

Sickle cell disease in Oman and HbS Oman: a brief review

Keywords: chronic anaemia, haemoglobinopathy, acute ischaemic, haemolytic, splenomegaly, heterozygosity, heterozygous

Abbreviations: SCD, sickle cell disease; HU, hydroxyurea; FDA, food and drug administration; G6PD, glucose-6-phosphate dehydrogenase; BMT, bone marrow transplantation

Introduction

The first medical case of SCD was described by James Herrick in 1910. It is one of the most common hereditary haemoglobinopathies with most cases from African and or Arab-Indian origin. SCD complications can be divided into two major groups, chronic anaemia and acute ischaemic incidents.¹ Chronic hemolytic anemia of varying severity is a day-to-day struggle. Additionally, patients suffer from sporadic pain-crisis incidents arising from thrombus formation in the vascular system. The most life threatening of these is acute chest syndrome,² cerebral vasculopathy³ and renal failure.⁴ These and other complications contribute to a high mortality of SCD patients, especially before seven years of age in areas with poor healthcare. SCD is also associated with a poor quality of life and severe organ damage.⁵ Moreover, treatment of SCD is still only supportive, employing periodic blood exchange transfusions and hydroxyurea (HU), which is the only US Food and Drug Administration (FDA) approved SCD therapy.⁶

Historically, Oman was the principal trading port of the Arabian Gulf region. Its high trade activities resulted in mixed social and ethnic background of the Omani people. Zanzibar, Pakistan and part of Iran were classified as malaria endemic areas as well as some part of the Arabian Peninsula (Malaria Belt). Malaria is one of the main reasons of the occurrence of sickle cell disease (SCD), thalassaemia, glucose-6-phosphate dehydrogenase (G6PD) deficiency and other erythrocyte defects which are the most common Mendelian diseases of mankind. Different populations have evolved different genetic variants to protect against malaria.⁷ The recent statistics shows that there are around 400 patients with thalassaemia major and 3000 with sickle cell disorders in Oman.⁸ The birth prevalence of infants with haemoglobin disorders was 3.5-4.7/1,000.⁹ Around 6% of Omanis are carriers of the gene for sickle cell anaemia, 2-3% for β -thalassaemia and 45% are carriers of the α -thalassaemia gene.¹⁰⁻¹³ The other red cell abnormality common in Oman is G6PD deficiency which is found in 28% of males and 12% of females.^{10,14}

Although Oman started diagnosing SCD in early 1980's; however, there is no published data on the first case. In Oman, almost 40% of the patients were diagnosed before the age of one year. The severity index correlated well with the age of diagnosis. More than two thirds of SCD cases were running a mild course of the disease. The majority of the patients (61.2%) were homozygous sickle cell anemia followed by double heterozygous types mainly sickle cell β -thalassaemia. African Haplotypes were predominant (68.53%) and 80% of those screened for α -globin gene mutations were heterozygous or homozygous for α -Thalassaemia. There was no significant correlation between

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phenotype and haplotype forms and the severity of the disease. About half of the patients had splenomegaly and preserved splenic function which may relate to the low incidence of infections observed in our patients compared to other reports. There was low documentation of acute chest syndrome and cerebrovascular accidents compared to published data. Other complications are comparable to other studies. Factors possibly influencing the severity of the disease are the presence of alpha thalassaemia gene mutation and high Hb F levels.^{15,16}

In 1989 Lang down and co-workers from Cambridge reported the first case of HbS-Oman. HbS/S-Oman is a severe variant of sickle haemoglobinopathy that results from 2 simultaneous mutations in the same B globin chain. The first is the classic Bs mutation (B6 Glu→val) and the second is in position 121 (B121 Glu→lys).^{17,18} Previous reports explained that carriers of this disease in Oman present in 2 different clinical syndromes:

- i. High expressors of HbS/S-Oman and concomitant- α/α thalassaemia (expressing about 20% HbS/S-Oman) presenting in the heterozygote state with clinical manifestations of Sickle Cell Disease of varying severity.
- ii. Low expressors of HbS-Oman with concomitant- α/α thalassaemia (expressing about 14% of HbS-Oman) and they are asymptomatic with no clinical syndrome.¹⁹

In the literature only 6 carriers have been described so far.¹⁷⁻¹⁹ Recently, we observed quite a number of carriers in our OPD presenting as severe forms. Also, we have identified for the first time in Oman compound heterozygotes HbS-Oman that resulted in a very severe clinical manifestations presenting as transfusion dependent thalassaemia major with hypersplenism early in life that was not controlled, solely, by hypertransfusion and needed both splenectomy at the age of one year and bone marrow transplantation in the second year of life. Recently we studied 4 affected families through pedigree evaluation and screened all family members by Hb variant analyses and HPLC. We identified 62 patients with Hb S Oman heterozygosity of which 6 patients had compound heterozygosity for HB S-S Oman.

Conclusion

Of the 6 patients with compound heterozygosity for Hb S-S Oman, 2 patients underwent Bone marrow Transplantation (BMT). The first patient underwent BMT at the age of 5 years. This patient had an extremely severe course of the disease with recurrent splenic sequestration despite receiving regular blood transfusions since 6 months of age. The other patient underwent BMT recently at age of 16 years due to severe course of the disease with h/o stroke and regular blood transfusion. We evaluated the 56 patients with HbS Oman heterozygosity, their clinical features range from being asymptomatic to severe course of the disease. We compared the Red Cell Indices of patients with Heterozygous HbS Oman and compound heterozygous HbS-S Oman and detected lower mean Hb, MCV, MCH and higher RDW values in compound heterozygous patients compared to SCD patients. We are currently investigating the genetic modifiers and the red cell biology of these patients.

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Conflict of interest

The author declares no conflict of interest.

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