Case Report

S-Beta Thalassemia leading to avascular necrosis of left hip joint in a young male - A rare case report

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Abstract

Sickle beta thalassemia is a disorder which represents the double heterozygous state for the Hb-S and the beta-thalassemia genes. The clinical and hematological manifestations of sickle beta thalassemia are highly variable due to existence of two types of genes, beta⁰ thalassemia gene and beta⁺ gene. Beta⁺ gene leads to complete absence of Hb-A levels, whereas beta⁺ gene leads to production of Hb-A levels 10-30%. This disorder is diagnosed by levels of HbS, HbA2 and HbF in Hemoglobin Electrophoresis. We are presenting one such young male patient with features of Sickle Beta⁺ thalassemia who presented with anemia, fatigue and joint pain with characteristic features of avascular necrosis of left hip joint in X-Ray and MRI. For the etiological diagnosis further investigation in the form of capillary haemoglobin electrophoresis and for final confirmation genetic analysis by PCR is done.

Key words

Anemia, Avascular necrosis, Sickle-Beta Thalassemia, Hb Electrophoresis, Genetic analysis by PCR.

Introduction

Hemoglobinopathies are a group of genetic disorders of hemoglobin [1]. Thalassemia and other structural hemoglobinopathies are the major genetic disorders prevalent in certain parts of the world including India. The general incidence of thalassemia trait and sickle cell Hemoglobinopathy in India varies between 3-17% and 1-44% respectively [2] but, because of consanguinity, caste and area endogamy, some
communities show a very high incidence, making the disease a major public health problem in our
country [2, 3]. Inherited disorders of hemoglobin
synthesis are an important cause of morbidity
and mortality worldwide. They place a large
burden on the patients, their families and even
the community. They can be managed by
expensive bone marrow transplantation, which is
always not possible in a developing country like
ours. Population screening, genetic counseling
and prenatal diagnosis can prevent these genetic
disorders; as it has been a success in countries
like Greece, Cyprus and Italy.

Population screening has identified the
prevalence of Beta-thalassemia carrier status as
high as 17% in certain communities in India [4].
The prevalence of hemoglobinopathies varies in
different parts of India. Sickle beta thalassemia
prevalence was found to be relatively low in
contrast to the prevalence of beta-thalassemia
trait in various studies [5-11]. Sickle beta
thalassemia is a disorder which represents the
double heterozygous state for the Hb-S and the
beta-thalassemia genes. The overall prevalence
of sickle beta thalassemia in India is 0.02% with
highest prevalence in Bangalore (0.06%). The
overall prevalence of beta-thalassemia trait in
India is (2.78%) with highest prevalence in
Kolkata (3.64%). The overall prevalence of HbS
trait in India is 0.70% with highest prevalence in
Vadodara (2.94%). The overall prevalence of
HbE trait in India is 3.63% with highest
prevalence of 23.9% in Dibrugarh [5]. This case
is presented due to uncommon occurrence of
sickle beta thalassemia.

Case report
A 40 year old Hindu male from Jaipur, Rajasthan
presented with acute onset of intermittent fever
with chills, rigor, backache, fatigue and joint
pain since one week. He did not have any other
complaints suggestive of cardiac, respiratory and
haematological disorders. There is no significant
family or personal history. On examination, he
was conscious, oriented and mildly icteric with
mild pallor. Other systemic examinations were
unremarkable. Radiological findings on X-Ray
showed avascular necrosis in left femoral head
(Figure - 1) and MRI showed avascular necrosis
in left hip joint, stage 4.

Figure – 1: X-Ray showing avascular necrosis of
left femoral head.

His complete blood count revealed anaemia Hb
10.1 gm%, RBC’s 5.14 million/cubic mm, MCV
56.1 fl, MCH 19.3, MCHC 34.5, RDW 21.6%
with normal total count and platelets with ESR
10 mm/hr. Peripheral smear showed microcytic
hypochromic RBC’s with moderate
anisopoikilocytosis in the form of target cells,
eliptocytes, sickle cell, few fragmented RBC’S
with polychromatic cells. Reticulocyte count was
4.7%.

