International Journal of Advances in Medicine
Sharma KV et al. Int J Adv Med. 2022 May;9(5):616-618
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20221101

Case Report

A rare case of bronze diabetes in a patient with thalassemia

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Received: 13 March 2022
Accepted: 02 April 2022

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ABSTRACT

Secondary haemochromatosis (also known as bronze diabetes) is a perilous medical condition that can occur as a complication of frequent blood transfusions. Thalassemia major which occurs due to a decrease in the beta globulin chain can lead to severe anemia, extramedullary hematopoiesis and splenomegaly. Because of this, the affected patients required continuous blood transfusions throughout their life and as a consequence, it may lead to iron overload. A 26-year-old male presented with a complaint of darkening skin, joint pain and fever. He was a known case of thalassemia major and was undergoing blood transfusions three times a week. Further laboratory findings revealed decreased hemoglobin, abnormal liver function tests and increased blood glucose levels. The patient was managed with IV insulin and chelation therapy. The patient responded to treatment and was better on subsequent follow-up. The diagnostic and therapeutic challenges along with the epidemiological data emphasize the need of raising the awareness of physicians to this devastating condition.

Keywords: Bronze diabetes, Chelation therapy, Thalassemia major, Iron overload

INTRODUCTION

Hemochromatosis is a condition in which there is an abnormal deposition of iron in specific organs. There are two types of hemochromatosis; primary and secondary. primary haemochromatosis is a hereditary disorder while Secondary hemochromatosis is transfusion-related. Patients with beta-thalassemia where both alleles of the gene are affected suffer from severe anemia starting at approximately six months of their age after fetal hemoglobin (HbF) reserve is depleted.[1] As a result, patients also suffer from secondary hematopoiesis and splenomegaly. Therefore, patients require frequent blood transfusions.

Due to continuous blood transfusions, excess iron accumulates in the tissues and forms reactive oxygen species resulting in organ damage. Prophylactic chelation therapy is started in patients who receive greater than ten units of packed red blood cells.[2] In our case, the patient was suffering from multiple end-organ damages due to iron deposition. He was managed with chelation therapy and phlebotomy and his symptoms improved after adequate treatment.

CASE REPORT

A 26-year-old male patient presented with the complaint of darkening of skin for three months, increased thirst and urination for two months, joint pain in hands since one hand a half month, Feeling of weakness for one month and dull abdominal pain for one week. Upon further history taking, the patient and his relatives were informed that he was a known case of thalassemia major which was diagnosed when he was one year old. He had been requiring frequent blood transfusions for the last twenty years and past two years, he had been undergoing blood transfusions two to three times a week. Physical examination revealed that the abdomen was soft and tender in the right upper quadrant upon

palpation and the liver was palpable five centimeters below the right costal margin indicating hepatomegaly. Pelvic examination revealed small firm testes. There was mild to moderate pain when the patient was asked to move the extremities. The patient also reported stiffness in metacarpophalangeal joints. The skin of the patient was diffusely hyperpigmented. Large areas of hyper-pigmentation were seen in the dorsal palms, legs and back of the patient.

Table 1: Parameters indicative of the diabetic status.

Laboratory investigations	Values	Reference range
Random blood sugar (RBS) (mg/dl)	223	70-140
PP2BS (post-prandial blood sugar) (mg/dl)	322	100-140
Fasting blood sugar (FBS) (mg/dl)	213	70-100

Table 2: Hematologic indices.

Laboratory Investigations	Values	Reference range
Haemoglobin (g/dl)	10.6	12-16
PT	16.0	15.2
INR	1.64	
APTT (seconds)	33.5	26.1-34.5

Table 3: Liver function tests.

