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Review Article

Genetically Confirmed Hereditary Spherocytosis About 3 Cases

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Abstract

Hereditary spherocytosis, also known as Minkowski chauffard disease, is a constitutional red blood cell disease most common in North Africa with a prevalence of 1/2000. Autosomal dominant transmission. The disease is revealed by a chronic hemolysis chart made of a pallor, an icterus and a huge splenomegaly. The diagnosis is usually confirmed by a globular resistance test or better flow cytometry. It is easier when there is a family history associated with regenerative hemolytic anemia with the presence of spherocytosis. This assessment must be made before any transfusion of globular pellet. The red blood cell has a capacity of deformation and elasticity that ensures its permanence in the blood circulation, red blood cells are limited in their physical performance by genetic irregularities affecting different proteins of the membrane skeleton usually the anykrine, band 3, protein 4, 2 as well as the alpha or beta chains of the spectrin This assessment must be done before any transfusion of globular pellet. If necessary, a genetic study may be proposed to confirm the diagnosis. In this work we report 3 observations of genetically confirmed hereditary spherocytosis in children. The objective of our work is to raise the diagnostic difficulties of hereditary spherocytosis in patients who receive an emergency transfusion before the diagnosis confirmation and who have significant transfusion needs.

Keywords

Hereditary Spherocytosis, Genetic Testing, Child

1. Introduction

Hereditary spherocytosis (HS), formerly known as Minkowski disease, is a constitutional red blood cell disease. It is a morphological disorder of erythrocytes whose shape is more rigid and spherical. Due to morphological change, they are most often sequestered and destroyed in the spleen, which leads to chronic hemolytic anemia. Some forms are severe and require significant transfusion needs [1].

Its transmission is usually autosomal dominant in 75% of cases. While 25% of cases may be autosomal recessive, this explains the sporadic cases of this disease [2]. Hereditary spherocytosis can be diagnosed at an early age. Symptoms can be expressed from birth to the fourth decade of life. Her patients may be asymptomatic in some cases and severe in others with symptoms requiring frequent transfusions [3].

Diagnostic confirmatory tests have improved significantly in terms of specificity and sensitivity, allowing for accurate diagnosis of hereditary spherocytosis. The diagnosis of hereditary spherocytosis is based on clinical, family history,

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presence of spherocytes on blood smear, the globule resistance test or better the screening test for hereditary spherocytosis by flow cytometry or the eosin 5'maleimide (EMA) test. Its treatment is based on blood transfusions in cases of severe anemia, an iron chelator and a possible splene.

2. Materials and Methods

We report three observations of patients with genetically confirmed hereditary spherocytosis and followed up in the pediatric department.

3. Results

Observation 1

A 6-year-old girl, followed since the age of 3 for chronic hemolytic anemia. She is from a non-consanguineous marriage and has no similar family history. Clinical examination shows normal facies, paleness with generalized mucosal-cutaneous jaundice and 5 cm splenomegaly without hepatomegaly. The blood count shows a severe regenerative normochromic normocyte anemia at 4 g/dl, ferritinemia is elevated to 217 ng/l, Coombs test is negative, globule resistance test is normal, G6PD dosage is normal, The electrophoresis of hemoglobin is normal and blood smear indicates anisopoïkylocytosis. Abdominal ultrasound confirmed isolated homogeneous splenomegaly. Therapeutically, the patient initially received an emergency globular cell transfusion. The evolution is marked by monthly transfusion needs and the appearance of signs of hypersplenism. Due to diagnostic difficulties, a complete exome sequencing was performed after 3 years of evolution. It revealed a mutation of the SPTB gene NM_001024858 (SPTB) in the heterozygous state at exon 25, confirming the genetic diagnosis of hereditary spherocytosis. After this confirmation, the patient was treated with a splenectomy and the outcome was favorable with a disappearance of transfusion needs.

