Beta Thalassemia Major with Diabetes Mellitus: A Case Report

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Abstract:

Thalassemia occurs due to defects in normal hemoglobin production. Globally it is most common inherited anaemia. Diabetes is a complication of b-thalassemia major. We report a case of Diabetes mellitus in a known case of beta thalassemia major. Patient had undergone splenectomy 1 year back. Patient is taking chelating agent Defasirox 1000mg orally once a day in the morning. Family history reveals, born through third degree consanguineous marriage. The patient was then subjected for laboratory examination reveals BSL was 490, urine ketone 2+, urine sugar 3+, ABG was normal, HbA1c was 13 & 3 month old report of serum ferritin 1200 ng/dl. TFT and GH studies normal. Multidisciplinary management was instituted. Blood sugar level got controlled over subcutaneous insulin. Patient may have landed in Diabetic ketoacidosis but was promptly diagnosed & treated. This case is presented for its rarity. Due to increase in life expectancy of patient with thalassemia major, patient will expose more years of hyperglycemia and diabetes. Sustaining metabolic control and controlling cardiovascular risk factors helps to prevent future complications.

Key Words: Thalassemia, Diabetes Mellitus, Iron chelation, Blood transfusion, Hyperglycemia

Introduction:

Thalassemia occurs due to defects in normal hemoglobin production. Globally it is most common inherited anaemia. Patients with severe form of thalassemia i.e. Thalassemia major or transfusion dependent thalassemia require regular blood transfusions to maintain an appropriate hemoglobin level. Although, life expectancy of Thalassemia Major patients has improved substantially due to regular blood transfusions but there is increased risk of secondary hemosiderosis due to increase iron overload and multiple organ dysfunctions due to excess iron deposition causes cardiomyopathies, endocrinopathies, gonadal insufficiency and osteoporosis as a complications of thalassemia major.[1,2]

This disease is presented as chronic anaemia and iron overload due to blood transfusion therapy. Excessive iron overload and inadequate chelation leads to deposition of excess iron in various tissues mainly heart and liver and endocrine glands. Other factors contributing to toxicity of iron including long term hypoxia due to chronic anaemia, individual susceptibility and risk for viral infections and it also contribute to the endocrinal dysfunction.[3-4] Detection of the exact prevalence of endocrinopathies in thalassemia patient is challenging because of different studies which partly relates its association with ages of patient and suboptimal chelation therapy. Prior studies shows the major endocrine complications are delayed puberty or hypogonadism and growth retardation, hypothyroidism, hypoparathyroidism, osteoporosis and adrenal insufficiency, diabetes mellitus seen among patients with thalassemia major.[5]

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Diabetes is a major complication of b-thalassemia major. The prevalence varies from 1% to 21%.[6,7] This variability in estimation of prevalence is partly relates to the early introduction of iron chelation therapy and its optimal use as well as relates to the ages of patients being studied, as less prevalence seen in younger patients. There are various risk factors may cause development of diabetes in thalassemia. Transfusional iron overload is major etiological factor responsible for impairing pancreatic b-cells. Impaired glucose metabolism mainly seen in patients with poor compliance with chelating agent and advanced age during initiation of chelation therapy.[8] Other etiological factors responsible for altered glucose metabolism are impaired b-cell insulin secretion,[9] autoimmunity,[10] insulin resistance secondary to liver disease and Hepatitis C virus infection.[11] During management of patients with diabetes and thalassemia certain issues should be considered. First, early detection of impaired glucose metabolism and diabetes and regular screening with annual oral glucose tolerance tests from puberty or from age 10 years if there is a positive family history according to UK and international thalassemia management guidelines.[12,13] This allows for early treatment of hyperglycemia but also helps to increase potential of iron chelation therapy, which may improve glycemic control in patients.[14]

Case Report:

17 years old male child was admitted in PICU for history of polydipsia, polyuria, and weight loss of 6kg in last 1 month. Patients' past medical history revealed that my patient is a known case of β Thalassemia major since he was one and a half year old, for which he has been undergoing blood transfusion since then. Patient had undergone Splenectomy 1 year back. Patient is taking chelating agent Defasirox 1000mg orally once a day in the morning. Family history reveals, born through third degree consanguineous marriage. Other siblings are normal. On general examination, he was under-built, under-nourished with a short stature, weight 31.7kg, height 148cm with BMI 14.47kg/m2, evidence of icterus, and yellow tinged fingernails also present. His skin was ashen grey in color. Head and Neck examination revealed that he is having depressed cranial vault, frontal bossing, maxillary expansion, retracted upper lip and saddle nose, a classical "Chipmunk facies". Patient was in some dehydration. As patient was new to us detailed history was taken.

The patient was then subjected for laboratory examination reveals BSL was 490, urine ketone 2+, urine sugar 3+, ABG was normal, HbA1c was 13 & 3 month old report of serum ferritin 1200ng/dl. All other routine reports were normal, TFT, GH studies were normal. 2 D echo was not done due to non affordability issue but planned to do on upcoming follow up.

Patient was treated with increased dose of defasirox & was started on subcutaneus insulin for hyperglycaemic control. Blood sugar level got controlled over subcutaneous insulin. Patient may have landed in Diabetic ketoacidosis but was promptly diagnosed & treated.

Patient also given 1 packed cell volume for low Hb.

Patient advised to take subcutaneous insulin regularaly & do regular follow-up. Patient was also refered to higher center for combination chelation therapy for better control of iron overload.

Discussion:

The age of onset of diabetes in our patient is 17 years. This suggests that increased tissue iron overload with suboptimal chelation can impaires b-cell function at young age. It is necessary that effective iron chelation therapy is started early. Patients like tolerance and treatment consistency and adherence to chelation therapy regimens, must be discussed, addressed and treated.

Patient is on subcutaneous huminsulin R 5 units thrice a day and subcutaneous huminsulin N 8 units twice a day. Improvements in metabolic control were seen in patient after one month of follow-up (equivalent to a reduction in HbA1c of 0.7%). A reduction in serum ferritin level by 33% indicates reduction in tissue iron overload.

Thalassemia patients have complex medical management. In addition to managing thalassemia and related complications, the diagnosis of diabetes causes physical and mental trauma in patient with thalassemia major.

Psychological issues like anxiety and depression have been seen among these patients. Therefore management of diabetes in patients with thalassemia is challenging and should be tackled carefully. Clinics where both diabetic and thalassemia management provided together are more effective and provide high quality effective care in these patients.[15]

Glycemic control, prevention of micro and macro vascular complications and decrease in cardio vascular risk are main objectives for management of these patients. Intensive chelation therapy with des-40 Journal of the Ceylon College of Physicians Karuppiah D ferrioxamine and deferiprone are useful to gain β-cell function and may improve insulin secretion by pancreatic cell and increase glucose tolerance and reduction in iron deposition in organs like liver. Multiple studies conclude that an oral chelator deferasirox is effective in thalassemia patients.[16] In addition, weight loss and exercise are both established ways to reduce insulin resistance and prevent progression to diabetes.[17]

Insulin is used in patients with severe hyperglycemia and who are symptomatic and insulin deficient. There are two common treatment protocols. Premixed insulin is given before breakfast and evening meal twice a day. The second basal bolus regimen contain slow acting basal insulin (Isophane, Glargine or Levemir) once a day and rapid acting prandial insulin given with each meal thrice a day. The choice of insulin depends on many factors including the availability, affordability and preference by patient.18

Conclusion:

This was an overall improvement in case. Increasing life expectancy of patients with thalassemia will also increase years of suffering with hyperglycaemia and diabetes. Metabolic control and controlling cardiovascular risk factors helps for preventing diabetic complications in future. Early detection of impaired glucose metabolism as well as diabetes and it's regular screening with annual oral glucose tolerance tests from puberty or from age 10 years are useful for prompt treatment of hyperglycemia and also prevent progression of prediabetes to overt diabetes and diabetic ketoacidosis.

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