Case Report

Sickle cell hemoglobin C disease in Saudi Arabia

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ABSTRACT

Sickle cell hemoglobin C (HbSC) is a disease confined to people of West African ancestry and it has not been reported in the Kingdom of Saudi Arabia (KSA). We are reporting 2 patients with HbSC disease from the western province of KSA (Madinah); one patient presented with severe form of the disease which include transient hypertension.

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Sickle cell hemoglobin C (HbSC) disease occurs as a result of inheritance of the gene for hemoglobin S (HbS) from one parent and the gene for hemoglobin C (HbC) from the other, the disease was confined to people of West African ancestry and occurs at high prevalence in Ghana and Barkina Faso.[1,2] It also occurs in black populations of North and South America, the Caribbean and Europe but it is not seen elsewhere in Africa, around the Mediterranean, Kingdom of Saudi Arabia (KSA) or India.[3] To the best of our knowledge the clinical and laboratory findings of HbSC disease have not been reported in KSA.[4] We are reporting 2 patients with HbSC disease from Madinah, western province of KSA. Sickle cell hemoglobin C disease is considered relatively more benign than hemoglobin SS (HbSS) disease. The unique features we have found in one of our cases are severe form of the disease characterized by early hand-foot syndrome, recurrent severe vaso-occlusive crisis and transient hypertension.

Case Report. ***Patient One.*** A 3-year-old black Saudi girl was diagnosed with sickle cell anemia in another local hospital at early infancy, her initial clinical presentation was of hand foot syndrome and subsequently she had frequent episodes of acute painful crisis requiring hospital admission, she did not require blood transfusion (BT) during her follow-up at local hospital, her outpatient follow-up was not regular. Parents are not relatives. The first admission in our hospital in Madinah Maternity and Children's Hospital (MMCH), Madinah, Kingdom of Saudi Arabia (KSA) was in February 2001 with acute painful crisis; she received conservative treatment and was discharged within 3 days in a stable general condition. Two months later she was readmitted with severe acute painful crisis in the form of abdominal pain, limb pain, along with fever and vomiting. Physical examination revealed an ill looking girl, febrile, (temperature 39^0C), pulse rate 155 per minute, respiratory rate 58 per minute, and blood pressure (BP) was 150/105 mm Hg. She had congested tonsils, hepatomegaly of 3 cm below costal margin; spleen was not palpable and other systems were unremarkable. Laboratory tests revealed white blood cell (WBC) $15x10^9$/L, Hb 88 g/L, platelet 260 x 10^9/L, peripheral blood smear showed Howell Jolly bodies, significant number of target cells and sickle cells **(Figure 1)**. Blood culture grew *Staphylococcus aureus*. In hemoglobin electrophoresis by cellulose acetate at

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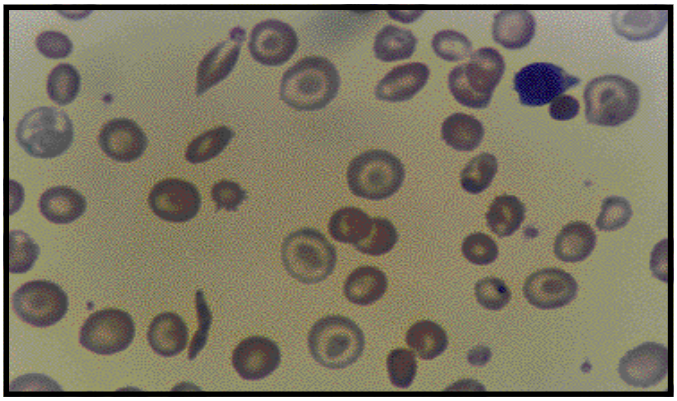

Figure 1 - Peripheral blood film of patient one demonstrating Howell Jolly bodies, target cells and sickle cells.

