CASE REPORT
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The Clinical Approach toward Hereditary Persistence of Fetal Hemoglobin: A Case Report

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ABSTRACT

Fetal hemoglobin is the principal hemoglobin in the human fetus, and the adult levels of fetal hemoglobin (HbF) are less than 1% of total hemoglobin. A steady increase of HbF in patients with hereditary persistence of fetal hemoglobin (HPFH) is associated with complications. The present report describes HPFH in a 26-year-old man with emphasis on its hemoglobin electrophoresis. The patient was admitted with complaints of recurrent weakness and lethargy, weight loss, abdominal pain, and dyspepsia. Splenectomy was planned due to massive splenomegaly and gastrointestinal complications. Ultimately, electrophoresis confirmed the diagnosis of HPFH.

Keywords: Blood protein electrophoresis; Fetal hemoglobin; Hemoglobinopathies

INTRODUCTION

Fetal hemoglobin, also known as hemoglobin F, HbF, or α2γ2- is the principal hemoglobin in the human fetus. HbF makes up 60 to 80 percent of the total hemoglobin of the infant. In normal healthy individuals, hemoglobin A replaces HbF at 6 to 12 months, and the adult levels of HbF are less than 1% of total hemoglobin.[1] Congenital or acquired increase in HbF is the characteristic of some hemoglobinopathies.[2-4] Because this type of hemoglobin has a high affinity to bind with oxygen; it improves clinical symptoms in patients with hereditary hemoglobinopathies such as sickle cell hemoglobin and β-thalassemia.[3,5-7] Despite the benefits of high production of HbF in patients with hemoglobinopathy, a steady increase of HbF in patients with Hereditary Persistence of Fetal Hemoglobin (HPFH) is associated with complications, especially in the presence of other hemoglobinopathies.[8,9] These complications include but are not limited to splenomegaly, dyspnea on exertion, pulmonary hypertension, and right heart failure.[10] HPFH appears in two homozygous and heterozygous types and is a rare form of hemoglobinopathies.[11] In this case report, we attempt to describe a patient with HPFH.

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CASE PRESENTATION

The patient was a 26-year-old man frequently referred to Gastroenterology Clinic (Shahid Mofateh clinic, Yasuj, Iran) with recurrent weakness and lethargy, weight loss, abdominal pain, and dyspepsia. At the time of the admission, there was no history of drug consumption except pantoprazole (20 mg capsule), and clidinium-c (Chlordiazepoxide/clidinium bromide tablet). The patient did not report any known family cancer history for first-degree relatives. The patient's sister has 98% hemoglobin F on electrophoresis without a history of blood transfusions, which is a sign of congenital hemoglobin F.

In the initial examination, vital signs were stable, and distal pulse was weak. There were symptoms of weight loss, cachexia, and temporal atrophy. Physical examination of the abdomen and touch inspection of the solid organ revealed splenomegaly. The estimated size of the liver was about 18 cm. Nothing abnormal was discovered in the examination of the heart, lung, and other organs.

Sonography revealed hepatosplenomegaly (HPM) with liver and spleen sizes 194 mm and 254 mm, respectively. Liver tissue was normal. Sonography showed a right Duplex kidney, and this finding was reported in favor of the horseshoe kidney. Respectively multiple 6-8 mm stones and a 6mm stone were observed in the right and the left kidneys.

Due to HPM, A fibroscan and upper endoscopy were performed, and the outcomes indicated no parenchymal diseases, including steatosis, fibrosis, and the absence of esophageal varices ruled out the cirrhosis. Mild gastric congestion and superficial erosions in the antrum were observed. Convincingly these findings were reported to be in favor of gastritis.

As seen in Table1, laboratory tests upon admission included depressed White blood cell (WBC), Red blood cell (RBC), and platelet (PLT) count. Bone marrow aspiration and biopsy were proceeded to evaluate and rule out the possibility of blood malignancies and other diseases related to bone marrow. The biopsy results confirmed no abnormalities but mildly hypercellular marrow with erythroid hyperplasia and decreased megakaryocytes.

