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Congenital hypothyroidism in a child with Sickle cell anemia (a case report)

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A B S T R A C T

Sickle cell disease (SCD) is an autosomal recessive disease common in negros and Arab.1 The main pathological cause is the substitution of valine with glutamic acid in the β-chain of hemoglobin producing abnormal hemoglobin called hemoglobin S.1,2,3 The production of this abnormal hemoglobin is responsible for the sickling of red blood cells in deoxygenated conditions. The symptoms include chronic intravascular hemolysis, vaso-occlusion and painful crisis.1,3 Over time, multiple organ damage can develop.1,3,4 Patients with SCD display a defective activation of the alternate complement pathway, the combination of SCD and Autoimmune disease (AID) is rare, potentially underdiagnosed, and its prevalence is unknown.4However, the frequency of coexisting SCD and AID has not been evaluated and the data mainly demonstrated from case reports. Case presentation In this case we report a rare combination of Sickle cell anemia and congenital hypothyroidism in a 4 years old Libyan boy. This patient referred to our Hematology department due to severe anemia, the patient diagnosed as Sickle cell anemia and congenital Hypothyroidismwhen he was 32 days old. Genetic counseling for the family showed sickle cell anemia, congenital hypothyroidism and celiac disease in the other familymembers. However, the association of SCD and congenital hypothyroidism were not reported before, this combination could be due to new gene mutation since the high consanguinity and multiple affection in siblings with SCD, Celiac disease and Hypothyroidism separately or combined. Conclusion SCD, congenital hypothyroidism in toddler are newly reported in this study. The combination of AID and SCD detected in many members of this family. Genetic counseling and testing are important in developing countries to educate individuals on SCD and also offer those at risk. Further studies are needed to determine the frequency of congenital hypothyroidism in patients with SCD to look for a new cause of combination.

1.0 Inroduction

Breast Sickle cell disease (SCD) is a common inherited condition in African, Caribbean, and Mediterranean countries.1,3,6 SCD is one of big health problems in developing countries because of high consanguinity rateand large families.6 Pathogenesis of SCD include a point mutation in the gene responsible for production of hemoglobin, this mutation leads to production of abnormal hemoglobin S.2,3 Abnormal heamoglobin S forming sickle-shaped erythrocytes, which disrupt blood flow in

capillaries, and causing occlusion of small blood vessels leading to distal tissue ischemia and inflammation, with symptoms defining the acute painful sickle-cell crisis.1,5,6 The morbidity and mortality is quite high in those cases due to repeated blood transfusion and hemolysis leading to parenchymal injury and chronic organ.1,4,7 It was suggested that complement abnormalities could predispose to autoimmune disease (AID). 2,3 However, the frequency of coexisting SCD and AID has not been evaluated, and most data come from case reports.1 The combination of SCD and congenital hypothyroidism is newly reported and discourage the role of functional A-splenia in causing AID in such patients. This case also covers the strategies governing newborn screening for hemoglobinopathies. However, the coexistence of Congenital hypothyroidism and SCD seems to be rare, potentially underdiagnosed, and its prevalence is unknown

Case presentation

A 4 years-old Libyan boy referred to hematological department in Central Sirte Polyclinic due to severe Anemia. The patient is a known case of SCD, Congenital Hypothyroidism. General examination of the patient showed hyperactivity and no response to the orders, By abdominal examination he has splenomegaly,laboratory investigation: Hb: 6.2 gm/dL, white cell count of 9,300/mm (39% neutrophils, 52% lymphocyte), platelet count of 343,000/m, Ferritin: 287.4 ng/ml, Iron: 178ug/dl, TSH:11.8Uiu/ml, 25- OH Vitamin D: 28.27 ng/mL. This patient diagnosed in earlier age afterdiagnosis of the other sisters with SCD. The child investigation when he was 32 days old revealed the following results: Hemoglobin electrophoresis Hb F: 39.9% Hb S:58.2% Hb A2: 1.9% , T4: 25.9 mmol/ml, the patient running on Levothyroxin tab 25mg. Blood film showed picture of sickle cell disease. Figure 1 show blood film result.

