

# Compound heterozygosity for Hb S and Hb S-Oman

## Case report

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### تَغَايُرُ الزِّيْجُوتِ الْمُرْكَبِ لِلْهِمُوغْلُوبِينَ الْمِنْجَلِيِّ وَالْهِمُوغْلُوبِينَ الْمِنْجَلِيِّ الْعَمَانِيِّ تَقْرِيرُ حَالَةٍ

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**المخلص:** أظهرت نتائج فحوص الدم والفحوص السريرية لطفلة عمانية عمرها ثلاث سنوات التَّمَطِّ الظَّاهِرِيَّ الْمُرْكَبِ لِتَغَايُرِ الزِّيْجُوتِ لِلْهِمُوغْلُوبِينَ الْمِنْجَلِيِّ وَالْهِمُوغْلُوبِينَ الْمِنْجَلِيِّ الْعَمَانِيِّ . ودعمت هذه النتائج فيما بعد بدراسة التاريخ العائلي . نؤكد هنا على أهمية وضرورة مراجعة حالات الإصابة بفقر الدم المنجلي في عمان.

**مفتاح الكلمات:** الهيموغلوبين المنجلي العماني . الهيموغلوبين المنجلي . الهيموغلوبين غير الطبيعي . أمراض الدم . فقر الدم المنجلي . خَلَّةُ الْكُرْبَةِ الْمِنْجَلِيَّةُ . عمان.

**ABSTRACT** The haematological and clinical findings of a three year old Omani girl, phenotypically compound heterozygote for Hb S and Hb S Oman, are presented, further substantiated by family studies. The necessity of reviewing cases with sickle cell haemoglobin in Oman is stressed.

**Keywords:** Haemoglobin S Oman; Haemoglobin S Disease; Abnormal haemoglobin; Haemoglobinopathies; Sickle cell anaemia; Sickle cell trait; Case report; Oman.

**T**HE CLASSICAL SICKLE CELL TRAIT HAS ONE  $\beta$ s mutation ( $\beta 6$  Glu  $\rightarrow$  Val). Hb S-Oman has two mutations *in cis*. in the same  $\beta$  chain, one the classical  $\beta$ s mutation ( $\beta 6$  Glu  $\rightarrow$  Val), and the second ( $\beta 121$  Glu  $\rightarrow$  Lys), identical to that found in a variant namely Hb O Arab. Hb S-Oman increases the sickling tendencies, but the clinical symptomatology is influenced by co-existing alpha thalassaemia. No homozygous Hb S-Oman has been reported in the literature.

### CASE REPORT

A three year old Omani girl from the Al-Kindi tribe from Barka, a town on the coast about 80 km north-

west of Muscat, presented to the Ear, Nose and Throat department of Al-Nahdha hospital in September 2007 with complaints of recurrent sore throat, 5-6 times a year. The clinical diagnosis was recurrent acute follicular tonsillitis. The past history revealed that she was diagnosed to have sickle cell anaemia with a history of haemolytic crises and frequent admissions to a tertiary care hospital and had had a recent blood transfusion. A tonsillectomy was planned and a complete blood cell count (CBC) and sickling test were requested as preoperative investigations. The CBC showed, among other parameters: Hb - 9.34g/dl; red blood cell count -  $3.45 \times 10^{12}/L$ ; haematocrit - 22.4%; mean cell volume - 65fl; mean cell haemoglobin - 27.1pg;

mean cell haemoglobin concentration - 41.7g/dl and red cell distribution width - 18.9%. The sickling test was positive. From the blood film examination, the most important feature was the presence of many Napoleon hat x-shaped red blood cells and classical sickle cells [Figure 1]. The white blood cell count was  $5.53 \times 10^9/L$  (normal 6 -18) and platelet count was  $552 \times 10^9/L$  (normal 150 - 450). Given the presence of numerous Napoleon hat x-shaped red blood cells in the blood film with moderate anaemia and a positive sickling test, the presence of Hb S-Oman was suspected and the patient was referred to the genetic blood screening unit of our hospital. The results of this screening were as follows: G6PD activity was normal; the high performance liquid chromatography (HPLC) profile showed: Hb A - 49%; Hb A2 - 2.3%; Hb F - 30.8%; Hb S - 12.3% and a presumably Hb S-Oman - 5.6% in the HbC window. The presence of Hb A was believed to be due to the recent blood transfusion. The family studies revealed the HPLC profile of the father (also from the Al-Kindi tribe) to be: Hb A - 70%; Hb A2 - 3%; Hb F- 1%; Hb S- 26% and he was diagnosed as having sickle cell trait. He was clinically asymptomatic. The HPLC profile of the mother showed: Hb A - 83%; Hb A2 - 3%; Hb F - 1%, and an abnormal component in the HbC window, very likely Hb S-Oman - 13%, so she was diagnosed to have having the Hb S-Oman trait. The two brothers of the index case had normal HPLC profiles.

