



Transient Hyperphosphatasemia Associated with Human Bocavirus Infection

Human Bocavirüs Enfeksiyonu ile İlişkili Geçici Hiperfosfatazemi

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University of Health Sciences Turkey, Ankara Dr. Sami Ulus Gynecology, Child Health and Diseases Training and Research Hospital, Clinic of Pediatric Emergency Care, Ankara, Turkey

ABSTRACT

Transient hyperphosphatemia is a rare benign condition in children characterized by elevated serum alkaline phosphatase levels in infancy and childhood without metabolic bone or liver disease. As it can occur with many different conditions, temporary hyperphosphatasia can be seen especially in gastrointestinal, ear, urinary and respiratory tract infections. It is believed to be triggered by a viral infectious disease. It is important to raise the awareness of clinicians on this issue in terms of facilitating the diagnosis and not requiring additional research. Here, a case of transient hyperphosphatasemia with acute bronchiolitis caused by human bocavirus infection is presented.

Keywords: Alkaline phosphatase, transient hyperphosphatasemia, acute bronchiolitis, infant

ÖZ

Geçici hiperfosfatemi, metabolik kemik veya karaciğer hastalığı olmaksızın bebeklik ve çocukluk döneminde yüksek serum alkalik fosfataz seviyeleri ile karakterize, çocuklarda nadir görülen iyi huylu bir durumdur. Birçok farklı durum ile ortaya çıkabileceği gibi özellikle gastrointestinal, kulak, idrar ve solunum yolu enfeksiyonlarında geçici hiperfosfatazemi görülebilmektedir. Viral bulaşıcı bir hastalık tarafından tetiklendiğine inanılır. Klinisyenlerin bu konuda bilinçlendirilmesi tanıyı kolaylaştırması ve ek araştırmalar gerektirmemesi açısından önemlidir. Burada human bocavirüs enfeksiyonu ile ilişkili akut bronşiolit ile birlikte geçici hiperfosfatazemi saptanan olgu sunulmaktadır.

Anahtar kelimeler: Alkalen fosfataz, geçici hiperfosfatazemi, akut bronşiolit, bebek

Received: 08.04.2022

Accepted: 18.05.2022

Corresponding Author

Raziye Merve Yaradılmış MD,
University of Health Sciences Turkey,
Ankara Dr. Sami Ulus Gynecology,
Child Health and Diseases Training
and Research Hospital, Clinic of
Pediatric Emergency Care, Ankara,
Turkey

✉ karaomermive@hotmail.com

ORCID: 0000-0003-1202-8564

Cite as: Yaradılmış RM, Bodur İ,
Göktuğ A, Güneylioğlu MM, Öztürk
B, Güngör A, Tuygun N. Transient
Hyperphosphatasemia Associated with
Human Bocavirus Infection.
J Dr Behcet Uz Child Hosp.
2022;12(3):230-232

INTRODUCTION

Transient hyperphosphatasemia is characterized by elevated serum alkaline phosphatase (ALP) levels in infancy and childhood without metabolic bone or liver disease⁽¹⁾. It can be seen concomitantly with many viral infections, especially gastroenteritis and upper respiratory tract infections⁽²⁾. Here, a case of transient hyperphosphatasemia with acute bronchiolitis caused by human bocavirus (HBoV) infection is presented.

CASE REPORT

Eight-month-old boy (who was healthy) was admitted to pediatric emergency service with complaints of cough

and wheezing. He was admitted with a diagnosis of acute bronchiolitis. At admission his head circumference 43.5 cm was [-1.28 standard deviation (SD)], body weight 9,600 gr (0.5 SD), body length 74 cm (0.82 SD), body mass index 17.5 (0.01 SD) and growth and development was normal. From laboratory findings, ALP level was 4647 IU/L (age-adjusted normal range: 110-302 IU/L). Aspartate aminotransferase, alanine aminotransferase, glutamine transferase, bilirubin and serum creatinine levels were within normal ranges, therefore hepatic and renal pathology was excluded. One month ago, the patient had a serum ALP level of 149 IU/L. No rachitic changes were detected in the wrist X-ray of the patient. Serum calcium level was 10.3 mg/dL (reference range:

8.9-10.9 mg/dL), serum phosphate 4.8 mg/dL (reference range: 4.5-6.7 mg/dL), serum 25-hydroxyvitamin D [25(OH)D] 25 ng/mL (reference range: 25-80 ng/mL) and serum parathyroid hormone (PTH) 29 pg/mL (reference range: 11-67 pg/mL). Thus, rickets and other bone metabolism disorders were also ruled out. HBoV was identified in respiratory specimen by means of reverse transcription-polymerase chain reaction. The patient, who was followed up with oxygen and fluid therapy with a simple mask in our emergency department, was discharged home with the recommendation of control. On the 14th day of follow-up, ALP level decreased to 576 U/L and other laboratory values were within normal ranges. Without any treatment, serum ALP concentration returned to age-adjusted normal values in the first month of follow-up (Figure 1). Verbal consent was obtained from the patient's family.

