

Mosapride is a gastroprokinetic agent that acts as a selective 5HT₄ agonist which accelerates gastric emptying and is used for the treatment of acid reflux and functional dyspepsia. 5HT₄ receptors are located in the alimentary tract, urinary bladder, heart and adrenal gland as well as the central nervous system (CNS) [4]. In the CNS, receptors appear in the putamen, caudate nucleus, nucleus accumbens, globus pallidus and sub-stantia nigra and to a lesser extent in the neocortex, raphe and pontine nuclei and some areas of the thalamus [5]. Mosapride acting on 5HT₄ receptors in basal ganglia may have produced the symptomatic improvement in our patient. This case report suggests that mosapride (5HT₄ agonist) may become a novel tool in the treatment of blepharospasm.

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A case of Hb Hofu in Sri Lanka

D S N Samaraweera¹, R Das², S Chhabra², J Kaur²

Ceylon Medical Journal 2014; **59**: 27-29

Introduction

Hb Hofu (HBB:c. 380T>A) is a rare inherited haemoglobin variant due to substitution of valine with glutamic acid at codon 126 of the beta globin gene. It is a mildly unstable haemoglobin. This rare haemoglobin abnormality has not been described from Sri Lanka and there are only few case reports in the world literature [1-5]. This report describes a case of Hb Hofu in a Sinhalese family from the central province of Sri Lanka.

Case report

A three year old boy of Sinhalese origin presented with moderate anaemia to the paediatric haematology clinic. Investigations showed that he was compound heterozygous for beta thalassaemia and an unknown haemoglobin variant. Screening of his parents found that father was heterozygous for beta thalassaemia and mother was heterozygous for an unknown haemoglobin variant.

Later the grandparents and the child's aunt were screened with haemoglobin HPLC. All the tests were performed as per guidelines for the laboratory diagnosis of haemoglobinopathies.

Venous blood samples were taken for red cell indices and blood picture followed by HPLC. The focus of this case report is on the mother of the index case whose blood was further analysed at the Department of Haematology, Postgraduate Institute of Medical Education and Research, Chandigarh, India with haemoglobin HPLC, electrophoresis followed by gene sequencing of alpha₂, alpha₁ and beta globin genes.

Investigations of the child with microcytic anaemia (Hb 7.6 g/dl) showed red cell indices of RBC 3.83 x 10⁹/l, MCV 66.7 fl, MCH 20.2 pg, MCHC 30.3 g/l and RDW 15.6%. Serum ferritin was 68.3 ng/ml. Blood picture showed marked morphological abnormalities suggestive of thalassaemia/haemoglobinopathy syndrome. On screening of parents, the father was found to have micro-

¹Haematology Unit, Sirimavo Bandaranayake Specialized Children's Hospital, Peradeniya, Sri Lanka and ²Department of Haematology, Postgraduate Institute of Medical Education and Research, Chandigarh, India.

Correspondence: DSNS, e-mail: <amaanil@hotmail.com>. Received 4 October 2013 and revised version accepted 20 November 2013. Competing interests: none declared.

cytic red cell indices (Hb 120 g/l, RBC 5.79 x 10⁹/l, MCV 65.4 fl, MCH 20.7 pg, MCHC 31.7 g/l, RDW 15.4%) His haemoglobin HPLC showed elevated HbA2 level of 3.9%, HbF 1.5% and HbA0 of 83%. He was diagnosed as beta thalassaemia trait.

