

A Non-Symptomatic Elevated Alkaline Phosphatase in a 3-Year-Old Child; A Rare Iranian Report

Fateme-Sadat Tabatabaei¹, Sahab-Sadat Tabatabaei², Seyyed-Mohsen Hosseininejad^{3,4} and Hossein Zaeri^{5*}

¹Resident of Pediatric, Neonatal and Children's Health Research Center, Golestan University of Medical Sciences, Gorgan, Iran

²Resident of Internal Medicine, Department of Pediatrics, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

³Resident of Orthopedics, Bone, Joint and Related Tissue Research Center, Akhtar Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁴Neonatal and Children's Health Research Center, Golestan University of Medical Sciences, Gorgan, Iran

⁵Assistant Professor of Pediatric Endocrinology, Neonatal and Children's Health Research Center, Golestan University of Medical Sciences, Gorgan, Iran

***Corresponding Author:** Hossein Zaeri, Assistant Professor of Pediatric Endocrinology, Neonatal and Children's Health Research Center, Golestan University of Medical Sciences, Gorgan, Iran.

Received: September 19, 2018; **Published:** May 29, 2019

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 mainly occurs in infants and children and infrequently happened in adults. The differential diagnosis may include liver, bone, kidney, intestinal, placental and blood diseases as well as accidental or non-accidental bone fracture.

In this report, we present a 3-year-old boy with TH and compare their clinical course with the natural history of TH mentioned in literature.

Keywords: Alkaline Phosphatase; Hyperphosphatasemia; Transient; Idiopathic; Iran

Introduction

Transient Hyperphosphatasemia (TH) is a benign condition characterized by marked elevation of serum alkaline phosphatase (ALP) with absence of other associated disease such as in liver, bone or kidneys. In addition, TH is also characterized by a return of ALP to normal levels within weeks or months of initial observation [1-3].

It may be common for physicians to meet children with elevated alkaline phosphatase (AP) levels. Given the possibility of underlying asymptomatic hepatobiliary diseases, these patients are usually referred to either a pediatric gastroenterologist or an endocrinologist for further evaluation and management. Likewise, to determine the cause, apart from referral to a specialist, the diagnostic work-up can be quite costly, reflecting the broad scope of hepatobiliary and skeletal diseases known to be associated with AP elevation. Importantly, in a significant proportion of these patients, elevated AP is benign, and gradually resolves without any intervention, inquiring the rationale for an exhaustive evaluation of every patient with such a biochemical derangement [1,2].

The exclusion of such causative illness before establishing a diagnosis of TH is of a dominant importance. As elsewhere, TH is generally rare to see in children managed in the inpatient and outpatient clinics at Gorgan, Iran. Yet the awareness of this condition, which is rarely encountered in practice, is important for both patients/parents and clinicians and also medical costs and time. This will inspire the prevention of unnecessary concerns and investigations [4-9].

We report a rare pediatric TH to highlight the classic presentation as well as the natural history of the disease with a focused review of literature on the subject.

Case Presentation

A 3-year-old male child was visiting in our pediatric clinic of Taleghani Hospital, Gorgan, Iran as routine height and weight follow-up. He was healthy with normal development. She fed on breastfeeding, regular diet and he was on no treatment. On examination, her anthropometric indices and growth were relevant to his age and thus normal with unremarkable systemic examination suggesting organic disease or child abuse. His initial screening blood tests at first year of age, out of the blue, he was found to have an elevated serum alkaline phosphates (ALP) level of 7298 U/L, which had decreased to 2580/L a week after (child normal lab value 180 - 1200 U/L). All her other investigation was detected normal (Table 1). When followed in clinic, the ALP level started to drop dramatically from 2580 U/L to 636,354 U/L within a month. It remained within normal range while his twice a year visits until now (3 year-old); the patient’s family looked healthy and reported no systemic complaint.

Investigations	At presentation	After 1 month	After 3 months	After 2 years
ALP (N = 175 - 1200 u/l)	7298	2580	636	271
25(OH) VIT D (optimal = 30 - 50 ng/ml)	-	37	-	-
PTH intact (N = 14.5 - 87.1 pg/ml)	2.69	24.7	-	-
Ca (N = 8.8 - 10.8 mg/dl)	-	10.8	10.7	10.7
Phosphorus (N = 4 - 7 mg/dl)	-	6.55	6	6.1
AST (N = 10 - 31)	32	10		
ALT (N = 15 - 41 u/l)	37	13	-	-
WBC (N = 8000 - 1200)	9200	9000	-	8500
Urea (N = 1.8 - 6.4 mmol/l)	4.2	-	4.5	4
Serum creatinine (N = 27 - 62 umol/l)	26	-	40	38
Gamma-glutamyl transferase (GGT)	10	-	-	11
ESR 1hr (mm)	10	-	-	9
Radiology: Wrist X-ray, Growth plate	-	Normal	-	Normal
Ultrasonography: Abdomen and pelvic	-	Normal	-	-

Table 1: Assessment of our case at presentation and during follow-up.

Discussion

Transient Hyperphosphatasemia (TH) in infancy and early childhood is described as a noticeable raise of the serum Alkaline Phosphatase (ALP) activity in children below the age of five year-old in the absence of clinical or laboratory findings of a systemic disease which may result in similar biochemical condition [10]. ALP typifies a group of isoenzymes originating mostly from kidney, bone, liver, placenta intestine and white blood cells [11]. The ALP level alter with age, it is usually higher in children than in adults, with a peak in the first six months of age and during pubertal growth spurt, since they have higher osteoblastic activity in such age [12,13]. In TH, as in our patients,

the serum level of ALP is typically elevated four to five times above the upper limit of normal and tend to returns to normal range within six months [8,13,14].