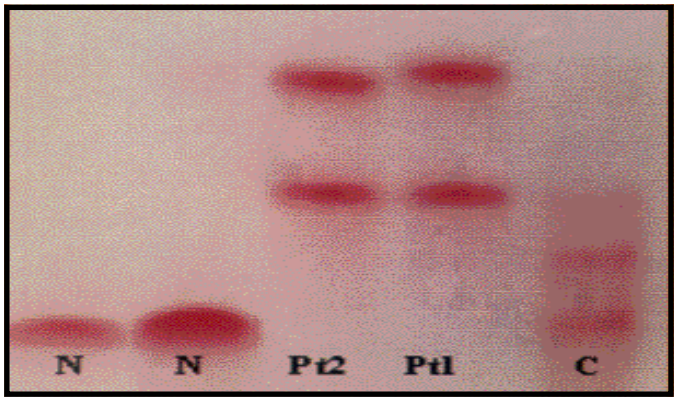

Figure 3 - Cellulose acetate of Hb electrophoresis at pH 8.4 showing Hb at A2 and S position of patients one and 2. N - normal, Pt 2 - patient 2, Pt 1 - patient one, C - control, Hb - hemoglobin, Hb at A2 - hemoglobin A2, Hb at S - hemoglobin S

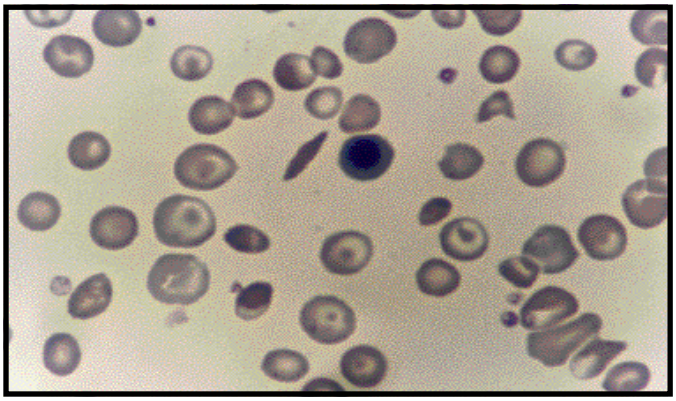

Figure 2 - Peripheral blood film of patient 2 demonstrating, sickle cells, target cells, polychromatic cells and few nucleated red blood cells.

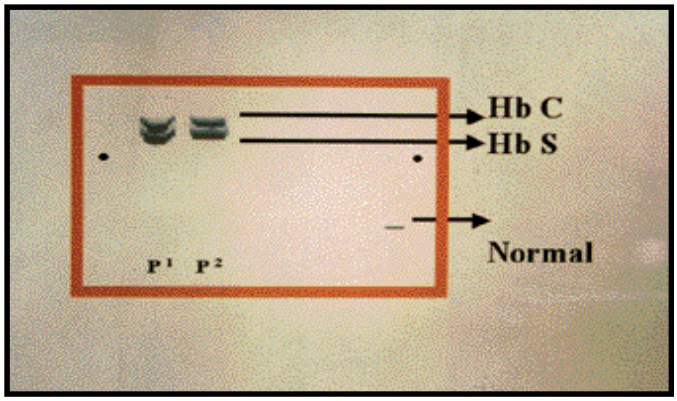

Figure 4 - Agar gel Hb electrophoresis at pH 6 showing HbS and HbC bands of patients one and 2. HB - hemoglobin, HbC - hemoglobin C, HbS - hemoglobin S, P1 - patient one, P2 - patient 2.

alkaline pH (pH 8.4) revealed HbS 47%, Hb band at A2 position 53% **(Figure 3)**. Agar gel electrophoresis at acid pH (pH 6) was performed and it revealed HbS 47%, HbC 53% **(Figure 4**). Hemoglobin electrophoresis for mother revealed HbAS and for father HbAC. The patient was managed conservatively with intravenous fluid, simple analgesics, intravenous (IV) antibiotics (ceftriaxone) and started on antihypertensive drug (hydralazine). Subsequently the patient improved clinically, BP became normal and hydralazine was discontinued over 2 weeks; the patient was followed at the outpatient department, BP remained normal during follow-up.

