EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 3
Issue: 4
433-435
Year: 2016

IMPENDING BONE INVOLVEMENT IN THALASSEMIA MAJOR PATIENTS- IS SERUM ALKALINE PHOSPHATASE AN EARLY MARKER?

Dr. Prakruti Dash*

Assistant Professor, Dept. of Biochemistry All India of Institute of Medical Sciences, Bhubaneswar, Odisha, India.

***Author for Correspondence:** Dr. Prakruti Dash
Assistant Professor, Dept. of Biochemistry All India Institute Of Medical Sciences, Bhubaneswar, Odisha, India.

Article Received on 08/02/2016 **Article Revised on 29/02/2016** **Article Accepted on 21/03/2016**

ABSTRACT
Thalassemia major is a genetic disorder with defective haemoglobin synthesis resulting in premature destruction of RBCs leading to haemolytic (pre-hepatic) jaundice with unconjugated hyperbilirubinemia. Life expectancy of patients has increased due to regular blood transfusion but associated side effects due to iron overload are always encountered which are tackled by chelation therapy. The liver function tests of such patients show typically a picture of unconjugated hyperbilirubinemia with no hepatic abnormalities detected which are indicated by the normal hepatic enzyme panel. Few cases showing unconjugated hyperbilirubinemia with isolated rise in alkaline phosphatase level are analyzed and the probable pathophysiology behind it will assist in elimination of diagnostic dilemma regarding probable hepatic involvement. This will also help in early diagnosis and prevention of bone abnormalities often associated with transfusion dependent Thalassemia patients.

KEYWORDS: Thalassemia, Alkaline phopshatase, Blood Transfusion, Chelation therapy.

INTRODUCTION
Alkaline phosphatase (ALP) is an enzyme of immense diagnostic importance, mainly in liver and bone disorders. Total ALP level as well as its various isoenzymes is in regular use for diagnosis of bone and liver diseases. .A raised level of ALP associated with hyperbilirubinemia usually indicates obstructive liver diseases. Similarly raised ALP level with abnormal serum calcium and phosphorus levels point towards bone diseases. Bile stasis in obstructive liver diseases leads to elevated serum ALP level with conjugated hyperbilirubinemia whereas in bone disorders like osteoporosis, rickets, malignant bone tumours , healing fractures, raised ALP maintains the ionic balance of calcium and phosphorus for optimal bone mineralization.

Thalassemia is a genetic disorder with high prevalence. Thalassemia is major cause of haemolytic jaundice or pre-hepatic jaundice usually manifest with indirect hyperbilirubinemia due to excessive RBC destruction. The outcome of the disease has improved significantly owing to blood transfusions and iron chelating therapy.[1] However, repeated blood transfusions and iron chelating therapy to prevent iron overload has negative effects leading to other associated abnormalities, mostly related to bone with few subtle changes indicative of impending bone abnormalities, which is mostly overlooked till major diseases like osteoporosis and pathological fractures are encountered.[1,2]

Few cases of Thalassemia major showing unconjugated hyperbilirubinemia with isolated rise in alkaline phosphatise level and the probable pathophysiology behind it are analyzed which will assist in elimination of diagnostic dilemma regarding probable hepatic involvement .This will also help in early diagnosis and prevention of bone abnormalities often associated with transfusion dependent Thalassemia patients.

Case Study 1
- Diagnosis- Thalassemia major
- Age-24 years
- Total Bilirubin-2.0mg%, Direct Bilirubin-0.7mg%, Indirect Bilirubin-1.3mg%, SGOT-62IU/L, SGPT-34IU/L, ALP– 246 IU/L, Serum Albumin -3.8gm%, Serum Total Protein – 6.4gm%, Serum Calcium – 8.0mg%, Serum Phosphorus – 6.0mg%

Case study 2
- Diagnosis – Thalassemia major
- Age – 18 years
- Total Bilirubin-6.8mg%, Direct Bilirubin-0.4mg%, Indirect Bilirubin-5.9mg%, SGOT-42IU/L, SGPT-39IU/L, ALP– 407 IU/L, Serum Albumin -3.9 gm%, Serum Total Protein – 6.6gm% Serum Calcium – 8.4mg%, Serum Phosphorus – 6.4mg%.

