## Pituitary Hemochromatosis in a Transfusion-Dependent Beta Thalassemia Patient: A Case Presenting with Endocrine Dysfunction and Diabetic Ketoacidosis

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## Key clinical message:

In patients with transfusion-dependent beta thalassaemia, this example emphasises the significance of early detection and treatment of endocrine dysfunction caused by pituitary hemochromatosis. This example highlights the possibility of multisystem iron overload and highlights the need of MRI in identifying pituitary involvement. The patient presents with panhypopituitarism and diabetic ketoacidosis. Endocrine replacement and timely chelation therapy can produce notable clinical improvements.

## Abstract

Beta thalassemia is an inherited blood disorder caused by defective synthesis of the beta globin chains of hemoglobin. Patients mostly present between six months and two years of age. Blood transfusions and iron chelation therapy remain the mainstay of treatment in low socioeconomic countries like Pakistan. However, this can lead to hemochromatosis in major organs of the body including the endocrine system. We present a case of a young female, known case of beta thalassemia with history of regular blood transfusions who presented with endocrine dysfunction and diabetic ketoacidosis.

## Introduction:

Beta thalassemia is an inherited blood disorder caused by defective synthesis of the beta globin chains of hemoglobin and has two clinically significant forms beta thalassemia major and intermedia, characterized by absent or reduced formation of beta globin chains, respectively (1). It is mainly prevalent in the Mediterranean, Middle East, and Southeast Asian regions, however, due to migration, its prevalence is now increasing in Europe and North America. (2-4)

Patients who have beta thalassemia major mostly present between six months and two years of age usually with complaints of pallor due to anemia, weakness and stunted growth (2). The only curative treatment currently present for this condition is hematopoietic stem cell transplantation

(5). However, in countries with low socioeconomic status (including Pakistan) the option of stem cell transplant is not readily available and therefore blood transfusions and iron chelation therapy remains the mainstay of treatment in these countries (6).

Inadequate chelation therapy can lead to excessive accumulation of iron i.e hemochromatosis, in major organs of the body such as heart, liver, pancreas and endocrine system. The consequence of iron toxicity in the heart is cardiomyopathy which ultimately leads to heart failure and is the leading cause of death in transfusion dependent thalassemia patients (7). One of the late complications of iron toxicity is hemochromatosis of the central nervous system including iron deposition in the choroid plexus and pituitary gland which leads to hypogonadotropic hypogonadism and short stature due to growth hormone deficiency (8).

## Case Presentation:

**History and examination**

We present a case of a 25 year old female, known case of beta thalassemia with history of regular blood transfusions. She presented to our emergency department with complaints of yellowish discoloration of skin for 10 days, abdominal pain for 5 days and altered level of consciousness for 1 day. On examination, the patient had altered mentation but was vitally stable.

**Laboratory and radiology investigations**

Initial management included maintenance of intravenous lines and lab workup was sent which included detailed report of urine, arterial blood gasses and electrolytes levels. Her serum glucose levels were elevated and arterial blood gasses showed an acidotic picture with raised anion gap. Urinary ketones came out to be positive and hence diagnosis of diabetic ketoacidosis was made and relevant treatment was given. Her iron work up showed raised ferritin levels and endocrinological workup was suggestive of panhypopituitarism. Contrast enhanced MRI brain with sella protocol was done as a part of management plan which showed hypointense signal in the anterior pituitary gland on both T1 and T2-weighted sequences, with signal drop out on susceptibility sequence. No diffusion restriction or abnormal enhancement was demonstrated in the pituitary gland.

These findings were concluded as pituitary hemochromatosis (Figure 1).

**Management**

She was admitted to a special care unit for further management and work up. Patient was started on treatment for diabetic ketoacidosis and chelation therapy with deferoxamine.

**Outcome and followup**

Throughout hospital stay there was significant improvement in patient's symptoms and clinical status. She was discharged after stabilization on levothyroxine and oral hydrocortisone and advised to follow up regularly as an outpatient.

## Discussion:

Beta thalassemia is the most common genetic hematologic disorder which is clinically categorized into major, intermediate and minor subclasses depending on the severity of symptoms. The only curative treatment for beta thalassemia is hematopoietic stem cell transplant. However, due to its cost and availability, it is not usually the treatment of choice in low socioeconomic countries and these patients are generally treated with lifelong blood transfusions and iron chelation. As a result, problems related to transfusion hemosiderosis are now a leading cause of morbidity and mortality in thalassemia patients.

Cardiomyopathy secondary to iron deposition in the cardiomyocytes causing arrhythmias and heart failure is now the leading cause of mortality in transfusion dependent beta thalassemia patients.

Ucler et al. in 2015 and Lu et el. in 2001 described cases of pituitary iron overload manifesting as hypogondotropic hypogonadism (9,10).

In a multicenter study cinducted in Tehran, hypothyroidism was reported in 7.6% of the patients (11).

In a study reported by Nameq et al (12), higher rates of echographic abnormalities were encountered in adult transfusion dependent thalassemia patients when compared to a similar cohort of non transfusion dependent thalassemia patients.

Multiple endocrinological organs are also likely to be affected by the iron overload in transfusion dependent thalassemia (TDT) patients, leading to diabetes mellitus, hypogonadism, hypothyroidism and other such abnormalities.

Pituitary gland, also called the master gland, plays a critical role in regulation of multiple physiology functions of the body. However, in cases of iron overload secondary to chronic transfusions and inadequate chelation therapy, pituitary hemochromatosis is not uncommon, resulting in stunted growth and delayed puberty. MRI is an important diagnostic imaging modality to detect pituitary iron deposition and the most sensitive sequences for this purpose are T2\* and SWI. Loss of signal of anterior pituitary on T2 weighted sequence without any enhancement is also a useful radiological sign when assessing for pituitary iron deposition (13). Hyperintense signal of the posterior pituitary is usually preserved.

Similar findings were reported by Fuji et al (14) in which multiple red blood cell transfusions due to anemia secondary to alcoholic cirrhosis and lymphoma lead to pituitary iron deposition.

In our case the patient was transfusion dependent due to thalassemia with significantly raised serum ferritin levels of 12207 ng/ml (normal: 10-120).

In conclusion, MRI features of the CNS manifestations of iron overload, particularly in the pituitary gland, are highly important for timely management and favorable outcomes in patients with thalassemia. This case report provides a good example of such an instance where timely identification of this condition resulted in adequate management in this patient.

# Protection of humans and animals:

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association.

# Data confidentiality:

The authors declare having followed the protocols in use at their working center regarding patients’ data publication.

# Patient consent:

Written informed consent was obtained from the patients to publish the case series.

# Conflicts of interest:

All authors report no conflict of interest.

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