beta-thalassemia in a child whose both parents, as well as the eldest child in the family, have a heterozygous form of Beta-thalassemia without clinical manifestations is presented.

Case report: At the age of 1 year and 8 months, the patient was diagnosed: HbF – 94.98%, HbA -1.17%, the presence of IVS2-1 (G-A) replacement in a homozygous state. The molecular genetic studies of both parents and the eldest child in the family showed heterozygous form of Beta-thalassemia. The basis of thalassemia treatment is regular blood transfusions to maintain normal levels of haemoglobin, which this patient is receiving (haemoglobin levels from 67 to 90 grams per litre).

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Due to the high levels of serum iron (>30mcmol per litre) and ferritin (>1000 mcg per litre), chelation therapy was prescribed to prevent complications. At the age of 7, the girl underwent a Magnetic Resonance by Images of the abdominal organs, which revealed grade 3 iron overload of the liver, signs of hemosiderosis of the liver and bone marrow. Additional ursodeoxycholic acid therapy was prescribed.

Conclusions: Despite the necessary and regular treatment, as the patient grows older, the therapy did not prevent development of complications such as hemosiderosis of the liver, spleen, bone marrow, and the formation of bilirubin stones in the bile ducts.

Keywords: children; homozygous form of Beta-thalassemia; chelation therapy; haemotransfusion; hemosiderosis.

RESUMEN

Introducción: La beta-talasemia es una hemoglobinopatía hereditaria caracterizada por la supresión de las cadenas beta de la globina.

Objetivo: Se presenta un caso grave de beta-talasemia en un niño cuyos padres, así como el hijo mayor, presentan una forma heterocigótica de beta-talasemia sin manifestaciones clínicas.

Presentación del caso: A la edad de 1 año y 8 meses, se diagnosticó al paciente con los siguientes niveles de HbF: 94,98 %, HbA: 1,17 %, y la presencia de la sustitución IVS2-1 (G-A) en estado homocigótico. Los estudios de genética molecular de ambos padres y del hijo mayor de la familia confirmaron la presencia de beta-talasemia heterocigótica. El tratamiento de la talasemia se basa en transfusiones sanguíneas regulares para mantener niveles normales de hemoglobina, las que recibe este paciente (entre 67 y 90 gramos por litro). Debido a los altos niveles de hierro sérico (>30 mcmol/L) y ferritina (>1000 mcg/L), se prescribió terapia de quelación para prevenir complicaciones. A los 7 años, se le realizó una resonancia magnética de los órganos abdominales, que reveló una sobrecarga de hierro de grado 3 en el hígado y signos de hemosiderosis hepática y de la médula ósea. Se prescribió terapia adicional con ácido ursodesoxicólico.

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Conclusiones: A pesar del tratamiento necesario y regular, con el paso del tiempo, la terapia no impidió el desarrollo de complicaciones como hemosiderosis hepática, esplénica y de la médula ósea, ni la formación de cálculos de bilirrubina en los conductos biliares.

Palabras clave: niños; forma homocigótica de beta-talasemia; terapia de quelación; hemotransfusión; hemosiderosis.

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Introduction

The homozygous form of beta thalassemia is a hereditary haemolytic anemia caused by a violation of the synthesis of haemoglobin chains, in which partial deficiency of a certain chain or its complete absence is possible due to a predominance of another chain.[1,2]

This pathology can be seen equally often in both boys and girls, and within the last decade the spread across the world is around one in a hundred thousand people.[1,3].

Pathogenesis of Beta-thalassemia is linked with mutation in the beta-globin locus in the 11th pair of chromosomes, which disrupts the beta-globin chain's synthesis. Due to the lower production of beta-globin chain, non-damaged alpha chains start to collect in excess within erythropoiesis cells, which leads to the damage of the membrane and destruction of cells of erythroid series within bone marrow and red blood cells in peripheral blood. Haemolysis of red blood cells, in turn, leads to the hypoxia of organ systems and tissues, resulting in development of ineffective erythropoiesis.[1,4,5,6]

Destruction of erythrokaryocytes within bone marrow leads to increased absorption of iron, which, with time, leads to development of secondary hemochromatosis.[7]

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The following clinically significant variations of beta thalassemia: severe form of beta thalassemia (homozygous form, Cooley anemia), intermediate form of beta thalassemia, minor beta thalassemia (heterozygous form).[2]

The inheritance type of this disease is autosomal recessive. Inheritance of pathology from one (heterozygosity) or both (homozygosity), the type of a broken chain determines the severity of clinical manifestations.[1,2]

Long term haemolysis, frequent transfusion of red blood cells leads to development of secondary complications such as hemosiderosis liver, spleen, bone marrow and myocardium. Often times bilirubin stones start to form in the gall bladder.[2,7,8]