The mother was 28 years old, from Kandy in the central province of Sri Lanka. Her red cell indices (Hb 123 g/l, RBC 4.3 x 10⁹/l, MCV 85.4 fl, MCH 28.6 pg, MCHC 33.5 g/l, RDW 13.8%) and blood picture were within normal limits. Her HPLC findings showed an unknown peak just before the A0 peak with a retention time ranging from 2.22 to 2.25 minutes (Figure 1 A). On further investigation it showed a fast moving band ahead of HbA on alkaline Hb electrophoresis (Figure 1 B). Genomic DNA was extracted from peripheral blood leucocytes and alpha-globin gene deletions were tested by gap-PCR. Automated sequencing of alpha 2, alpha 1 and beta globin genes was performed on the ABI Prism 310 sequencer

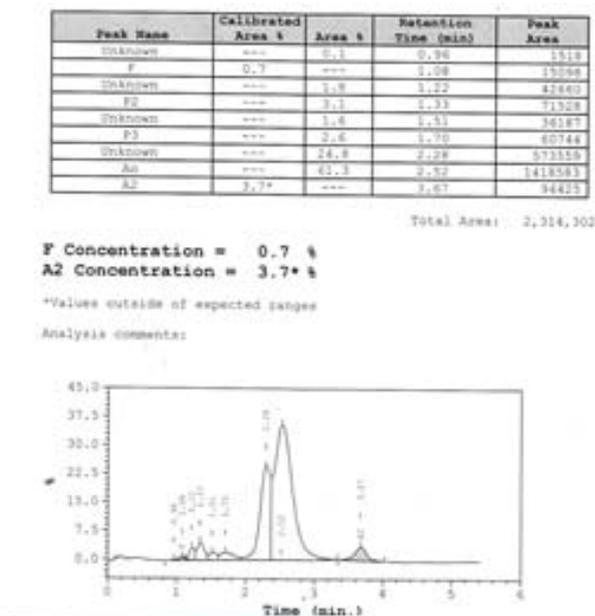


Figure 1A. HPLC of mother of index case showing a hump splitting the HbA0 and constituting 24.8% of total Hb.

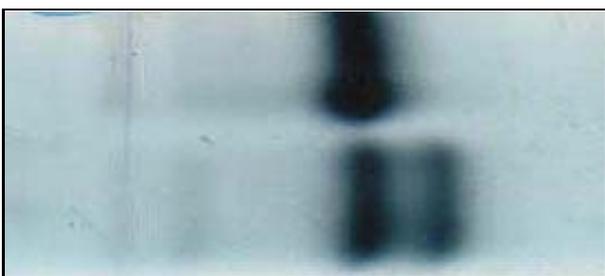


Figure 1B. Alkaline Hb electrophoresis at pH 8.6 showing a fast moving band.

(Applied Biosystems, Foster City, CA, USA). It showed a mutation in the beta gene with substitution of valine with glutamic acid (GTG>GAG) at codon 126 of the beta globin gene (Figure 2). This mutation gives rise to the abnormal haemoglobin, Hb Hofu. Family screening showed the grandfather of the index case also to be a carrier of Hb Hofu.

The child (index case) was diagnosed as compound heterozygosity with beta thalassaemia Hb Hofu.

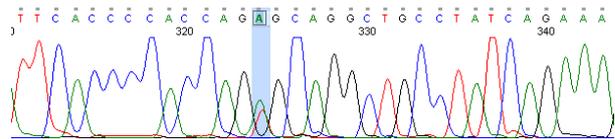


Figure 2. Chromatogram showing heterozygosity for Hb Hofu beta 126(H4) Val>Glu; T-A.

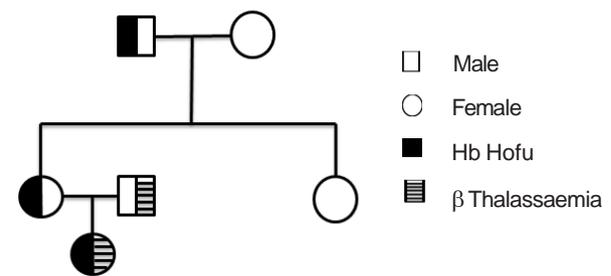


Figure 3. Pedigree of the family with Hb Hofu.