Patient 2. A 5-year-old black Saudi girl, known case of Down's syndrome with congenital heart disease (ventricular septal defect) underwent cardiac surgery at early infancy referred to the Hematology Clinic at MMCH from a private hospital with a history of mild recurrent lower limbs pain and anemia. She did not require hospital admission or any treatment previously. Parents were not relatives, and there was no family history of sickle cell disease (SCD). Physical examination was unremarkable apart from obvious features of Down's syndrome. Her investigations revealed WBC 17 x 10^9/L, Hb 80 g/L, platelet 170 x 10^9/L, reticulocyte 7%; peripheral blood film showed few sickle cells, some target cells, polychromatic cells and occasional nucleated red cells **(Figure 2)**. Hemoglobin electrophoresis with cellulose acetate at alkaline pH (pH 8.4) revealed HbS 45%, Hb band at A2 position 55% (**Figure 3)**. Agar gel electrophoresis at acid pH (pH 6) revealed HbS 45%, HbC 55% **(Figure 4)**. Hemoglobin electrophoresis from the father and mother of the patient revealed HbAS and HbAC. She is being followed regularly at the hematology clinic.

Discussion. The clinical and laboratory finding of HbSC disease have not been reported in KSA.[4] This is the first reported case of HbSC disease in KSA. This

disease was confined to people of West African ancestry. It occurs in black populations of North and South America, the Caribbean and Europe but is not seen elsewhere in Africa, around the Mediterranean, KSA or India.[3] The disease is generally benign with mild symptoms and near normal survival.[5] In the United State of America, HbSC disease is the most common compound heterozygous form of SCD occurring in approximately one in 800 African American live births.[6] In our study, both patients were black and they were from West African ancestry (Nigeria), this observation is consistent with that reported previously that HbSC disease occurs in black populations and was confined to people of West African ancestry.[3] Most of the African Saudis are localized in the western province of KSA particularly in the Holy Cities of Makkah and Madinah. Their grand generation had migrated over the years from Western African countries to the Holy Cities of the KSA. As the sickle cell genes in the western province of KSA are of benin haplotypes[7,8] it indicates that these genes originate in Western Africa. This suggest that HbSC disease does exist in KSA among black Saudis of west African origin. Although HbSC disease is known as benign,[5] patient one had a severe form of the disease with early manifestation of hand-foot syndrome and recurrent severe painful crisis. She also presented with transient hypertension during acute vaso-occlusive crisis, this finding has been reported earlier in SCD;[9] however, the occurrence apparently rare. Generally BP is lower than normal in patients with SCD.[10,11] Ernst et al[12] found no patients of SCD with hypertension during acute vaso-occlusive crisis, neither did they reported a lower BP in female patients, HbSS disease and patients with bilateral pain. The cause of low BP in SCD is not known; however, it has been suggested that the lower BP in SCD was attributed to low body weight[13] and to significantly higher daily urinary volume and sodium excretion,[14] which results in a decrement in intra vascular volume status and finally a decreases in cardiac output. Although transient hypertension occurs rarely during sickle cell crisis, the possible etiology for this occurrence includes associated sepsis following BT.[9,15-17] In patient one, peripheral smear shows Howell Jolly bodies which indicate functional asplenia, she had septicemia with *Staphylococcus aureus.* Although HbSC disease is a benign form of the disease functional asplenia has been documented in children and adults,[18-20] also fetal pneumococcal septicemia had been reported in HbSC disease.[21] Thus, we agree with the recommendation that pneumococcal vaccine should be administered to all children with HbSC disease and that acute febrile illnesses should be investigated and treated promptly by antibiotics such as ceftriaxone.[22] We also recommend routine use of penicillin prophylaxis in infancy and childhood for all HbSC disease. Patient 2 had a mild disease consistent with others.[5] This study demonstrates that HbSC disease exists in KSA, particularly in the western province among black Saudis of West African ancestry.

We conclude that HbSC disease is not always a benign condition and transient hypertension can also manifest during acute vaso-occlusive crisis of SCD. Finally, we recommend performance of Hb electrophoresis on sicklers from West African ancestry by both cellulose acetate at pH 8.4 and citrate Agar at pH 6.

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