Even though TH has been well recognized for several, the etiology and pathophysiology remains still unclear. It is considered to be a benign condition in young children and has also infrequently been reported in adults [15]. The prevalence of TH is not known in Iran. In a series of 260 healthy infants, 1.5% (n = 3) had unexplained and transient elevations in ALP, all of them had more than three times the upper limit of the normal range [15,16].

There are criteria used to diagnose the transient hyperphosphatasemia: age below 5 years; symptoms like respiratory infections, diarrhea, vomiting; absence of clinical and biochemical signs of liver and bone disease; increased ALP level; elevated activity of osseous and/or hepatic isoenzymes; and return to normal levels within 6 months [1-4]. Most children with TH are healthy although TH can be incidentally recognized in association with a variety of clinical problem comprising gastroenteritis, respiratory infections, failure to thrive, chronic otitis media, eczema and asthma [1,17] however our current case had no complaint; This evidently signifies the challenge in differentiating benign TH from an organic condition or constant serious condition like associated physical child abuse and neglect warranting a watchful attention to family and social history as well. Follow up is required to document the return of serum ALP level to normal and it is critical for confirmation of the diagnosis. The sustained elevation of ALP beyond three to four month of primarily being high should prompt reassessment of other causes of Hyperphosphatemia [18]. Conversely, children with TH should be spared from wide-ranging investigations and unnecessary vitamin D treatment attempts. An initial detailed evaluation such as detailed social history, with infrequent biochemical follow up of ALP is the whole mark of diagnosing this condition and evading missing out other pathology [1].

Conclusion

Though no accurate estimation of its prevalence worldwide, transient Hyperphosphatasemia (TH) seems to be rarely encountered in our community, as elsewhere in the world. Our report, which was the first case of Iranian TH, showed a classic natural history of the disease with emphasis on awareness to such condition in practice.

Informed Consent

A Standard informed consent was obtained from the family.

Conflict of Interest

The authors declare there is no conflict of interest.

Acknowledgment

The authors wish to give special thanks to the parents of our case for theirs sincere cooperation.

Bibliography

1. Huh SY, *et al.* "Prevalence of transient hyperphosphatasemia among healthy infants and toddlers". *Pediatrics* 124.2 (2009): 703-709.
2. Čvorišćec, *et al.* "Harmonizacija laboratorijskih nalaza u području opće medicinske biokemije". Hrvatska komora medicinskih biokemičara (2004): 8.
3. Dodig S, *et al.* "Cut-off values of total serum IgE between nonatopic and atopic children in north-west Croatia". *Clinical Chemistry and Laboratory Medicine* 44.5 (2006): 639-647.
4. Eboriadou M, *et al.* "Acute laryngotracheobronchitis and associated transient hyperphosphatasemia: a new case of transient hyperphosphatasemia in early childhood". *Journal of Paediatrics and Child Health* 42.3 (2006): 149-150.
5. Suzuki M, *et al.* "Viral infection of infants and children with benign transient hyperphosphatasemia". *FEMS Immunology and Medical Microbiology* 33.3 (2002): 215-218.

6. Arikan C, *et al.* "Transient hyperphosphatasemia after pediatric liver transplantation". *Pediatrics International* 48.4 (2006): 390-392.
7. Ranchin B, *et al.* "Transient hyperphosphatasemia after organ transplantation in children". *Pediatric Transplantation* 6.4 (2002): 308-312.
8. Behúlová D, *et al.* "Transient hyperphosphatasemia of infancy and early childhood: study of 194 cases". *Clinical Chemistry* 46.11 (2000): 1868-1869.
9. Dodig S, *et al.* "Alkaline phosphatase isoenzymes in children with respiratory disease". *Biochemia Medica* 17.1 (2007): 102-108.
10. Wolf PL. "The significance of transient hyperphosphatasemia of infancy and childhood to the clinician and clinical pathologist". *Archives of Pathology and Laboratory Medicine* 119.9 (1995): 774-775.
11. Moss DW. "Alkaline phosphatase isoenzymes". *Clinical Chemistry* 28.10 (1982): 2007-2016.
12. Stein P, *et al.* "Transient hyperphosphatesemia of infancy and early childhood: clinical and biochemical features of 21 cases and literature review". *Clinical Chemistry* 33.2 (1987): 313-318.
13. Turan S, *et al.* "Serum Alkaline Phosphatase Levels in Healthy Children and Evaluation of Alkaline Phosphatase-scores in Different Types of Rickets". *Journal of Clinical Research in Pediatric Endocrinology* 3.1 (2011): 7-11.
14. Carroll AJ and Coakley JC. "Transient hyperphosphatesemia: an important condition to recognize". *Journal of Paediatrics and Child Health* 37.4 (2001): 359-362.
15. Schambeck CM, *et al.* "Transient hyperphosphatesemia in infancy and adult: Biochemical Peculiarities". *European Journal of Clinical Chemistry and Clinical Biochemistry* 35.6 (1997): 441-444.
16. Asanti R, *et al.* "Serum alkaline phosphatase in healthy infants. Occurance of abnormally high values without known cause". *Annales Paediatricae Fenniae* 12 (1966): 139-142.
17. Dori N, *et al.* "Transient hyperphosphatesemia in children revisited". *Pediatric International* 52.6 (2010): 866-871.
18. Tolaymat N and deMelo MC. "Benign Transient hyperphosphatesemia of infancy and childhood". *Southern Medical Journal* 93.12 (2000): 1162-1164.

Volume 2 Issue 3 June 2019

©All rights reserved by Hossein Zaeri, *et al.*