Rheumatological tests have been performed to evaluate the patient for rheumatic diseases. Antinuclear antibodies (ANA), anti-double-stranded DNA (anti-dsDNA), and antiphospholipid antibody (APL) tests were negative, indicating no underlying rheumatic diseases.

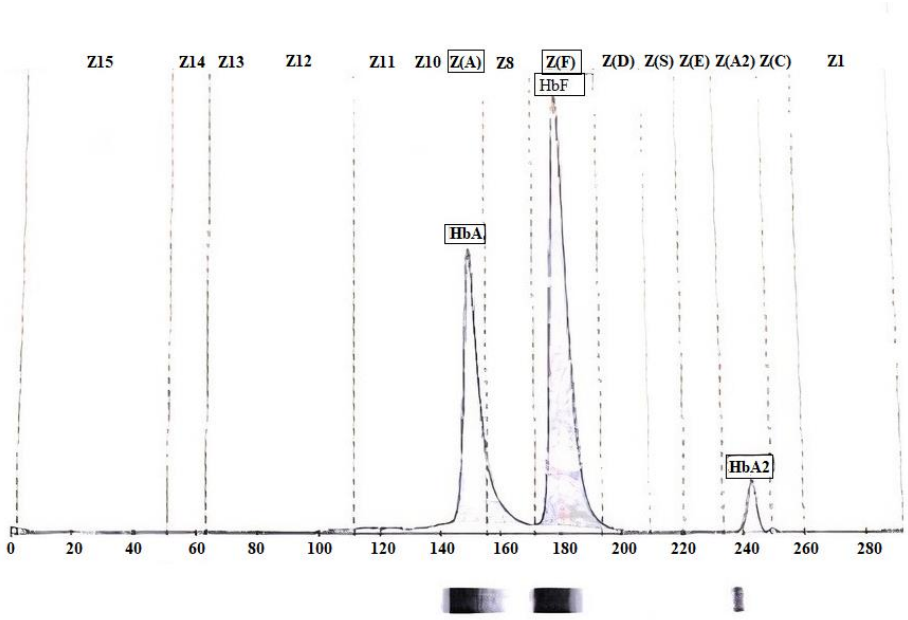
Considering anemia with high ferritin and hepatosplenomegaly, hemoglobin electrophoresis was performed to evaluate the possibility of hemoglobinopathies. The results indicated that HbF makes up 61 percent of the total hemoglobin of the

Table 1. Laboratory tests upon admission

Parameter	Results	Normal range
White blood cell (WBC) (1000/µL)	4.3	4.5-10
Red blood cell(RBC) (10^6/uL)	3.19	4.7-6.1
Hemoglobin (HB) (gr/L)	8.5	14-18
Mean corpuscular volume (MCV) (f/L)	79.6	80-100
Platelet (PLT) (1000 mm^3)	59	150-450
Erythrocyte sedimentation rate (ESR)(mm/H)	14	0-15
Ferritin (ng/mL)	1198	20-300
Reticulocyte (%)	0.7	0.5-.5
Lactate dehydrogenase (LDH) (U/L)	801	180-280
Alanine aminotransferase (ALT) (U/L)	33	Up to 41
Aspartate transaminase (AST) (U/L)	68	Up to 37
Albumin (gr/dL)	4.2	3.4-5.4
Protein (gr/dL)	6.4	6-8.3
Prothrombin time (PT) (Second)	12	11-13.5
International normalized ratio (INR) (Second)	1	Up to 1.2
Partial thromboplastin time (PTT) (Second)	46	25-35

patient (Figure 1). Sampling was performed two days after packed cell transfusion. Since the patient did not use any particular drug, the hereditary persistence of fetal hemoglobin F diagnosis was confirmed based on hemoglobin electrophoresis.

The patient underwent splenectomy due to massive splenomegaly and gastrointestinal complications (Figure 2). The post-splenectomy pathology report stated only an increase in red pulp due to hemoglobinopathy.



