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Hereditary Spherocytosis Across Four Generations of the Single Family

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Abstract

Hereditary spherocytosis (HS) is an important cause of inherited nonimmune hemolytic anemia in which defects of protein producing the biconcave shape of red cells result spleen trap the spherocytic cells and shorten the red cell life span. HS is usually transmitted as an autosomal dominant inheritance form and less commonly as nondominant inheritance form. Some patients without family history have de novo mutations. There are no actual estimates of the prevalence in general populations. And the more, as the family size are getting smaller with few relatives and cultural pressure against genetic disease is persisting, it is difficult to know family inheritance pattern and genetic mutations. We report an informative family with their pedigree in which the HS occurred in four generation with literature reviewing.

Key Words : Genetic counseling, Hereditary, Pedigree, Spherocytosis

Introduction

Hereditary spherocytosis (HS) is an important cause of inherited nonimmune hemolytic anemia in which defects of protein producing the biconcave shape of red cells result spleen trap the spherocytic cells and shorten the red cell life span. HS is usually transmitted as an autosomal dominant inheritance form and less commonly as nondominant inheritance form [1,2]. As many as 25% of patients without family history is due to a de novo mutation, which tends to occur at CpG, and is associated with small insertions or deletions [2]. For these patients it is possible to have an autosomal recessive

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form of the disease, although it cannot exclude the dominant form of HS with reduced penetrance or new mutation [1].

As surveys of some diagnostic test about osmotic fragility test suggest that mild forms of the disease may be more common than believed, the prevalence and genetics is probably underestimated [1]. There are no actual estimates of the prevalence in general populations. And the more, as the family size are getting smaller with few relatives and cultural pressure against genetic disease is persisting, it is difficult to know family inheritance pattern and genetic mutations [3]. There are few reports about family study of hereditary spherocytosis and one study showed just three generation in a family [4]. Here we describe an informative family in which the HS occurred across four generations with literature reviewing.

Case Report

Two siblings, males aged four years and one year, were brought to our hospital for the complaints of neonatal jaundice within their first week after birth. From family history, several members of their family had done splenectomy. They are maternal great-grand-father, two grand-father, and mother. The family tree is shown in the (Fig. 1). The diagnosis of hereditary spherocytosis was made of the history and clinical findings.

The older brother's laboratory findings at diagnosis revealed hemoglobin 13.8 g/dL, reticulocyte 11%, total indirect bilirubin 22 mg/dL, direct bilirubin 0.9 mg/dL. Direct and indirect coombs test ware negative. His peripheral blood smear showed many spherocytic red cells. Phototherapy and exchange transfusion was done for him. When

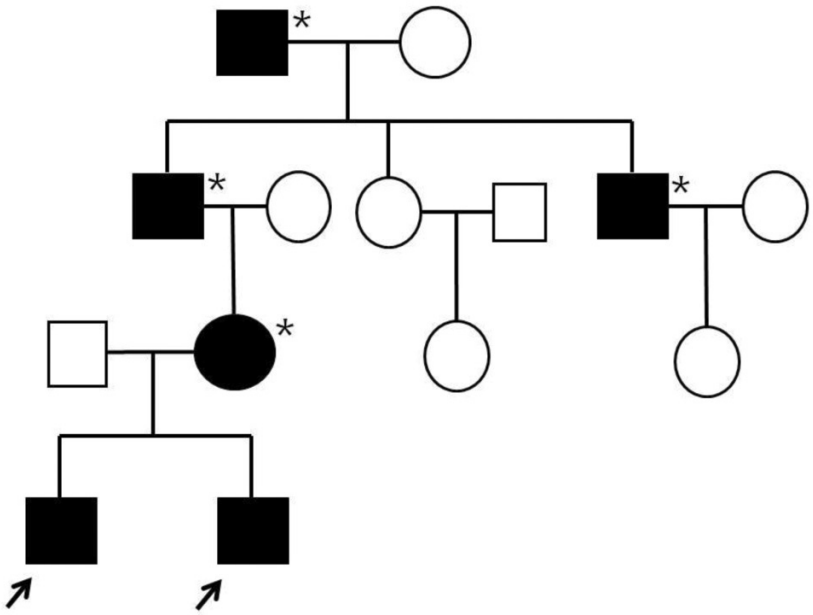

Fig. 1. Family pedigree. The sibling patients are indicated by arrows. (□ ○ : Normal phenotype, ■ ● : Affected, * : Splenectomy).

he was 3 years old, he suffered severe anemia of aplastic crisis and admitted for treatment and transfusion.