Discussion

We document Hb Hofu in a Sinhalese family in Sri Lanka in heterozygous as well as in compound heterozygous states in combination with beta thalassaemia. The Hb Hofu heterozygotes were asymptomatic with completely normal red cell parameters and only Hb HPLC revealed an abnormal peak (approximately 25-30%). Since this haemoglobin variant has been described as mildly unstable, there is quantitative reduction in the amount of the variant Hb.

Compound heterozygosity with beta thalassaemia Hb Hofu resulted in worsening of anaemia compared to beta thalassaemia trait. In our patient the haemoglobin level was 75 to 77 g/l (without any red cell transfusion) with a normal serum ferritin level. There was a similar case report from central India of thalassaemia intermedia in an Indian female with Hb Hofu beta thalassaemia [4]. Considering these findings, it can be concluded that coinheritance of Hb Hofu with beta thalassaemia can result in

thalassaemia intermedia. Independent mutation is the most likely explanation for the occurrence of Hb Hofu in individuals of Japanese, Spanish, Indian and Sri Lankan origin [1-5].

Routine baseline thalassemia screening involves automated FBC to evaluate red cell indices. This does not detect any abnormality in the heterozygous state of Hb Hofu. Hb Hofu was detected by Hb HPLC but can be overlooked due to a close association with Hb A0. Hence, partner screening of a known carrier, especially with beta thalassaemia trait, should include haemoglobin HPLC with careful interpretation.

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Thrombotic microangiopathy following Russell's viper (*Daboia russelii*) envenoming in Sri Lanka: a case report

S A M Kularatne¹, S Wimalasooriya¹, K Nazar³, K Maduwage²

Ceylon Medical Journal 2014; **59**: 29-30

Introduction

Thrombotic microangiopathy (TMA), though uncommon, is a recognized complication of snake envenoming [1]. Characteristically, it comprises of the triad of microangiopathic haemolytic anaemia, thrombocytopenia and acute renal failure [1]. Association of TMA with hump-nosed viper (*Hypnale* species) envenoming has been described recently in Sri Lanka [2]. However, association of TMA with Russell's viper (*Daboia russelii*) envenoming had not been clearly defined except in a publication in 1975 in India which described manifestations of TMA in 5 patients [3]. It appears that TMA is a rare manifestation of Russell's viper bite, despite the fact that its bites are common in Sri Lanka [4]. We present a patient with severe anaemia, thrombocytopenia and mild acute renal failure after Russell's viper bite in Kandy district suggestive of TMA.

Case report

A 43 year-old woman was working in a paddy field in

a remote village in the Central Province. At about 11 am her foot was bitten by a Russell's viper. With a vigorous shake the snake was dislodged and she ran to find help. But she stumbled and fell down on her face and stuck the forehead. Then she started to bleed heavily from the nose and fainted within a few minutes. After regaining consciousness, she managed to wave her hands and got the attention of another farmer. She was brought to a local hospital within 30 minutes. On admission to the hospital she had ophthalmoplegia and passed red coloured urine suggestive of haematuria. The bleeding scalp laceration was managed with tight bandaging. She was given 10 vials of Indian polyvalent antivenom and transferred to a tertiary care hospital where she underwent CT scan of the brain which was reported normal. However, over the next two hours her blood pressure dropped and therefore she was sent to the intensive care unit of the Teaching Hospital, Peradeniya. Upon resuscitation with intravenous fluid and hydrocortisone her blood pressure increased to 110/70 mmHg. The radial pulse rate was 98 min. She had bilateral ptosis and external ophthalmoplegia, but respiration was normal. Fang marks were present over

Department of ¹Medicine and ²Biochemistry, Faculty of Medicine, University of Peradeniya and ³Teaching Hospital, Peradeniya, Sri Lanka.

Correspondence: SAMK, e-mail: <samkul@sltnet.lk>. Received 25 July 2013 and revised version accepted 9 October 2013. Competing interests: none declared.