CASE REPORT

TRANSIENT HYPERPHOSPHATASEMIA OF INFANCY AND EARLY CHILDHOOD: A LESS COMMON ENCOUNTER - A CONCERN FOR THE PAEDIATRICIAN

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Abstract

Transient hyperphosphatasemia (TH) is a benign condition in which serum alkaline phosphatase (ALP) is transiently elevated in the absence of other systemic diseases. It rarely occurs in infants and children under 5 years and is very rarely seen in adults. The differential diagnosis may include bone, intestinal, liver, kidney, intestinal, placental and blood diseases as well as other serious conditions, as well as bone fracture due to accidental or non-accidental injuries. The exclusion of such differential diagnosis before establishing the diagnosis of TH is crucial.

We present a case of a nine-month-old girl who was found to have transient hyperphosphatasemia, while she was being investigated for failure to thrive. This case report aims to reinforce that hyperphosphatasemia is a benign phenomenon and diagnostic procedures that are invasive and costly should be avoided.

Key words: Transient hyperphosphatasemia of infancy and early childhood

Introduction

The benign elevation of alkaline phosphatase (ALP) is referred to as transient hyperphosphatasemia (TH) and is occasionally observed in infants and children younger than 5 years of age, without evidence of bone, gastrointestinal or liver disease on history taking, physical examination or laboratory investigations[1,2] It has no adverse long-term consequences[3,4]. TH has shown to be a less common condition among healthy infants and toddlers and is detected incidentally during laboratory investigations for other illnesses[4].

The pathophysiology of transient hyperphosphatasemia is poorly understood. Previous authors have speculated that immaturity of the mechanisms responsible for ALP clearance, in the presence of trigger factors secondary to exogenous insults as the possible underlying reason for transient hyperphosphatesemia[5]. There are reports

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in the literature correlating transient rise in alkaline phosphatase to upper respiratory tract infections or gastro enteritis[6].

The awareness of this condition, which is rarely encountered in practice, is important for both patients, parents and clinicians. This will encourage the avoidance of unnecessary concerns and prevent over-investigation[7].

Case report

A nine-month old girl with severe failure to thrive presented with a lower respiratory tract infection. She was born to healthy, non-consanguineous parents following a complicated antenatal period with symmetrical growth retardation. Her birth weight was 1.55 kg at term and screening for congenital infections and brain imaging were normal.

During investigations, her ALP level was repeatedly noted to be very high (4540 IU/L). She had no clinical features suggestive of chronic liver, intestinal, renal or bone disease. There were no risk factors for nutritional rickets.

Her serum calcium (2.34 mmol/l), inorganic phosphorus (2.94 mmol/l) and parathormone (51.5 pg/ml) levels were within the normal ranges. There was no radiological evidence of rickets or hyperphosphatasia. Renal and liver profiles were normal. Both parents had normal ALP levels. A provisional diagnosis of TH was made and ALP levels were monitored. The ALP level was 519 IU/L (B- ALP 58.8, L- ALP 460.2, Placental ALP <1 IU/L) after 2 months and 135 IU/L after 3 months. Spontaneous reduction of ALP values to normal within three months confirmed the diagnosis of transient hyperphosphatasemia of infancy and early childhood.

The following table illustrates the summary of investigations performed during evaluation over the three months duration.

Table 1- Summary of investigations performed in the child

Analysis	On Admission	2 Weeks	2 Months	3 Months	Normal Reference Range
Calcium (mmol/l)	2.26	2.34	-	-	2.15-2.57
Phosphate (mg/dl)	2.97	2.94	-	-	2.5-4.9
SGOT/SGPT U/L	38/22	-	-	-	34/35
S. Creatinine (mmol/l)	90	-	-	-	60-120
S. Albumin (mg/dl)	42	-	-	-	37-50
PTH (pg/ml)	-	51.5	-	-	8.8-75.5
L/Wrist X Ray	-	No rickets	-	-	-
GGT	-	12.1	-	-	11-50
ALP (U/L)	4540	3474	519	135	98-279
Bone- ALP (U/L)	-	-	58.8	14.8	-
Liver- ALP (U/L)	-	-	460.2	120.1	-
Placental- ALP(U/L)	-	-	<1	<1	<1

Discussion

Recognition and differentiation of transient hyperphosphatesemia from bone, liver, renal and intestinal pathology is important to avoid unnecessary investigations[3]. It needs to be differentiated from familial hyperphosphatesemia, which is inherited in an autosomal dominant manner and is associated with persistent and asymptomatic elevation of alkaline phosphatase levels.

ALP includes tissue nonspecific isoenzymes that are predominantly produced by the liver and bone tissues, and to a lesser degree by the kidneys, intestine, placenta and placental-like isoenzymes (expressed in the testes, thymus and lungs)[8]. The catalytic activity of ALP is greater in childhood and puberty due to increased bone growth, compared to adults. ALP can be increased up to 20 times the upper limit for age, in serum of infants and children in the absence of hepatic or bone disease [9].

The criteria for diagnosis of THP are (1) age below 5 years, (2) elevation of serum ALP ranging from 3-50 times the upper normal value for the given age, (3) isoenzyme analysis showing elevation in bone or liver fraction, (4) lack of clinical or biochemical evidence of bone or liver disease, (5) return to normal ALP values within 4 months and (6) presence of unrelated illnesses such as failure to thrive, respiratory infections, diarrhea and vomiting.

The child in this instance had respiratory symptoms on presentation and fulfilled all the other criteria during subsequent evaluation. She had severe failure to thrive, which needed further evaluation.

The aetiology of THP remains unclear without guidelines for evaluation. Thus, it is important for paediatricians to consider THP of infancy and childhood in the differential diagnosis of a markedly elevated serum ALP, especially when it is an isolated finding, in order to avoid unnecessary and extensive diagnostic evaluation, given the spontaneous and uneventful resolution of this condition[10].

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