

# A case of hereditary persistence of fetal haemoglobin

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## Introduction

Thalassaemia syndromes comprise a large clinical spectrum and a well recognized observation is the inverse link between clinical severity and quantity of fetal haemoglobin (HbF) present<sup>1</sup>. It is now known that three types of globin that produce haemoglobin (Hb) change from e-globin (epsilon) to g-globin (gamma) in the fetus and to b-globin (beta) around birth. This process of change is termed "globin switching". Rarely, due to a genetic defect, the g-globin gene continues to function, producing gamma chains. Therefore HbF is present throughout life giving rise to the condition hereditary persistence of fetal haemoglobin (HPFH)<sup>2</sup>. Such persons are often asymptomatic and lead normal lives. Persons with thalassaemia major who have concomitant HPFH have low transfusion requirements due to the persistence of HbF, making up for the deficiency of b-globin<sup>3</sup>. HPFH provides a basis for a genetic approach to cure haemoglobinopathies in the future.

## Case report

A 9 year old girl from the south of Sri Lanka presented to us, at the age of 9 years, with pallor and hepatosplenomegaly. She was the product of a non consanguineous marriage and a maternal uncle had died at the age of 20 years due to "thalassaemia". No other details were available.

She had been well until five years when she presented to the local hospital with fever, jaundice, pallor, hypochromic microcytic anaemia with target cells, a positive alkaline denaturation test and absence of bile in the urine and received a blood transfusion. A similar episode one year later resulted in the diagnosis of thalassaemia intermedia being made. Menarche at 9 years was followed by fever, enlarged liver and spleen of 3 cm and 2 cm respectively.

We found the following haematological findings: Hb 6g%, MCH 22 pg, MCV 63 fl, MCHC 35 g/dl; white cell count  $9.2 \times 10^9/l$  (N50%, L45%, E3%, M2%); platelets  $235 \times 10^9/l$ ; reticulocyte count 4.2%.

*Blood picture* showed hypochromic markedly distorted red blood cells with anisocytes, poikilocytes, microcytes, target cells, spherocytes, fragmented and crenated cells, polychromatic cells and normoblasts. White cells and platelets were normal..

*Alkaline denaturation test* was positive with 37% HbF.

Acid elution test was 95% positive in neonatal blood (positive control), 100% negative in adult blood (negative control) and almost 100% positive in patient's blood.

*Haemoglobin electrophoresis* detected only HbF with no adult Hb or Hb E. Coombs test and sickling test were negative. G6PD test showed normal enzyme activity. Osmotic fragility showed initial haemolysis at 0.5% and not completed at 0.1%.

Mother's and father's blood showed alkaline denaturation tests of 1.2% and 0.9% and Hb A2 levels of 3.1% and 2.6% respectively. A diagnosis of HPHF was made. She remained well until 14 years when she needed her fourth transfusion.

## Discussion

Our patient had a non transfusion dependent chronic haemolytic anemia and presented with a fragmentation syndrome in the blood picture due to an acute crisis of haemolysis precipitated by an intercurrent febrile illness. Her Hb electrophoresis result indicates HPHF or homozygous thalassaemia with HPHF.

Increased levels of fetal haemoglobin (HbF) can ameliorate the clinical course of inherited disorders of beta globin gene expression, such as beta thalassaemia and sickle cell anaemia<sup>4</sup>. The continued production of Hb F compensates for the lack of Hb

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A<sup>5</sup>. A search for drugs to activate fetal haemoglobin production as a treatment option for thalassaemia and sickle cell disease is underway although clinical trials with hydroxyurea and butyrate have not yielded success<sup>6</sup>. Attempts to suppress the repressor proteins that bind to  $\gamma$ -globin genes are being researched.

## References

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