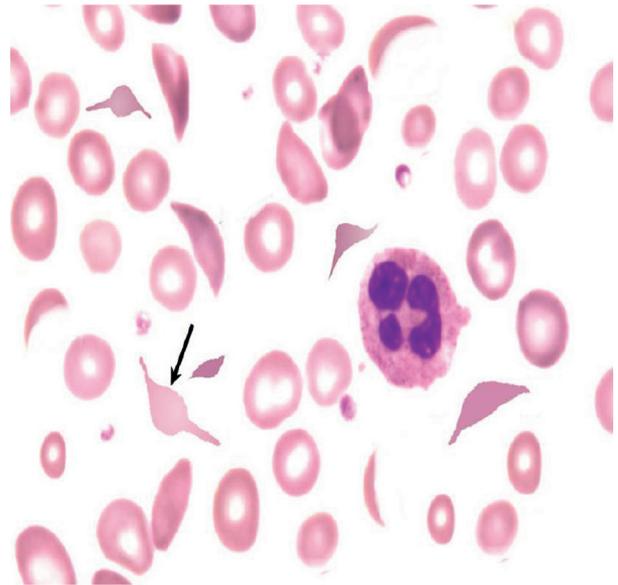
## DISCUSSION

This case report stresses the importance of examining the blood film, which revealed the presence of Napoleon hat x-shaped red blood cells [Figure1] characteristic of red blood cells containing HbS-Oman.<sup>1,2,3</sup>

The presence, in addition, of classical sickle cells in the smear, as seen in Figure 1, prompted family studies, and confirmed the inheritance of Hb S and Hb S-Oman in this patient. Thus she was diagnosed as compound heterozygote for Hb S and Hb S-Oman

During a follow up at Al-Nahdha Hospital, after the blood transfusion, the HPLC profile of the patient revealed the presence of Hb S-Oman at 12% and Hb S at 25% matching with the level observed in her parents for respective abnormal haemoglobins.

The first report of Hb S-Oman in the literature was by Langdown JV et al. in 1989.<sup>4</sup> The first description of compound heterozygosity for Hb S/Hb S-Oman in a one year old female from Oman was reported in 2002.<sup>1</sup>



**Figure 1:** Smear showing Napoleon hat x-shaped red blood cells, characteristic of red blood cells containing HbS Oman

The pathophysiology of the sickle syndrome in this compound heterozygote patient must be the result of interaction between HbS and HbS-Oman, the sickle mutation ( $\beta 6Val$ ) favouring sickling and the O-Arab mutation ( $\beta 121Lys$ ) favouring haemolysis and changes in red blood cell shape.<sup>5</sup> It is important to note that such patients who are compound heterozygotes for Hb S and Hb S-Oman behave clinically like sickle cell anaemia. Our case, who had frequent admissions to hospital with haemolytic crises and who received numerous blood transfusions, fully supports this fact. Our study highlights the importance of reviewing the sickle cell cases in Oman carefully, including those categorised as HbC trait or sickle cell disease (as HbS-Oman behaves as HbC on HPLC).

The mother of this patient, who is heterozygous for Hb S-Oman (13%), is clinically asymptomatic. Published reports state that the clinical manifestations in heterozygous Hb S-Oman are only observed in individuals having more than 20% of Hb S-Oman, whereas individuals with a lower percent of Hb S-Oman (14% and below), and concomitant homozygosity for single gene deletional alpha thalassaemia, are clinically asymptomatic, and have only slight to moderate red blood cell changes.<sup>3</sup> Thus both exploration of alpha thalassaemia and family studies will be useful in predicting the clinical outcome.

## CONCLUSION

A patient who has compound heterozygosity for Hb S and Hb S-Oman behaves clinically like a case of sickle cell anaemia. An awareness of existence of Hb S-Oman, an eye for Napoleon hat  $\chi$ -shaped cells on blood film, a review with HPLC in all cases of known sickle cell anaemias, along with family studies, is recommended to unearth cases of Hb S-Oman.

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