INTRODUCTION

Haemoglobin H is usually seen in inherited condition known as alpha thalassemia. However, it can be seen in acquired form, where it is associated with other conditions e.g. Myelodysplastic syndrome and haematological malignancies.

Disordered gene regulation is a common feature of transformed cells. This can manifest either by the synthesis of an inappropriate gene product, such as fetal hemoglobin synthesis, or by the loss of an appropriate product, such as deficient production of an α-globin chain resulting in acquired Haemoglobin H.

It is not completely clear whether the presence of Haemoglobin H is a marker for a particular subgroup of myeloproliferative disorders or whether it is a secondary event that may develop in neoplastic cells. The frequency of association between acquired haemoglobin H disease and clonal hematopoiesis is unknown, probably because reticulocyte preparations are not set up or adequately examined for the presence of haemoglobin H inclusions.

This case illustrates how a relevant physical examination and logical sequence of laboratory tests led to the diagnosis of Myelodysplastic syndrome. It is a rare but interesting association with acquired Haemoglobin H.

CASE REPORT

A 60-year-old Saudi male patient attended medical outpatient clinic for assessment of asthma. Patient was a known asthmatic and was stable. General experience showed that patient was having mild jaundice that prompted a detailed history. Patient told that this time the breathlessness was different from the previous episodes in that it had been persistent for the last few months. It increased on exertion, and partially relieved by inhalers. It was not necessarily associated with cough or wheeze. He disclosed on direct questioning that around 9 months ago, he went to another hospital for this breathing difficulty and generalized weakness, where he remained admitted for 4 days and was transfused 2 units of packed cells. There was an improvement in his general health after blood transfusion. At the time of discharge, he was asked to follow but he had no further follow-up.

Systemic review did not reveal fever, weight loss, bleeding or jaundice. There was no history of anemia, blood transfusion or jaundice in the family. He was taking salbutamol inhaler prn. He was able to do his routine work with some difficulty due to general ill health.

Examination revealed a middle aged male of normal built. His vital signs were within normal limits. He had mild jaundice and pallor. There were no petechiae or lymphadenopathy. Liver and spleen were not enlarged. The chest was mildly hyperinflated. Rest of the systemic examination was unremarkable.

Considering a history of blood transfusion, 9 months ago, and findings of pallor and jaundice, a clinical diagnosis of hemolytic anemia was made and investigations were accordingly done to confirm the diagnosis of hemolysis and to find out its cause.

ABSTRACT

A 60-year-old male patient presented with jaundice. Initial investigations showed anemia, indirect hyperbilirubinemia, raised Lactic Dehydrogenase (LDH) and increased reticulocyte count suggestive of hemolysis. Considering hemolysis low MCV and basophilic stippling on peripheral film, hemoglobin electrophoresis was done that showed Haemoglobin H (15.5%) that in the absence of family history was thought to be acquired. After bone marrow examination, the final diagnosis was Myelodysplastic Syndrome (MDS), Refractory anemia with excess of blast (RAEB) associated with acquired Haemoglobin H (Hb H) disease.

Key words: Myelodysplastic syndrome. Hemolytic anemia. Acquired Hemoglobin H.

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On initial investigations, Hb was 8.0 g/dl with normal total and differential leukocyte count and normal platelets. The MCV was 65 fl. Peripheral film showed dimorphic film with basophilic stippling and occasional nucleated RBCs. Reticulocyte count was 6.0%. Total bilirubin was 36 µmol/l, conjugated bilirubin was 9 µmol/l, unconjugated bilirubin was 28 µmol/l, and LDH was 808 u/l, which were all of raised values. Coomb’s test was negative. Serum ferritin done because of low MCV was normal. Hb electrophoresis revealed a band of fast moving Hb H (15.5%) on cellulose acetate membrane electrophoresis at alkaline pH (Figure 1a and 1b).

Family history did not show any evidence of thalassemia. This finding of Hb electrophoresis was labeled as acquired Hb H disease. Bone marrow examination confirmed the finding of Myelodysplastic syndrome; Refractory anemia with excess of blast (RAEB).

He was sent to a tertiary care hospital for cytogenetic studies. It was decided, however, to follow him in the local hospital and to provide supportive care. During follow-up, once again he had symptoms of dizziness and tiredness and Hb dropped to 5.6 g/dl with no evidence of blood loss. He was transfused two units of packed cells. After transfusion, his symptoms improved. At present, he is on follow-up in outpatient clinic. He is in normal state of health and on tablet folic acid 1 mg daily.

**DISCUSSION**

Although abnormal pattern of haemoglobin synthesis are nearly always inherited, occasionally, individuals with previously normal haematology may develop aberrant haemoglobin synthesis as an acquired abnormality e.g. within the context of Myelodysplastic syndrome or aplastic anemia.4

In 1960, two groups described a series of previously normal patients suffering from clonal hematopoetic disorders who developed an unusual acquired form of thalassemia during their illness.5 This syndrome was characterized by a marked hypochromic and microcytic anemia and the presence of Hb H demonstrated by electrophoresis.

Acquired α thalassemia is not limited to the geographical regions in which the inherited forms of α thalassemia are common (e.g. Middle East, South East Asia, Africa). Most patients have been of northern European descent.

A second, striking finding is that most patients reported with acquired form of α thalassemia have been male and elderly. As more cases have been evaluated, it has become clear that acquired Hb H disease most commonly develops in the context of Myelodysplastic syndrome and this condition is now referred to as the “α thalassemia Myelodysplastic Syndrome” (ATMDS).6 Many of these features were present in the reported case. His high indirect bilirubin and high LDH was due to hemolysis and ineffective erythropoiesis. The acquired Hb H also explained the finding of low MCV in the presence of normal ferritin and raised reticulocyte gave the dimorphic picture on peripheral film.

Most patients with MDS have unexplained macrocytic or normocytic anemia.7 In contrast, typical findings in ATMDS show hypochromic, microcytic red blood cells and anisopoikilocytosis.

Does the coexistence of α thalassemia exacerbate the anemia and clinical picture of MDS?

The evidence indicates that not only does the presence of thalassemia cause additional dyserythropoiesis or hemolysis, a proportion of the high-affinity Hb H further reduces the capacity for oxygen delivery.8

It can be said that microcytic, hypochromic red blood cell indices or other markers of thalassemia in a patient with MDS should prompt further evaluation for acquired Hb H disease.

**REFERENCES**