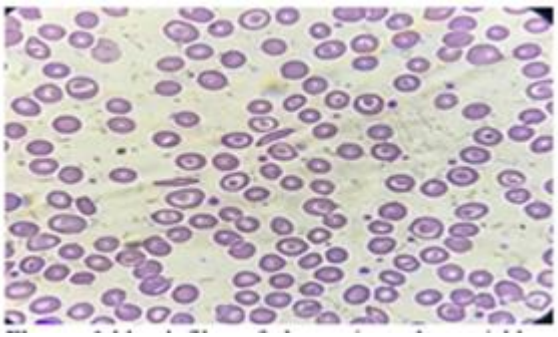

Figure 1 Blood film of the patient show sickle cells hemoglobin c and some target cells

Genetic counseling The patient refereed with his family to genetic counseling clinic, after taking the family pedgree we demonstrated that this child is the number 8 in his family and the earlier diagnosis established due to the affected older siblings with both SCD and congenital hypothyroidism, there are 2 girls diagnosed as SCD, one boy is carrier HbSs, one girl with congenital hypothyroidism and ASD. There is a consanguinity and the parents are carrier. However, the mother is known case of hypothyroidism, from the pedigree we noticed that mother family is very big and there are 2 affected males with SCD and 3 passed away males in her family while there are 4 unaffected males and 1 health female. The father family is small, has 1 healthy brother and 1 health sister, and another 2 brothers from his mother side, one is healthy and one is passed away with unknown cause. Moreover, the family has a causes of death which is unknown and there was many misunderstand and preservation from the family about some information.Figure 2 show the family pedigree of the patient.

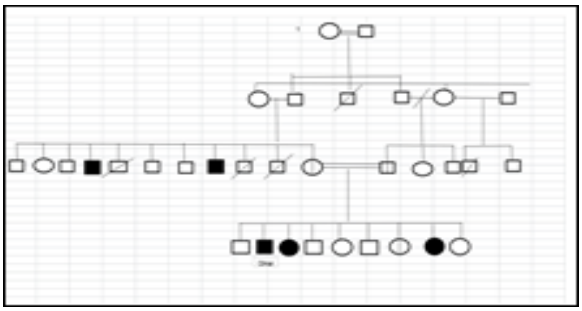

Figure 2: Family pedigree of the patient

Discussion

In this case report we demonstrated a rare combination of SCD and congenital hypothyroidism in toddler. We do not found a literature for those combination before. However, Coexisting of Hypothyroidism and SCD reported in adults which demonstrated to be due to the complications of blood transfusion.1,3,6 Iron overload has been associated with multiple endocrine abnormalities.6The high Autoimmune antibody in serum of SCD patients is the cause of combined sickle cell disease and SLE, Juvenile rheumatoid arthritis which were reported before.8,9 This patient diagnosed in an earlier age due to the previous affected siblings, came from a large family with a different range of Autoimmune diseases and SCD. Even though the above generation cannot be determined to have a SCD because no previous diagnosis. However, we considered two cases who died from jaundice at younger age as SCD. The 2nd generation of the family pedigree revealed two cases with Lymphoma. The combined different autoimmune disorders and SCD in this family need a more close study to determine the main cause of this combination. This can be done through whole exome sequencing of the patient and his family. However, this can be a challenge in Libya, because of the limited

facilities, but it can be done through collaboration studies. In Libya genetic counseling for inherited disorders is not well known. Although, the high consanguinity rate and the burden of inherited diseases is more due to large families, which increase the number of affected people. Premarital counseling and testing can indeed reduce the prevalence of inherited disorders of Hb, principally by identifying and offering counseling to intending couples of high-risk marriages.10 In countries with universal genetic counseling and screening for endemic-inherited disorders, information gathered from such exercise not only gives insight into the epidemiology of these disorders but also could most importantly be a useful resource for health planning in such countries.9,10,11 A number of the Mediterranean and the Middle Eastern countries like: Saudi Arabia, Emirates and Bahrain have a successful experience in genetic counseling and prenatal screening for inherited heamoglobinopathies.11,12 That programs have diminished the number of that disorders significantly. There were another success story of premarital genetic testing in Greece, Cyprus, and Italy.11,1,14 In Cyprus in particular, the religious bodies play very significant roles in enforcing mandatory premarital testing and give appropriate counseling to at-risk individuals with very remarkable results.14

Conclusion

Sickle cell disease combined with congenital hypothyroidism in toddlers is newly reported in this study. Coexisting AID and SCD detected in many members of the family. Further studies are needed to determine the prevalence of AID in patients with SCD to look for a new cause of combination. Genetic counseling and testing are important in developing countries to educate individuals on SCD and also offer those at risk. Whole-exome sequencing is needed to detect whither there is a novel gene mutation in this family.

Conflicts of interest The authors declares there are no conflicts of interest

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