CASE REPORT

A case report of benign transient hyperphosphatasaemia: What can we learn from this?

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SUMMARY

We report a case of benign transient hyperphosphatasaemia (BTH) which was noted incidentally when the patient was admitted for acute tonsillitis. Blood result showed alkaline phosphatase (ALP) at admission was markedly elevated with value of 2481 U/L [normal range 34 – 104 U/L]. He had no history or physical findings to suggest liver or bone disease. Various blood and radiographic investigations were performed to determine the cause but results were normal. He was followed-up with repeat blood test and the alkaline phosphatase normalised after 42 days.

INTRODUCTION

The common causes of elevated ALP in children are vitamin D insufficiency, bone fractures and liver disease. Physicians often face challenges investigating for the causes of raised ALP as many hospitals do not have the facility to perform parathyroid hormone (iPTH) and 25-hydroxyvitamin D level. Blood samples are sent to a centralised laboratory and the test result will only be available after several weeks. Consequently, most patients would be treated with vitamin D supplement considering high prevalence of Malaysian children with vitamin D insufficiency.[1] Usually, the ALP level is less than twice the upper limit of adult value. If the level is 5 or 10 times higher, physicians may embark on various blood and radiological investigations. Some patients may even be referred to the gastroenterologist or endocrinologist thus incurring further cost, unnecessary tests and needless anxiety.

BTH is a diagnosis of exclusion and an entity under-recognised in this region. We hope to use this case to create awareness that raised ALP level can have a benign cause.

CASE ILLUSTRATION

A 2 year-old boy presented to the emergency department with symptoms of upper respiratory tract infection for 3 days duration. He had no significant past medical history but his blood investigation revealed markedly elevated ALP.

There was no evidence to suggest bone disease (bone fracture, bone pain, or significant family history of bone diseases) or liver disease (jaundice, tenderness over right hypochondrium, pale coloured stool, or dark coloured urine). He was well nourished with height of 90cm (50th percentile) and weight of 13.6kg (50th to 75th percentile) and his general examination was unremarkable except for inflamed tonsils.

Blood investigations taken at presentation (day 0) are as follow: (A) Blood counts: hemoglobin 12.7 g/dl, white cells 8 x 10^9 per litre, platelet 379 x 10^9 per litre, normal differential (B) Biochemical investigations: urea 2.06 mmol/L, sodium 134.2 mmol/L, potassium 4.36 mmol/L, chloride 104.2 mmol/L, creatinine 35 µmol/L, calcium 2.36 mmol/L, magnesium 0.91 mmol/L, phosphate 1.76 mmol/L, lactate dehydrogenase 303 U/L, creatine kinase 163 U/L; (C) Hepatic biochemical profile: protein 73.5 g/L, albumin 43.9 g/L, globulin 29.7 g/L, total bilirubin 5.3 U/L, alanine transferase 30 U/L, aspartate transferase 49 U/L.

ALP was significantly raised at 2481 µmol/L but the local laboratory was unable to perform isozyme fractionation of ALP to determine the source of the elevated enzyme. X-ray of the right wrist showed no evidence of rickets.

The patient was treated with intravenous penicillin and was discharged on day 4 of hospitalisation. A repeated ALP on day 2 was 3110 µmol/L and prior to discharge (day 4) was 2992 µmol/L.

Parathyroid hormone and 25-hydroxy vitamin D level were normal with values of 1.1 pmol/L and 88.0 nmol/L respectively. Mycoplasma serology and anti-streptolysin-O titre were also negative.

On subsequent follow-up, his ALP level dropped to 1742 µmol/L on Day 10, 506 µmol/L on Day 24 and 322 µmol/L on Day 42 after his first presentation.

DISCUSSION

Serum ALP is contributed mainly by bone isoenzyme (about 85%) with the remainder by the liver (about 15%), intestine, white blood cells, kidneys and endothelium. A raised ALP level is often associated with conditions such as cholestasis, intrinsic liver disease, rickets or fracture. However, it is known that children have a higher ALP level in view of physiological higher rates of osteoblastic activity. The level is highest in infants aged 1 to 6 months old where the level can be three times the upper reference limit of the adult but falls to two-

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Table I: Serial Level of Alkaline Phosphatase, Vitamin D, Parathyroid Hormone, Calcium and Phosphate

Normal Range	Alkaline phosphatase (µmol/L) [34 - 104]	Vitamin D (mmol/L) [60 – 160]	Parathyroid hormone (nmol/L) [1.5 – 7.6]	Corrected Calcium (mmol/L) [2.2 – 2.65]	Phosphate (mmol/L) [0.84 – 1.45]
On admission (day 0)	2481	88	1.1	2.28	1.76
Upon discharge (day 4)	2992			2.35	1.82
Day 10	1742			2.36	2.14
Day 24	506			2.48	1.90
Day 42	322		1.5	2.30	1.69

fold when the child reaches 2 years old. There is a second peak during puberty when the child experiences maximum height velocity.

BTH is not a new entity as it was first recognized by Bach[2] in the year 1954. In 1985, Kraut[3] published a 7-point criterion to clearly define the diagnosis of BTH. The criteria are (1) elevated alkaline phosphatase level 3 – 50 times above normal limit (2) patient's age of less than 5 years, (3) presence of variable unrelated symptoms, e.g. gastroenteritis or neurologic impairment, (4) absence of physical signs of bone or liver disease, (5) normal laboratory investigations for liver and bone diseases, (6) isoenzyme analysis showing elevations in both bone and liver activity, and (7) serum alkaline phosphatase value which normalise within four month. It was not mentioned in the paper the minimum number of criteria to fulfil to diagnose of BTH. In our patient, he fulfilled 5 of the 7 criteria mentioned above.

Most of the patients with BTH were relatively well and about 60% of them had history of recent mild infection.[4] This was seen in our patient who was treated for tonsillitis and he recovered within short span of time.

His ALP level showed a downward trend even while in the ward. It was highest on the second day with value of 3110 µmol/L but declined to 2992 µmol/L on the last day. He was reviewed every 2 to 3 weeks with repeat ALP, calcium and phosphate level. His ALP level returned to normal 42 days after the first abnormal result. Systemic review of all published reports showed that 20% of the patients with BTH had persistent elevation of ALP for ≥ 4 months.[5]

Samples for parathyroid hormone and 25-hydroxyvitamin D assay of this patients were sent to a local private laboratory and vitamin D insufficiency was excluded early. Should the tests be made readily available in most centres, many patients will not need to endure the anxiety of waiting for test results.

CONCLUSION

BTH is relatively common (prevalence of 7.9%) [5] but under-recognised condition among children less than 5 years old. We hope to use this case report to highlight the possibility of diagnosing BTH in a child with raised ALP after thorough history and physical examination have ruled out liver and bone diseases.

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