His biochemical investigations showed normal
liver fuction and renal function test. Serological
tests like coomb’s test, ELISA for HIV, dengue
and malaria card test, VDRL, ASLO Titre and
RF were all negative. Immunological test like
Quantitative CRP is 22.6mg/dl and is positive.

In view of anaemia and sickle cells in peripheral
smear, patient was investigated further and hence
sickling test and capillary Haemoglobin
electrophoresis was ordered. Sickling test came positive with Hb electrophoresis revealing HbS 73.2%, HbA level 2.7%, HbA2 4.8%, HbF 19.3% suggestive of S-Beta Thalassemia (Figure - 2). We further advised him for parental screening and DNA analysis.

**Figure – 2:** Capillary Hemoglobin Electrophoresis shows HbS 73.2%, HbA2 4.8%, HbF 19.3% and HbA 2.7% suggestive of S-Beta Thalassemia.

On Allele specific Polymerase chain reaction codon 6 (A-T) mutant allele detected which confirms sickle cell carrier and IVS 1-5 (G-C) mutant allele detected which confirm a Beta thalassemia minor. The genetic study confirms the patient is compound heterozygous for Beta thalassemia and sickle cell and is likely to suffer from disease.

**Discussion**
Differentiation of sickle cell anaemia and some of the sickle beta thalassemia syndromes has to be done carefully due to close similarity of symptoms and laboratory features. Mean corpuscular volume (MCV) may be normal or low in all thalassemia syndromes. Symptoms and blood picture of patients with HbS beta⁰ thalassemia are similar to those of homozygous sickle cell disease (HbSS) with microcytosis, marked hypochromia, target cells and sickle cells in the peripheral smear and can be differentiated only by Hb electrophoresis. The Hemoglobin Electrophoresis pattern of the sickle-beta⁰ thalassemia consists almost totally of HbS with a mild increase in HbF and HbA2 and absent HbA [12]. They also have similar symptoms of homozygous sickle cell disease like frequent painful vasoocclusive crises, hand-foot syndrome and aseptic necrosis of bone with autosplenectomy. The beta⁺ thalassemia type consists of Hb-S, along with 10-30% of Hb-A and a mild increase in Hb-F and Hb-A2. Patients with HbS beta⁺ thalassemia are characterized by mild anemia associated with moderate splenomegaly, in contrast to autosplenectomy of sickle cell anaemia [13]. Sickle beta⁺ thalassemia patients have Hb-S composition of approximately 60–70%, Hb-A 25%, and an elevated level of Hb-A2 [14]. They also can have few symptoms like occasional vasoocclusive crises and aseptic necrosis of the bone. Patients with HbS-HPFH (HbS and Hereditary Peristence of Fetal Hemoglobin) are asymptomatic and not anemic. HbA2 levels are elevated above 3.5% in HbS beta thalassemia and are low or normal in patients with HbS-HPFH. HbF level in patients with HPFH are generally more than 20% [15]. Thus a careful evaluation of symptoms and signs along with Hb electrophoresis helps us to distinguish between various sickle beta thalassemia syndromes.

**Conclusion**
Hemoglobinopathies are a group of genetic disorders of hemoglobin in which there is abnormal production or structure of the hemoglobin molecule. These hereditary disorders are major public health problem in many parts of the world including India. The clinical spectrum of the disorders varies from asymptomatic

conditions to serious disorders like thalassemia major that requires regular blood transfusions and extensive medical care. As per World Health Organization (WHO) report, around 7% of the global population carries an abnormal haemoglobin gene [16].

As in this 24 year old male who presented with pain in left pelvic girdle and fatigue was diagnosed by MRI as a case of avascular necrosis of left hip joint stage 4 and was further investigated for the etiology by haematological parameters which suggested S-Beta thalassemia. Further DNA analysis was done which revealed codon 6 (A-T) mutant allele which confirms sickle cell carrier and IVS 1-5 (G-C) mutant allele which confirms Beta thalassemia minor. The genetic study confirms the patient is compound heterozygous for Beta thalassemia and sickle cell and is likely to suffer from disease.

References