Name	%		Normal Values%
HbA	35.6	L	96.5-98.5
HbF	61.0	H	=<2.0
HbA2	3.4		1.5-3.5

Figure 1. Hemoglobin electrophoresis. Hemoglobin F (HbF) makes up 61% of the hemoglobins, and this increase in HbF indicates the persistence of Hbf.

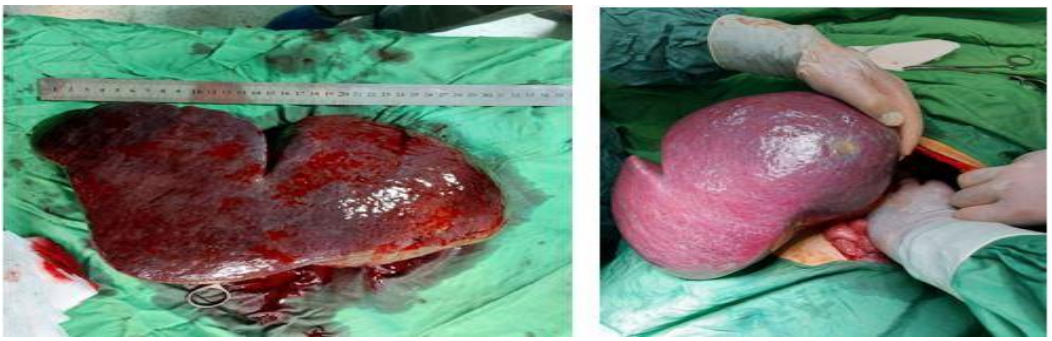


Figure 2. The patient underwent splenectomy due to massive splenomegaly and gastrointestinal complications. The size of the spleen is shown on the left.

DISCUSSION

Hemoglobin F has a high affinity to bind with oxygen, and this specific property of HbFmight be considered a therapeutic effect. Drug-induced production of HbF may be effective in treating other hemoglobinopathies' complications.[3,5,6,12] In a homozygous type of HPFH, the entire hemoglobin chain comprises hemoglobin F and is usually not accompanied by severe symptoms and complications.[13] But if it occurs concomitantly with other hemoglobinopathies such as hemoglobin S or β-Thalassemia, the defect in the other hemoglobin occurs in patients. The range of symptoms depends on the rate of production of HbF and the other hemoglobin.[3,4,6] On account of massive HSM, no history of blood transfusion, and hemoglobin electrophoresis, it can be concluded that the patient has HPFH in association with β-thalassemia intermedia. Hepatosplenomegaly is seen in patients with β-thalassemia intermedia, but blood transfusion is usually unnecessary.[14]

Blood cell count is of paramount importance in laboratory parameters in weight loss.[15] A gastrointestinal examination is performed if there is a low level of Hb and average MCV count on a CBC test.[16] In this patient, no gastrointestinal involvement causing weight loss was detected in medical examination.

Cirrhosis should be assayed as one of the most critical complications of hepatosplenomegaly.[17] Thereupon, our patient was examined for cirrhosis because of depression in two cell lines in CBC and hepatosplenomegaly. Cirrhosis was ruled out due to normal liver function.

Because hepatosplenomegaly is seen in some patients with blood malignancies,[18] bone marrow biopsy was proceeded to evaluate and rule out blood malignancies. There was no evidence in favor of malignant cells in this patient.

The patient was referred to the hematology department, considering anemia with high ferritin, hepatosplenomegaly, low hemoglobin, and normal MCV. Hemoglobin electrophoresis was performed as the last assessment to evaluate the possibility of hemoglobinopathies.[19]

In a patient with HPFH, there could be a normal MCV. Therefore, a missed diagnosis can occur. Eventually, the diagnosis was confirmed with the outcomes of electrophoresis.

This study highlighted the importance of hemoglobin electrophoresis in weight loss and hemoglobinopathies etiology. According to the diagnosis process in this patient, it might be concluded that hemoglobin electrophoresis should be considered a principal assessment, especially in areas where hereditary persistence of fetal hemoglobin is prevalent.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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