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ENDOCRINE DYSFUNCTION IN β THALASSEMIA – A CLINICAL REPORT

Swati Bhattacharyya , Sanghamitra Chakraborty, Sharmistha Chatterjee

Department of Biochemistry, Medical College, Kolkata, West Bengal, India

E-mail of Corresponding Author: drsanghamitra84@gmail.com

ABSTRACT

Hypoparathyroidism is one of the rare endocrinopathy in β thalassemic patients as a consequence of iron overload. Hypogonadotropic hypogonadism, hypothyroidism are still prevelant in β thalassemic patients inspite of intensive chelation therapy. Though regular blood transfusion may increase the life expectancy, yet growth disturbances and growth hormone defects in these children may be noticed. We present a rare case of multiple endocrinological defects following splenectomy in a known case of β thalassemia noted during biochemical investigations. The literature regarding the prevalence of hypoparathyroidism has been reviewed. Moreover, literature survey depicts that serum concentration of ferritin does not predict the occurrence of hypoparathyroidism, thus the case being reported.

Keywords: Hypoparathyroidsm, Endocrinopathy, β Thalassemia, Hypogonadotropic Hypogonadism

INTRODUCTION

The inherited disorders of haemoglobin are the commonest single-gene disorders, with an estimated carrier rate of 7% among the world population.[1] Though regular blood transfusion and intensive chelation therapy may increase the survival of thalassemia affected child, yet growth disturbances and endocrinopathy like hypogonadotropic hypogonadism,diabetes mellitus, hypothyroidism and rarely hypoparathyroidism in these children may be noticed.[2,3,4]Hypoparathyroidism may or may not be associated with hypocalcemia and present with neurological symptoms like tetany, carpopedal spasm, paresthesia.[5,6,] Majority of the hormonal defects like growth hormone-insulin like growth factor axis, hypogonadotropic hypogonadism is solely from iron overload and later age of initiation of chelation therapy. So, regular hormonal profile assay in thalassemic patients is warrented.

CASE REPORT

A 14 year old girl, known case β thalassemia, presented to the outpatient department of Medical College Hospital, Kolkata with carpopedal spasm and fever for last two months. About 1 year back she had a history of splenectomy because of increased requirement of blood transfusion and hypersplenism. She was diagnosed to be suffering from β thalassemia major by clinical symptoms and HPLC of Hemoglobin at the 2nd year of birth. She received repeated monthly blood transfusions there after till next 10 years. There was no family history of haemolytic anaemia. Both the parents of the girls were found to be thalassemia carrier on screening by HPLC.

On general examination, the girl was of thin built with height 90cm and weight 18 kilograams (expected 22kgs). The girl was having moderate degree of pallor with mild icterus. The facies was with high arched palate, prominent malar prominences and frontal bossing. There was severe bowing of both the legs and a scar of splenectomy in the left hypochondrium. The left

axillary lymph node were enlarged. Fine needle aspiration cytology, however, suggested reactive hyperplasia of lymph node due to infection. On systemic examination, the liver was just palpable and other systems were within normal limit. The girl had no pubertal changes (Tanner I) and did not attained menarche till then.

As admitted with carpopedeal spasm she was treated with 2gm intravenous calcium gluconate injection. The investigations before admission revealed 2.56million/cmm of RBC, 6.7 g/dl of haemoglobin and 3% reticulocyte count. The peripheral blood showed hypochromic and microcytic red blood cells with target cells. The serum electrolytes were found to be Na-132 meq/L, K-3.4 mg/dl, PO_4^{3-}4.4 mg/dl and Mg^{+2}-1.6mg/dl measured by ISE. Both free calcium (5.1mg/dl) and ionised calcium (1.6mg/dl) were found to be low. Both serum vitamin D_3 8.265 nmol/l (recommended reference interval 36-144nmol/l) and parathyroid hormone iPT= 3pg/ml (the recommended reference interval 10-65pg/ml) were estimated by ELISA and found to be reduced. The fasting plasma glucose was 79mg/dl. On laboratory investigation for hypogonadism, gonadotropins (3 pooled serum assay) were estimated by ELISA. Serum FSH concentration was 1.37mIU/ml, lower than the cut off 2mIU/ml as per IAP recommendation. Thyroid profile (serum TSH, fT4,fT3) and cortisol at 8.a.m was determined to exclude other causes of delayed property. As the patient was on chelation therapy (desferrioxamine), monitoring of the ocular examination was normal with visual acuity of 6/6, but the audiometric system showed central perforation with mild sensorineural deafness. Serum insulin like grow factor 1 was estimated to determine the cause of retarded growth and found to be74ng/ml (286-660ng/ml). Hepatic enzymes showed transient rise of transaminases and hepatitis serology was within normal limits. The renal functions were normal but the urinary calcium excretion increased from 83.2mg/dl to 206 mg/dl and serum calcium raised to 8.4mg/dl after treatment with calcium gluconate suggested severe parathyroid hormone deficiency. Serum ferritin was many folds higher than the threshold, about 2213.8 mg/dl suggesting iron overload.

DISCUSSION

In our present case, the 14 year girl is suffering from iron-overload due to repeated blood transfusion, as reflected by her serum ferritin status. It has already been established that the iron overload is the prime cause of endocrinopathy in such patients.[6] The growth retardation in the girl is mainly due to a dysfunction of the growth hormone-insulin like growth factor axis. It is well known that bone metabolism and skeletal consolidation are dependent on a variety of hormonal factors like GH, IGF-I, sex hormone and their receptors. [7]Growth hormone insensitivity at the post receptor level, rather than growth hormone reserve may be more important in IGF-I deficiency in β thalassemia patients. This finding has been seen in case series reports where the basal insulin like growth factor levels significantly increased after administration of human growth hormone.[9] As in this case, transfusion dependent thalassemia major patients, chelation therapy may also be an important cause of growth retardation. Desferrioxamine though reduces hemosiderosis, may also lead to bony lesions like genu-valgum, metaphyseal changes and impaired spinal growth.[10] The underlying cause of hypogonadotrophic-hypogonadism may be due to pituitary dysfunction attributed by iron toxicity. Hypogonadism, bone marrow expansion, increased iron store and desferrioxamine toxicity may also lead to osteoporosis and osteopenia in such transfusion dependent thalassemia patients. [11,12,13] Osteopenia may also result from hypocalcaemia and Vitamin D deficiency. The increased serum ferritin due to increased iron overload may be a cause of reduced parathyroid

secretion and this may lead to Vitamin D deficiency.

CONCLUSION

From the above discussion it is evident that endocrinopathy is still a clinically significant cause of morbidity despite the newer advent of chelation therapy, so this case has been reported. But the proper cause effect relationship between endocrinopathy and transfusion associated iron overload is yet to be established in these patients. This can be done only by conducting further case series in such patients in this part of the subcontinent. These studies may be helpful for clinicians for effective management of transfusion dependent patients.

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Photograph1 showing severe bowing due to carpopedal spasm

Abbrebiations Of Terminology Used In The Case Report.

1. HPLC- High Performance Liquid Chromatography
2. ELISA- Enzyme Linked Immunosorbent Assay
3. ISE-Ion Selective Electrode
4. iPT- Intact Parathyroid Hormone
5. FSH-Follicle Stimulating Hormone
6. TSH- Thyroid Stimulating Hormone
7. IGF-I – Insulin Like Growth Factor I
8. GH-Growth Hormone