Case study 3
- Diagnosis – Thalassemia major
- Age – 8 years

- Total Bilirubin-1.2mg%, Direct Bilirubin-0.3mg%, Indirect Bilirubin-0.9mg%, SGOT-49IU/L, SGPT-62IU/L, ALP– 259 IU/L, Serum Albumin -4.1gm%, Serum Total Protein – 6.8gm% Serum Calcium – 9mg%, Serum Phosphorus – 5.2mg%

The normal level of hepatic enzymes in our laboratory is
SGOT – 5-35 IU/L
SGPT – 5-40 IU/L
ALP – 38-93 IU/L

In all the three cases indirect hyperbilirubinemia was observed giving a typical picture of pre – hepatic haemolytic jaundice. Optimal liver functions were also indicated by normal SGOT and SGPT levels and normal serum total protein and albumin levels in all the cases. However, serum ALP levels were found to be high in all the three cases, the rise being more marked in case 1 and case 2 compared to case 3.Considering the age of case 3 which is 8 years where higher value of ALP is normally encountered the rise of ALP is less compared to the other two cases. Hypocalcaemia and hypophosphataemia were also notable in the first two cases whereas the values were in borderline in the third case.

DISCUSSION

Thalassemia major is a common hemoglobinopathy mostly presenting with pre-hepatic haemolytic jaundice where other liver enzyme markers are usually normal. Hence, cases as discussed showing an indirect hyperbilirubinemia with raised ALP is an indication of other organ involvement, most like impending osteoporosis which is very commonly associated with Thalassemia.[2] Associated serum abnormalities were low serum Calcium level in case 1 and case 2 along with raised serum Phosphorus value which again was indicative of abnormalities related to bone .There were no obvious complains of bone diseases but abnormal serum Calcium, phosphorus and ALP values definitely calls for early diagnosis and prevention of bone involvement.[3]

Probable explanations regarding rise of serum ALP in Thalassemia major patients with repeated blood transfusions and Iron chelating therapy with no obvious liver involvement is put forward by many authors as:

1. Frequent blood transfusion leads to iron deposition in the parathyroid gland which has a detrimental effect on its normal functioning and raised level of serum alkaline phosphatase may have an association with osteomalacia, hypocalcaemia and hyperphosphatemia associated with hypoparathyroidism.[4]

2. Vitamin D deficiency is yet another contributing factor even before hypoparathyroidism is established. Vitamin D deficiency significantly contributes to low bone mass in thalassaemia. Thalassemia patients gradually develop iron overload, and a possibility is that it adversely affects liver hydroxylation of vitamin D, or in vitamin D absorption, more common in older thalassemic patients.[5]

3.Deferoxamine induced toxicity is linked with evidence of cartilaginous dysplasia of the long bones and spine which may also lead to low serum Calcium, high serum Phosphorus and raised serum ALP levels. Actions of vitamins and minerals like Vitamin C, zinc, copper on bone growth and metabolism is observed to be repressed in thalassemic patients on high doses of desferrioxamine. Desferrioxamine also cause bone damage by inhibiting cell proliferation, DNA synthesis, and collagen formation resulting in platyspondylosis with flattening of the vertebral bodies and consequently shortening of the spinal height.[6]

CONCLUSION

Bone involvement and abnormalities are of common association in thalassemia having multi factorial aetiology. Endocrine complications like hypoparathyroidism in addition to progressive marrow expansion, iron and desferrioxamine toxicity on bones, as well as liver involvement add to the pathophysiology of bone disorders like osteoporosis in thalassaemia patients which adversely affects the quality of life of patients with Thalassemia. Regular and meticulous follow-up, early detection of osteopenia, and proper management are vital for every thalassemic patient. In diagnosis, management and follow-up of a Thalassemia patient with an aim to prevent bone involvement at an early it is highly recommended that the biochemical investigations apart from liver and renal function tests, should also include

- Regular assessment of serum calcium , phosphorus and alkaline phosphatase status
- Parathyroid hormone status and Vitamin D status

REFERENCES

1. Borgna-Pignatti C, Rugolotto S, De Stefano P, Zhao H, Cappellini MD, et al. Survival and complications in patients with thalassemia major treated with transfusion and deferoxamine, Haematologica, 2004; 89: 1187-1193.
2. Salama OS, Al-Tonbary YA, Shahin RA, Eldeen OA .Unbalanced bone turnover in children with beta-thalassemia, Hematology, 2006; 11: 197-202.
3. Modi AS, Poornima RT, Jayaprakash Murthy DS. Serum calcium and phosphate levels in patients with ß-Thalassemia major, IJPBS, 2012; 2: 156-160.
4. Goyal M, Abrol P, Lal H .Parathyroid and calcium status in patients with Thalassemia, Indian J Clin Biochem, 2010; 25: 385-387.
5. A. Moulas, A. Challa, N. Chaliasos, and P. D. Lapatsanis. Vitamin D metabolites (25-hydroxyvitamin D, 24, 25 dihydroxyvitamin D and 1, 25 dihydroxyvitamin D) and osteocalcinin β thalassaemia, Acta Paediatrica, 1997; 86(6): 594–599.
6. S. De Virgiliis, M. Congia, F. Frau, et al. Deferoxamine induced growth retardation in patients

with Thalassemia major, Journal of Pediatrics, 1988;
113(4): 661–669.