The foundation of the thalassemia treatment is regular blood transfusion therapy with intent to maintain haemoglobin levels.[1,9] To prevent or delay the development of complications from iron overload chelation therapy is conducted, which targets combining and removing excess iron from the system.[7] Such therapy is prescribed in case of serum ferritin indicator is above 1000 mkg per litre.[2,4,9]

A more radical method of treatment of thalassemia at the moment is a haematopoietic stem cells transplant from a relative or a suitable donor. However, due to the complexity of finding a suitable donor, as well as high risks of organ rejection, this isn't a primary method of treatment.[2,4]

The course of the disease is characterised with the development of a severe haemolytic anaemia, which becomes apparent by the age of 1 via hepatomegaly and splenomegaly, characterful bone modifications, especially with skull development, delays in physical development, yellowish and pale skin tones.[5,6]

Currently there are methods of genetic therapy that are being researched, including the collection of haematopoietic stem cells from patient's blood, their modifications and return into patient's system.[10]

The objective of this article was to report a severe case of Beta-thalassemia in a child whose both parents, as well as the eldest child in the family, have a heterozygous form of Beta-thalassemia without clinical manifestations is presented.

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Case presentation

A girl of 13 years old (nationality - Azerbaijani), from the second pregnancy carried through anaemia, second term birth, with weight at birth being 2700 grams, height - 48cm.

From the anamnesis it is known that she was breastfed up to 2 months of age, and at the age of 1.5yrs she moved from Azerbaijan to Russia.

During a routine outpatient examination at the age of 1.5 years the girl was diagnosed with anaemia, with haemoglobin levels registered at 80 grams per litre (N > 110 grams per litre), serum ferritin at 210 μmol/l (N under 140 μmol/l). Due to the findings of the examination, patient was directed to Ryazan's Scientific and Clinical Center for Hematology, Oncology and Immunology to confirm the diagnosis.

At the age of 2 years the girl's haemoglobin was analysed using electrophoresis. Quantitative determination of hemoglobin fractions from the child showed: HbF (fetal haemoglobin) -94.98%, HbA (adult haemoglobin) – 1.7%. Alongside that, a molecular genetic study of DNA samples of haemoglobin beta chains was performed via direct sequencing. The analysis of beta globin gene sequence HBB showed signs of replacement of IVS2-1 (G-A) in a homozygous state.

For the establishment of heredity of the disease the beta haemoglobin beta chain DNA was tested in both parents and the eldest child – all three have shown results of heterozygous form of the disease.

Considering family history, ethnicity of the child and the results of the tests the patient was diagnosed with homozygous form of beta thalassemia.

In April 2013 at the age of 3 the girl has suffered an acute respiratory viral infection, after which the paleness of skin, weakness and loss of appetite appeared. Haemoglobin levels were at 68 grams per litre, which lead to the girl being hospitalised at to the Department of Oncohematology of the State Budgetary

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Institution named after N.V. Dmitrieva in Ryazan with the diagnosis as homozygous beta thalassemia, hemolytic crisis.

Upon admission in somatic status the following were brought to attention: paleness of skin, sub icteric sclera, hepatorenal syndrome (liver +3 cm, spleen +3 cm from the edge of the costal arch along the midclavicular line). After observation the hbF levels were registered at 98%.

Due to a bad condition of the patient replacement therapy for erythrocyte suspension was prescribed for the first time. There were no post-transfusion reactions or complications detected. After this therapy the haemoglobin levels were at 132 grams per litre.

Following that the child was admitted to hospital monthly for the blood transfusion therapy due to haemolytic crisis (haemoglobin levels varied from 67 to 90 grams per litre)

Up until 5 years old the level of serum ferritin was up to 330 μmol/l (N under 140 μmol/l), and the level of serum iron has been within 19-26 μmol/l (N - 10-33 μmol/l). Since November 2015 the girl's serum iron level was > 30 μmol/l, and serum ferritin >1000 μg/l.

Considering the results of the testing, the severity and characteristics of the disease the patient has gone through chelation therapy with deferasirox (Exjade) orally at a dose of 250 mg per day, with the dose increasing to 375 mg per day at first, following the increase to 720 mg per day due to continuous high levels of serum iron.

According to the Magnetic Resonance by Images (MRI) and ultrasound of abdominal cavity at the age of 6 the following were detected: MRI signs of hemosiderosis of the liver (the average iron concentration in the liver parenchyma was 11.2 mg/g - iron overload of the 3rd degree) and bone marrow, cyst of the right lobe of the liver, hepatosplenomegaly; anechoic contents in the gallbladder; dense clots of bile were noted along the posterior wall.

Due to these updated findings an additional therapy with ursodeoxycholic acid (250 mg 2 times a day) was prescribed - for a long time.

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With a planned observation from October 2013 at the age of 13, the somatic status of the child shows light yellow tone of the skin, hepatosplenomegaly.

Currently the patient is receiving the following treatments: monthly replacement blood transfusions, chelation therapy (Deferasirox 720 mg - (23 mg/kg)), ursodeoxycholic acid - 1 capsule, 2 times a day.

