Transient hyperphosphatemia: a benign laboratory disorder in a boy with Gitelman syndrome

Hiperfosfatemia transitória: uma alteração laboratorial benigna em um menino com síndrome de Gitelman

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ABSTRACT

Transient hyperphosphatasemia of infancy and early childhood (THI) is characterized by transiently increased activity of serum alkaline phosphatase (S-ALP), predominantly its bone or liver isoform, in children under five years of age. There are no signs of metabolic bone disease or hepatopathy corresponding with the increased S-ALP. THI is benign disorder, rather laboratory than clinical disorder, which is usually accidentally detected in both healthy and sick children. When encountered in a child with either chronic bone, liver or kidney disease, it might concern the physician. We present a three year old boy with genetically confirmed Gitelman syndrome where THI was detected accidentally during periodic check-up. S-ALP peaked to 41.8 μkat/L, there were neither laboratory or clinical signs of liver or bone disease; the S-ALP dropped to normal value of 4 μkat/L 60 days later. Therefore, the patient fulfilled the criteria for THI. There were no further increases in S-ALP.

Keywords: alkaline phosphatase; bone diseases, metabolic; Gitelman syndrome.

INTRODUCTION

Transient hyperphosphatasemia of infancy and early childhood (THI) is characterized by transiently increased activity of serum alkaline phosphatase (S-ALP), predominantly its bone or liver isoform, in children under five years of age. There are no signs of metabolic bone disease or hepatopathy corresponding with the increased S-ALP, nor there is a disease common to all children with THI.

THI is benign, rather laboratory than clinical disorder, which is usually accidentally detected in both healthy and sick children.1,2 When encountered in a child with either chronic bone, liver or kidney disease, THI might concern the physician.2,3

CASE REPORT

Three year old boy with genetically confirmed Gitelman syndrome (three
Transient hyperphosphatemia and Gitelman syndrome

These criteria are not strict, as THI has been occasionally observed even in adult individuals, and the duration of THI has repeatedly exceeded the time limit of 4 months.\(^2\,\text{,}\,\text{3,}\,\text{7}\) Furthermore, the electromorphetic evaluation of the ALP isoenzymes in THI is characterized by an atypical transient pattern of cathodal and anodal migrating fractions, bearing some similarities to the isoforms of bone and liver origin.\(^8\) The incidence of THI has been estimated at 2.8\%.\(^9\)

The etiology of THI was presumed to be an infectious one, as some of the children with THI experienced signs of viral disease 2-3 weeks prior to the S-ALP elevation and THI was also observed either in siblings or in children who were hospitalised together.\(^10\,\text{,}\,\text{12}\) The exact mechanism of THI is unclear, however, the impaired clearance of ALP from circulation is still considered as the most likely one.\(^1\,\text{,}\,\text{2}\)

THI is generally considered a benign disorder. Furthermore, THI has to be differentiated from skeletal or liver diseases and can cause concern in patients with metabolic bone disorders.\(^13\) However, normal bone turnover has been observed in children with THI.\(^14\,\text{,}\,\text{15}\) In the presence of high S-ALP where basic biochemical markers (S-Ca, P, creatinine, ALT, AST) and radiograph of the wrist are normal, THI is the most likely diagnosis. Therefore, the children with THI should be spared from unnecessary early diagnostic procedures and therapeutic interventions. The monitoring of S-ALP on a monthly or two-monthly basis is recommended before any further diagnostic steps are undertaken.

Our patient with genetically confirmed GS presented with high S-ALP, thus drawing some concern about disturbed bone metabolism due to possible mineral dysbalance that may occur in GS.\(^4\) However, clinical signs of skeletal or liver diseases and normal bone turnover has been observed in children with THI.\(^14\,\text{,}\,\text{15}\) In the presence of high S-ALP where basic biochemical markers (S-Ca, P, creatinine, ALT, AST) and radiograph of the wrist are normal, THI is the most likely diagnosis. Therefore, the children with THI should be spared from further diagnostic procedures (such as \(^{99}\text{Tc}\) bone scans, radiographs and blood draws) and the S-ALP can be re-assessed after 2-3 months.\(^2\,\text{,}\,\text{16}\)

Our patient with genetically confirmed GS presented with high S-ALP, thus drawing some concern about disturbed bone metabolism due to possible mineral dysbalance that may occur in GS.\(^5\,\text{,}\,\text{17}\) However, the normal values of S-Ca, P, Mg, U-Ca/U-cr and normal wrist X-ray ruled out this possibility and pointed to the diagnosis of THI, which was further confirmed by normalisation of S-ALP within two months.

In conclusion, we presented a case of THI in a boy with GS. This case met the criteria for THI, which is a benign condition with good prognosis. Extremely high values of S-ALP can draw some concern, especially in children with chronic disorders of kidney, bone or liver.\(^2\,\text{,}\,\text{3,}\,\text{13,}\,\text{16-18}\) Children with THI should be spared from unnecessary early diagnostic procedures and therapeutic interventions. The monitoring of S-ALP on a monthly or two-monthly basis is recommended before any further diagnostic steps are undertaken.

**DISCUSSION**

Gitelman syndrome (GS) is a rare autosomal recessive salt-wasting nephropathy, characterized by hypokalemia, hypomagnesemia, hypocalciuria, metabolic alkalosis and low blood pressure. Typical clinical signs include fatigue, muscle weakness and muscle paralysis.\(^6\) Transient hyperphosphatasemia of infancy and early childhood (THI) has been reported in more than 800 subjects, both sick and healthy children.\(^13\) The definition of THI was delineated by Kraut in 1985 using the following criteria:

1) an age of less than 5 years; 2) variable, unrelated symptoms; 3) no bone or liver disease noted on physical examination or from laboratory investigations; 4) isoenzyme and isoform analysis showing elevations in both bone and liver activity; 5) a return to normal S-ALP values within four months.\(^4\)
REFERENCES