Laboratory Investigations	Values	Reference range
AST (U/l)	100	5-40
ALT (U/l)	69	5-40
ALP (U/l)	223	40-129

To get further clarity on right upper quadrant abdominal pain, ultrasonography was performed, which revealed enlarged liver; 16 cm (Figure 1). The patient's blood sample was collected and laboratory investigations were: serum ferritin was >15000 ng/dl and transferrin saturation was 98%. To confirm the diagnosis, a liver biopsy sample was collected and prussian blue staining showed deposition of iron in the sample (Figure 2). The diagnosis of secondary hemochromatosis was confirmed. The patient was started on injection human mixtard (30/70); 28 U before breakfast and 18 U BD to regulate elevated glucose levels. Chelation therapy was also started with tablet desferoxamine 500 mg (2000 mg/day) and tablet deferiprone 500 mg (2500 mg/day). Multivitamins along with vitamin C were also started. The patient responded to treatment and was symptomatically better on subsequent follow-up.

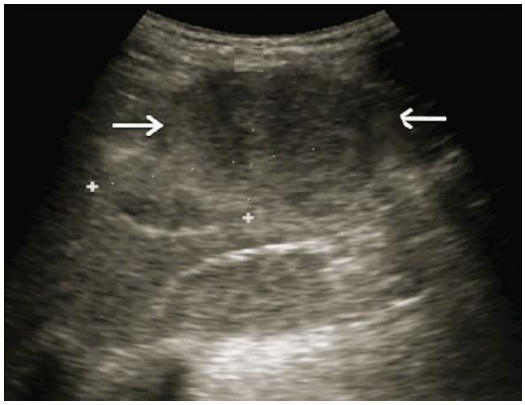

Figure 1: USG Showing enlarged liver.

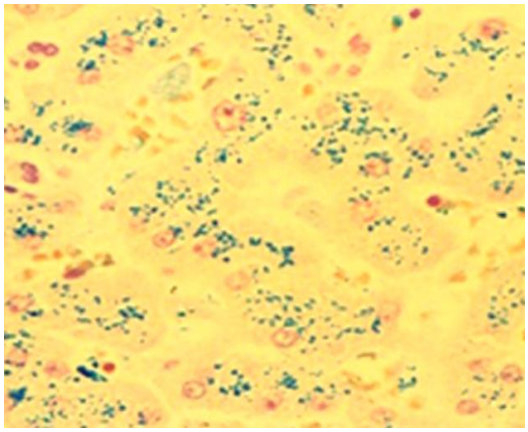

Figure 2: Prussian blue staining of liver biopsy sample.

DISCUSSION

Patients with thalassemia major need routine blood transfusions. Each unit of blood contains 200-250 mg of iron.[3] Deposition of excess iron can occur in several organs including the pancreas. This in turn results in damage to the pancreas and subsequent diabetes mellitus. This type of diabetes was called bronze diabetes due to the greyish color of skin developed from the deposition of excess iron. The American association for the study of liver diseases recommends that every patient with iron overload should be evaluated for Haemochromatosis even in the absence of symptoms.[4] Diagnosis of hemochromatosis were confirmed when the transferrin saturation was >45% and ferritin levels were elevated. Tubagus et al also reported a relationship between the increase in serum ferritin levels and T2 MRI of the liver in thalassemia major cases.[5] Monitoring of iron chelating therapy is mainly done by liver transaminases, bilirubin, creatinine, ferritin and cardiac function tests. Several studies have shown that monitoring of these parameters can help in the early detection of secondary hemochromatosis and thus starting chelation therapy early on.[6] To date, the best example of diabetes due to transfusional iron overload is in thalassemia major patients, although other causes like bone marrow

transplantation warranting repeated blood transfusion have also reported diabetes as a complication.[7]

CONCLUSION

Patients with thalassemia major require regular blood transfusions which predisposes them to iron overload. Therefore, period assessment of serum iron, serum ferritin, and transferrin saturation is required. This would help in preventing secondary hemochromatosis and additional burden in the management. Regular monitoring of the glycemic index is also required in patients with Bronxe diabetes to avoid complications from hypoglycemia and hyperglycemia.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Sharma KV, Khandhedia PB, Sharma VH. A rare case of bronze diabetes in a patient with thalassemia type of article: case report. Int J Adv Med 2022;9:616-8.