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Case Report

Biochemistry Section

Bronze Diabetes

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ABSTRACT

Thalassemia is a group of disorders characterized by deficient production of the β-globin sub unit of hemoglobin. The mandatory blood transfusions in patients with thalassemia to maintain adequate erythrocyte levels, leads to iron overload. The prevalence of diabetes in patients with thalassemia varies from 6 to 14%. We here by present a known case of thalassemia major in an 18 year old boy. He was diagnosed with thalassemia before the age of one year and is on regular blood transfusion every two weeks since then. The repeated blood transfusion is one of the common causes for haemochromatosis. Iron overload initially leads to glucose abnormalities such as insulin resistance and hyperinsulinemia, which is followed by impaired secretion of insulin. Diagnosed as a case of bronze diabetes, this patient is on insulin therapy for the last two years. Currently the patient is on iron chelation therapy at Kasturba Medical College Hospital, Mangalore, Karnataka, India.

Keywords: Serum ferritin, Thalassemia, Type I diabetes

CASE REPORT

We here by present a case of thalassemia major in an 18-year-old boy, (diagnosed before the age of one year) with bronze diabetes (diagnosed two years back when the patient presented with an episode of diabetic ketoacidosis). Informed consent was obtained from patient's mother. His complaints were joint pain and calf region pain aggravating on bending forwards and radiating to foot (dorsal aspect). He had poor endurance, easy fatigability with daily routine activities and was admitted for poor glycemic control at KMCH AT.

Patient is immunized to date, with developmental history appropriate to age and on regular blood transfusion, insulin and iron chelation therapy. History of death of a sibling due to complications of thalassemia in the past.

ON EXAMINATION

Patient was compliant, active and pale. Dry and scaly skin of darker complexion with no appreciable change in colour noted. Flattened nasal bridge and discolouration of teeth was seen. No icterus/ cyanosis/ pedal oedema/ clubbing/ enlarged lymph nodes.

SHORT STATURE

41.2 kg weight and 148 cms height (less than 3rd centile for age); head circumference: 52 cms;afebrile; HR: 86/ min; RR: 24/ min; BP: 100/60 mmHg;

PER ABDOMEN

Soft, liver palpable 5 cm below the right costal margin, splenomegaly 4 cm below left costal margin. Systemic examination had no detectable abnormality. Various investigations were done, which are tabulated in [Table/Fig-1-4].

MANAGEMENT

Serum creatinine, electrolytes were within normal range. CT scan brain was normal. Patient was treated with human mixtard (30/70) 28U-0-18U, multivitamin along with vitamin C preparations. Iron chelation therapy was initiated.

INVESTIGATIONS

[Table/Fig-1-4]

Biochemical parameters	Values	Reference Range
RBS	612 mg/dl	70-140 mg/dl
PPBS	567 mg/dl	100-140 mg/dl
HbA1c	12.6 %	Upto 6%
Insulin	4.25µU/ml	2.6-24.9µU/ml
Ferritin	10,297 ng/ml	30-400 ng/ml

[Table/Fig-1]: Parameters indicative of diabetic status and iron stores

Heamatological parameters	Values	Reference Range
Hb	9.1 g/dl	12-16 g/dl
PT	23.5 (15.0)	13.7-16.8 sec (15.2)
INR	1.66	
APTT	45.3 (31.5)	26.1-34.5 sec
Peripheral smear: Normocytic normochromic anemia		

[Table/Fig-2]: Status of haematological indices

LFT	Values	Reference Range
Total protein	6.2 g/dl	6-8.3 g/dl
Albumin	3.5 g/dl	3.2-5.5 g/dl
AST	149 U/l	5-40 U/l
ALT	119 U/l	5-40 U/l
ALP	243 U/l	40-129 U/l

[Table/Fig-3]: Status of Liver Function Tests

Lipid Profile	Values	Reference Range
TC	130 mg/dl	Upto 200mg/dl
LDL	76.3 mg/dl	Upto 100mg/dl
HDL	29 mg/dl	40-60 mg/dl
TG	133 mg/dl	Upto 150mg/dl
VLDL	26.6 mg/dl	Upto 40 mg/dl
TC/HDL	4.48	2.5-5