Outside of haemolytic crisis the child is feeling acceptable, no complaints, however the sub icterus of the skin tissue remains (figure).

Figure - Subicterism of the skin tissue.

Discussion

Most patients suffering from thalassemia live in the southern countries: Mediterranean, Central and South Asia. That is how the disease got its name, thalassemia, translated from Greek meaning “sea anaemia”. In Azerbaijan, thalassemia is the most common hereditary disease (up to 7-10 % of the population), with more than 1 million carrying the pathological gene. Within Russian Federation the patients suffering from Beta-thalassemia have roots from Caucasus region, Volga region and Central Asia.[3,4,10]

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Without proper treatment the prognosis for the homozygous form of beta thalassemia is unfavourable: patients die in infancy due to severe complications, with irreversible damage to organs and tissue.[9] In particular, the overload of myocardial iron leads to the development of heart failure, which is the main reason for deaths from this illness.[1,5,8]

Currently the main and most effective treatment from homozygous form of beta thalassemia is chelation therapy. The treatment that has been prescribed in due course allows levelling out clinical symptoms and sufficiently improving quality and duration of life of the patients.[2,7] However, despite the treatment, such therapy does not prevent from development of complications, such as hemosiderosis of the liver, spleen, bone marrow, formation of bilirubin stones in the bile ducts.[1,9]

Conclusions

This case demonstrates the development of severe case of Beta-thalassemia, despite adequate chelation therapy, against the background of prolonged hemolysis and frequent red blood cell transfusions, the girl had severe complications such as iron overload in the body, the development of hemosiderosis of the liver and spleen, and the formation of bilirubin suspension in the bile ducts.

In this regard, this clinical observation demonstrates the effectiveness of chelation therapy in maintaining the patient's quality of life. However, as the patient gets older, this therapy is not always able to prevent serious complications.

References bibliography

1. Alieva KA, Guseinova NT, Mamedova RF. Current state of prevention and treatment of thalassemia in Azerbaijan. Academy. 2022 [acceded 07/11/2023];1(72):6-9. Available at: https://cyberleninka.ru/article/n/profilaktika-

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posttransfuzionnyh-oslozhneniy-obuslovlennyh-antigenami-eritrotsitov-i-virusnymi-infektsiyami/viewer

2. Smetanina N.S. All-Russian Society of Orphan Diseases, "Thalassemia"; 2021 [accessed 07/11/2023]. Available at: http://talas.rare-diseases.ru/

3. Yusifova AA, Alekberova SA, Asadova BG. Statistical Indicators of Patients With Large and Intermittent Beta-thalassemia in Different Regions of Azerbaijan. Bulletin of Science and Practice. 2020;6(11):242-7. DOI: https://doi.org/10.33619/2414-2948/60/29

4. Botalova IV, Nikonova OE, Ryskal' OV. Development of acute leukemia in a child with thalassemia (clinical case). Pediatric Bulletin of the Southern Urals. 2020;(2):82-6. DOI: https://doi.org/10.34710/Chel.2020.38.92.011

5. Budnevsky AV, Simion AYu, Shapovalova MM. Pathophysiology of anaemic syndrome in cardiovascular diseases. Science of the young (Eruditio Juvenium). 2021;9(2):301-12. DOI: https://doi.org/10.23888/HMJ202192301-312

6. Eremina YO, Magalhães C. Reticulocyte haemoglobin content: 2020 update. I.P. Pavlov Russian Medical Biological Herald. 2020;28(4):605-12. DOI: https://doi.org/10.23888/PAVLOVJ2020284605-612

7. Forni GL, Kattamis A, Kuo KHM, Maggio A, Sheth S, Taher AT, *et al*. Iron chelation therapy for children with transfusion-dependent β-thalassemia: How young is too young? Pediatric blood & cancer. 2024; 71(8):e31035. DOI: https://doi.org/10.1002/pbc.31035

8. Vlachaki E, Venou TM. Iron overload: The achilles heel of β-thalassemia. Transfusion clinique et biologique: journal de la Societe francaise de transfusion sanguine. 2024;1(3):167-73. DOI: https://doi.org/10.1016/j.tracli.2024.06.001

9. Motta I, Bou-Fakhredin R, Taher AT, Cappellini MD. Beta Thalassemia: New Therapeutic Options Beyond Transfusion and Iron Chelation. Drugs. 2020;80(11):1053-63. DOI: https://doi.org/10.1007/s40265-020-01341-9

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10. Hamed EM, Meabed MH, Aly UF, Hussein RRS. Recent Progress in Gene Therapy and Other Targeted Therapeutic Approaches for Beta Thalassemia. Current drug targets. 2019;20(16):1603-23. DOI: https://doi.org/10.2174/1389450120666190726155733

Informative agreement

The authors declare that the patient gave informed consent for publishing this clinical observation.

Conflict of interest

Authors declare the absence of obvious and potential conflicts of interest related to the publication of this article.

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