The younger brother's laboratory findings at diagnosis showed hemoglobin 9.3 g/dL, reticulocyte 11%, total indirect bilirubin 12.8 mg/dL, direct bilirubin 0.3 mg/dL, and indirect coombs test ware negative. His peripheral blood smear showed many spherocytic red cells and polychromasia (Fig. 2). Phototherapy was done for him and packed red blood cell was transfused for several times for aplastic crises. Two siblings have been followed up regularly with folate medication until now.

Discussion

The severity of hereditary spherocytosis is variable from asymptomatic to very severe form. The diagnosis can be established clinically from the blood smear showing many spherocytes and reticulocytes with or without a family history. The osmotic fragility test can help confirming the HS but it is not specific test. The specific protein abnormality can be established in some patients just as research tool using gel electrophoresis or densitometric quantitation and molecular diagnosis also is also possible [3,5].

The most common molecular abnormalities are defects of spectrin or ankyrin, which are major components of the cytoskeleton preserving the red cell shape. The defect of alpha-spectrin shows a recessive pattern and severe disease severity. The dominant patterns have been showed in cases with the defects of beta-spectrin and protein 3, having mild to moderate disease severity. The defect of ankyrin can have both dominant and

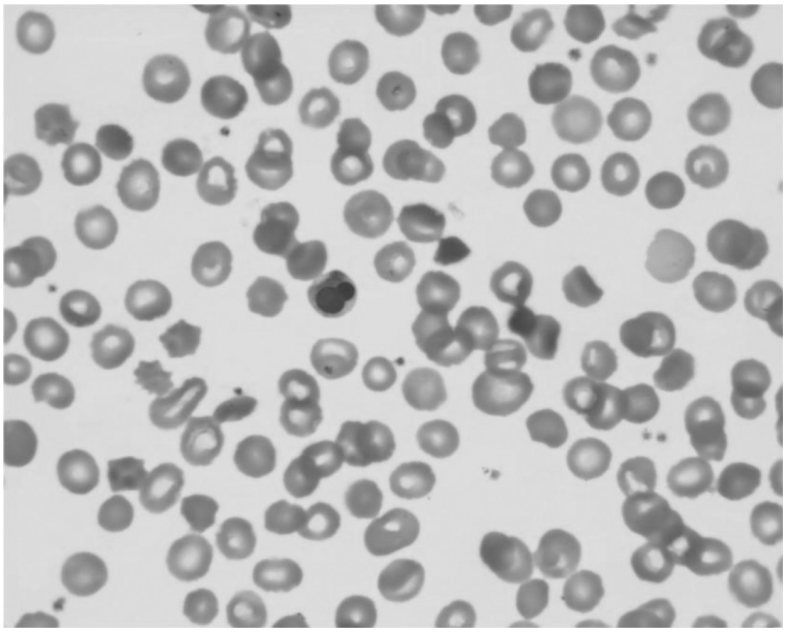

Fig. 2. The peripheral blood smear shows normochromic erythrocytes with many spherocytes and polychromasia (×1000).

recessive pattern [5]. By these molecular defects, the spherocytic red cells are trapped and destroyed prematurely in the spleen. The mild to moderate nature of the disease in this case report could be because of the dominant pattern of inheritance in them even though we could not perform the molecular analysis.

As a treatment, splenectomy eliminates most of the hemolysis that results in significant improvement in the clinical manifestations and prevents complications such as cholelithiasis. Recently, whether all patients with hereditary spherocytosis should perform splenectomy is controversial. Splenectomy is not recommended for the patients whose hemoglobin values exceed 10 g/dL and reticulocyte percentage is under 10% [5]. However for patients with more severe anemia and reticulocytosis or those with frequent or severe hypoplastic or aplastic crises, poor growth, or cardiomegaly, splenectomy is recommended after age of 5-6 year to avoid the possibility of postsplenectomy sepsis [3]. Three members of this family except two children patients did splenectomy.

Genetic testing involves analyzing genetic material to obtain information related to a person's health status using chromosomal analysis or DNA-based testing. One of the important purpose of genetic test and genetic counseling is to give the family information about risk of disease or carrier, natural history of the condition, how to manage the disease and follow-up, and to provide new information as it becomes available [5,6]. Under social pressure and ignorance against genetic disease, genetic counseling is very difficult. But it is very important part of the overall scheme of disease care as a communication process in which the genetic contribution to health is explained through risks of transmission of a trait and options to manage the condition and its inheritance.

We have observed a single family with hereditary spherocytosis across four generations. We report this family of our index case with this in mind and their family members now know the findings and their meaning.

Summary

As an important cause of inherited nonimmune hemolytic exhibiting both dominant and nondominant inheritance pattern, the single family with hereditary spherocytosis across four generations has been observed with literature reviewing. This is an informative family pedigree because nowadays it is difficult to know family inheritance pattern as the family size are getting smaller with few relatives and cultural pressure against genetic disease is persisting. With this genetic counseling is very important part of the overall scheme of disease care.

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