[Table/Fig-4]: Status of lipid profile

DISCUSSION

Studies have shown that thalassemia major patients, being dependent on regular blood transfusion are prone to iron overload which can affect various endocrine organs, heart, liver etc. over a period of time. Elevated ferritin concentration was considered as a marker for high body iron stores in this case [Table/Fig-1] which is in accordance with Eghbali et al., who reported a relationship between increase in serum ferritin levels and T2*MRI of liver in Thalassemia major cases [1]. The most frequently used indicator of body iron stores is the serum ferritin level in the investigative studies done so far [2,3].

Several studies over past few years have shown the importance of monitoring iron stores by serum ferritin estimation and hepatic/cardiac MRI which can help in early diagnosis of iron overload and timely intervention by iron chelation therapy can be instituted thus improving survival in such patients [4]. Iron chelation is a treatment option not only for thalassemia patients, but also for those with lower-risk myelodysplastic syndrome requiring long term transfusion therapy [5].

The association between body iron stores and risk of diabetes have been demonstrated in few prospective studies [2]. Study by Gattermann suggests that serum ferritin elevation in their study group was a marker of the metabolic syndrome with hepatic steatosis and insulin resistance, and not of iron overload, however the direct pathogenic mechanisms were not conclusive [6].

This iron overload can also damage pancreas leading to the development of diabetes as diagnosed in this case by the biochemical parameters [Table/Fig-1]. This type of diabetes is called “Bronze Diabetes” due to the greyish colour of skin developed from deposition of excess iron. However, no appreciable change in skin colour was noted in this case due to darker complexion of the patient. This patient also had frequent episodes of hypoglycaemia and hyperglycemia which required repeated hospitalisation thus emphasising the importance of regular monitoring of blood glucose in such cases.

The relationship between iron and diabetes became first evident from the studies of clinical cases like hereditary hemochromatosis and transfusional iron overload. Till 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

Frequent blood transfusion is the available therapeutic option in thalassemia which requires continuous periodic assessment of iron overload by estimation of serum ferritin to prevent foreseen long term complications which are of concern and adds to the burden in the management. Regular monitoring of blood glucose in bronze diabetes is also required to prevent further complications arising from episodes of hypoglycemia and hyperglycemia.

REFERENCES

[1] Eghbali A, Taherahmadi H, Shahbazi M, Bagheri B, Ebrahimi L. Association between serum ferritin level, cardiac and hepatic T2-star MRI in patients with major β-thalassemia. *Iran J Ped Hematol Oncol*. 2014;4(1):17-21.

[2] Montonen J, Boeing H, Steffen A, Lehmann R, Fritsche A, Joost HG, et al. Body iron stores and risk of type 2 diabetes: results from the european prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam study. *Diabetologia*. 2012;55(10):2613-21.

[3] Shahramian I, Razzaghian M, Ramazani AA, Ahmadi GA, Noori NM, Rezaee AR. The Correlation between Troponin and Ferritin Serum Levels in the Patients with Major Beta-Thalassemia. *Int Cardiovasc Res J.* 2013;7(2):51-55.

[4] Veríssimo MP, Loggetto SR, Fabron Junior A, Baldanzi GR, Hamerschlak N, Fernandes JL, et al. Brazilian Thalassemia Association protocol for iron chelation therapy in patients under regular transfusion. *Rev Bras Hematol Hemoter*. 2013;35(6):428-34.

[5] Gattermann N. The treatment of secondary hemochromatosis. *Dtsch Arztebl Int.* 2009;106(30):499-504.

[6] Brudevold R, Hole T, Hammerstrøm J. Hyperferritinemia is associated with insulin resistance and fatty liver in patients without iron overload. *PLoS One*. 2008;3(10):e3547.

[7] Simcox JA, McClain DA. Iron and diabetes risk. *Cell Metab*. 2013;17(3):329-41.

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