Observation 2

A 10-year-old woman from a non-consanguineous marriage, followed since the age of 1 for chronic hemolytic anemia. Clinical examination revealed mucosal skin pallor with jaundice and 7 cm splenomegaly. The hemogram showed normochromic anemia at 5 g/dl and a ferritinemia at 867 ng/l. The globule resistance test is normal, the Coombs test is negative, the hemoglobin electrophoresis is without abnormality and the blood smear reveals a poïkilocytosis. Abdominal ultrasound shows homogeneous splenomegaly with hepatomegaly and multiplexicular lithiasic gallbladder. Due to diagnostic difficulties and important transfusion needs, a complete exome sequencing was requested. This test, performed after 9 years of evolution due to lack of family resources, confirmed the diagnosis of hereditary spherocytosis, revealing a mutation of the SPTB gene NM_001024858.3 (SPTB): c.5266C>T p. (Arg1756*) in the heterozygote state at the level of the exon 25 of the SPTB gene.

Therapeutically, the patient initially received transfusions of phenotyped and filtered globular cells every 3 weeks. After the diagnostic confirmation, she underwent splenectomy and cholecystectomy with a good clinical outcome and no need for transfusion.

Observation 3

A 16-year-old teenager, followed since the age of 9 months for chronic hemolytic anemia, born from a non-consanguineous marriage with no similar family history. The clinical examination does not reveal facial dysmorphia, but shows a skin-mucous paleness, an icterus and a huge splenomegaly exceeding the umbilicus, associated with a staturo-weight delay of -3 standard deviations. The CBC shows a severe 3 g/dl regenerative normochromic anemia, negative Coombs test, no abnormal globule resistance test and blood smear showing poïkilocytosis. The G6PD is normal. Abdominal ultrasound shows a large homogeneous splenomegaly and lithiasis gallbladder. Therapeutically, the patient received transfusions of phenotyped and filtered globular cells with an iron chelator. The evolution is marked by significant twice-monthly transfusion needs and the appearance of signs of hypersplenism. To confirm the diagnosis of hereditary spherocytosis, a complete exome sequencing was performed after 14 years of evolution, revealing a mutation in the SPTB gene NM_001024858.3 (SPTB): c.2083C>T p. (Arg695*) at the heterocygote state at the exon 13 of the SPTB gene. After confirmation of the diagnosis, she underwent splenectomy and cholecystectomy with disappearance of transfusion needs.

4. Discussion

Hereditary spherocytosis is one of the hereditary causes of hemolytic anaemia in children. Easy to diagnose in the presence of a family history and obvious clinical signs including paleness, jaundice, splenomegaly and biological tests showing regenerative anemia with signs of hemolysis and decreased globule osmotic resistance. It becomes difficult in case of an emergency transfusion made before the diagnosis and important transfusion needs [6, 8, 10, 12, 14]. In this case, genetic diagnosis will be used. The most frequent genetic mutations are SPTA1, SPTB, ANK1, EPB42 or SLC4A1 genes causing a membrane skeleton of red blood cells deficient in alpha or beta spectrin anykrine, protein 4-2 at band 3 respectively. These proteins build the scaffold and vertical connections of the red blood cell membrane skeleton with the lipid membrane. Their deficiency allows the loss of membrane, hence the formation of spherocytes [4, 5, 7, 13, 15]. Bogus lawska et al reported cases with significant transfusion needs diagnosed late as hereditary spherocytosis by a genetic study and carrying heterozygous mutation in the SPTB exon 11 [11]. Similarly, our patients had significant transfusion needs and were diagnosed late by a genetic study objectifying SPTB gene mutations. In order to establish good therapeutic management in patients with significant transfusion needs, it

is desirable to carry out the rather a genetic test that is currently the most reliable.

In terms of treatment, splenectomy is the treatment of choice; [9]. it improves quality of life by eliminating transfusion needs. We found that our patients benefited from this treatment and all of them evolved positively.

5. Conclusions

Hereditary spherocytosis have significant needs for transfusion. In order to establish an early diagnosis of hereditary spherocytosis, genetic tests such as the search for a mutation of the SPTB gene may be used; this will help improve the quality of life of his children. may pose a diagnostic problem in patients who have been given emergency transfusions and who still.

Abbreviations

HS Hereditary Spherocytosis

Author Contributions

Angela Kibangou: Funding acquisition, Methodology, Project administration, Resources, Validation, Writing – original draft, Writing – review & editing

Mounia El Alaoui Hanafi: Investigation, Methodology, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

Salima Hajjaji: Methodology, Supervision, Validation

Noufissa Benajiba: Methodology, Supervision, Validation

Khadija Maani: Methodology, Supervision, Validation

Abdelhak Abkari: Methodology, Supervision, Validation

Conflicts of Interest

The authors declare no conflicts of interest

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