Forum Tunisien de Biologie Médicale
37èmes Journées Nationales de Biologie Clinique
2èmes Journées du Syndicat Tunisien des Biologistes Privés
N°201
STBC
FIFBCML
Hôtel Laico Tunis
3, 4 & 5 OCTOBRE 2024

Compound Heterozygous Sickle and alpha Thalassemia : A Case Report

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INTRODUCTION

Compound sickle cell syndrome with alpha thalassemia is a rare clinical entity, resulting from the coexistence of two distinct genetic abnormalities, sickle cell disease (SCD) and alpha (α) thalassemia. This unusual association gives rise to complex phenotypic variability depending on the type of α thalassemia (α-/α- or αα/α-), sometimes defying the conventional clinical patterns seen in each disease separately.

We would like to report a case which was diagnosed as sickle cell anemia; however, the case turned out to be compound heterozygous sickle cell and alpha thalassemia subsequently, highlighting the clinical manifestations and diagnostic challenges associated with this rare condition.

Case

A 6-year-old Tunisian girl, from the north-west, first product of non-consanguineous marriage, born at term with no significant perinatal history, presents with chronic anemia, fatigue and recurrent bone pain. Past medical history and family history was negative. Physical examination was normal with no splenomegaly. Initial laboratory workup showed: Hemoglobin (Hb) of 12.3 g/dl, Mean Corpuscular Volume (MCV) 67fL, Mean Cell Hemoglobin Concentration (MCHC) 32.8 g/dL, reticulocyte count of 36000/mm^3. Additional analysis showed no hemolysis. Hemoglobin electrophoresis showed low HbA value at 63.2%, HbA2 value at 3.4% and HbS value at 33.4%.

The family members: father,40 years old, mother, 33 years old and a 3 years old brother, with no pertinent past medical history, were tested. As for the father, the complete blood count (CBC) test showed Hb of 15.5g/dL, MCV 79fL, and the hemoglobin electrophoresis found a heterozygous SCD with 38.8% of HbS, 57.9% of HbA and 3.3% of HbA2.

The mother's CBC showed an Hb of 11.7g/dl, MCV 74fL, MCHC 22.7 and reticulocytes count of 73,000. Hemoglobin electrophoresis showed HbA at 97.6% and HbA2 at 2.4%, an electrophoretic profile that appeared to be normal. The brother had an Hb of 12g/dl, MCV 67.8fL and reticulocytes count of 39,000. Hemoglobin electrophoresis also appeared normal for the age, with HbA at 96.8%, HbA2 at 2.9% and HbF at 0.3%.

Considering the complete family picture and the strong suspicion of an association of heterozygous SCD and alpha thalassemia since the patient's HbS level is below 35% and the fact that heterozygous SCD alone does not explain our patient's symptomatology, the alpha gene was investigated by molecular biology in our patient and her family members.

Molecular testing using the Gap-PCR method revealed an alpha gene anomaly in our patient, her mother and her brother, and no alpha gene anomaly in the father. (1)

The 6-year-old Tunisian girl with chronic anemia and fatigue which is consistent with the literature (2), recurrent bone pain and atypical laboratory results was diagnosed with compound SCD alpha thalassemia. Peripheral blood smear revealed the presence of sickle cells. However, Hb electrophoresis showed an unusual electrophoretic profile, with a significant decrease in HbA at 63.2% and HbS at 33.4%, an increased value but still lower than 35%, thus suggesting a possible coexistent alpha thalassemia as described in the literature. (3,4)

In contrast to our study, in which the patient presented clinical manifestations such as bone pain, the majority of studies carried out showed a better clinical picture for patients with compound SCD alpha thalassemia, with mild, attenuated symptoms and even asymptomatic ones. This is thought to be the result of reduced intra-erythrocyte concentration of HbS, resulting in reduced density and polymerization, thus leading to improved tissue oxygenation. (5)

As for our patient's family, the father was identified as a heterozygous sickle cell carrier, with compatible laboratory results (6). However, the mother presented with microcytic hypochromic anemia, and Hb electrophoresis showed no clear evidence of alpha thalassemia (7). This atypical presentation suggests the possibility of masked alpha thalassemia. The patient's brother, although currently asymptomatic, presents a microcytosis.

The diagnostic findings in this family highlight the complexity of the situation, with a rare genetic association and potentially masked alpha thalassemia. The further molecular analysis to assess specific genetic variations revealed a homozygous alpha gene anomaly in the mother, clinically asymptomatic, and a heterozygous alpha gene anomaly in our patient and her brother, and no alpha gene anomaly in the father. (1)

CONCLUSION

The presented case of compound sickle cell disease alpha thalassemia illustrates the complexity and diversity of clinical presentations that can result from the coexistence of two inherited hemoglobin disordres. Moreover, early recognition of this rare entity is crucial for effective management, prevention of serious complications and improvement of patients' quality of life.

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