DISCUSSION

ALP is an enzyme with different isoenzymes secreted from many tissues such as bone, liver, kidney and intestines ⁽¹⁾. Serum ALP concentration increases in conditions such as hepatopathy (cholestasis, malignancy), metabolic bone diseases (rickets, osteomalacia), diseases with high bone turnover (bone tumors), chronic renal failure, tubulopathies, and during treatment with some medications (cotrimoxazole, antiepileptics) ^(1,3). ALP elevation in children can also present as a benign condition known as transient hyperphosphatasemia.

Transient hyperphosphatasemia is most common in young children, especially between 6 and 24 months of age ⁽²⁾. Its prevalence in children younger than 24 months (previously healthy) has been reported to

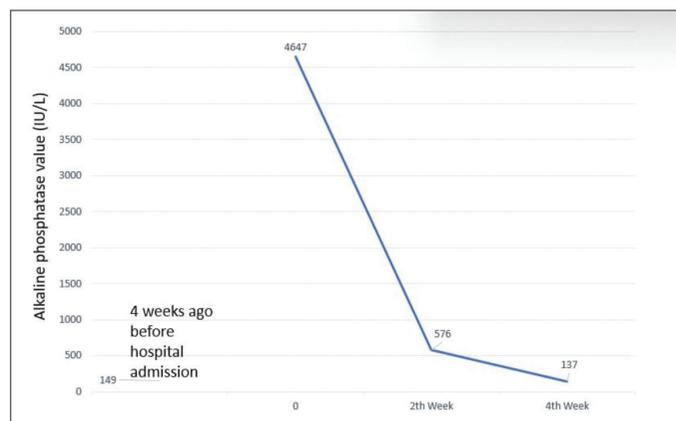


Figure 1. The time course of alkaline phosphatase elevation

range from 2.8 to 6.2 percent (between 400 and 1,000 units/L) ⁽⁴⁻⁶⁾. Often, an isolated elevation in serum ALP can be detected incidentally during laboratory testing for routine health care or as part of an evaluation for a particular complaint. Although various theories have been proposed regarding the etiology of benign hyperphosphatasemia, the pathogenesis of this clinical condition is not clear. It is a benign condition thought to be triggered by viral agents. In a study of 21 cases, it has been shown that temporary hyperphosphatasemia can be seen in especially gastrointestinal tract infections ⁽⁷⁾. In addition, it can be seen in conditions such as ear, urinary and respiratory tract infections, failure to thrive or gastrointestinal disturbances and coeliac disease ^(7,8). Pathogens such as rotavirus, echo 22, enterovirus, coxsackies, adenovirus have been associated with transient benign hyperphosphatasemia ⁽⁹⁾. It was thought that the transient hyperphosphatasemia in our patient might be associated with acute bronchiolitis caused by HBoV. Serum ALP concentration typically rises 4 and 5 times the upper reference limit ^(2,10). Rarely, elevations up to 20 times the upper reference limit have also been described in the literature. In our patient, ALP level increased 30 times compared to the ALP levels measured 1 month previously, while other laboratory values [including 25(OH)D and PTH] remained at normal levels during hospitalization and follow-up. On the 30th day of his admission, his ALP level also returned to normal limits.

CONCLUSION

Transient hyperphosphatasemia is a benign condition that accompanies many different diseases characterized by elevated serum ALP levels during infancy and childhood without metabolic bone or liver disease. It is important to raise the awareness of clinicians on this issue. In this case, recognizing the presence of transient hyperphosphatasemia may facilitate rapid diagnosis, and minimize anxiety for both the clinician and the patient's family.

Informed Consent: Verbal consent was obtained from the patient's family.

Peer-review: Externally peer-reviewed.

Author Contributions

Surgical and Medical Practices: A.G., Concept: R.M.Y., İ.B., Design: R.M.Y., İ.B., A.G., Data Collection and/or Processing: R.M.Y., A.G., M.M.G., A.G., Analysis and/or Interpretation: B.Ö., N.T., Literature Search: İ.B., M.M.G., N.T., Writing: R.M.Y., B.Ö., N.T.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Kutilek S, Cervickova B, Bebova P, Kmonickova M, Nemecek J. Normal bone turnover in transient hyperphosphatasemia. *J Clin Res Pediatr Endocrinol.* 2012;4(3):154-6. doi: 10.4274/jcrpe.680.
2. Gualco G, Lava SA, Garzoni L, Simonetti GD, Bettinelli A, Milani GP, et al. Transient benign hyperphosphatasemia. *J Pediatr Gastroenterol Nutr.* 2013;57(2):167-71. doi: 10.1097/MPG.0b013e3182922807.
3. Bakaloglu SA, Bacchetta J, Lalayiannis AD, Leifheit-Nestler M, Stabouli S, Haarhaus M, et al. Bone evaluation in paediatric chronic kidney disease: clinical practice points from the European Society for Paediatric Nephrology CKD-MBD and Dialysis working groups and CKD-MBD working group of the ERA-EDTA. *Nephrol Dial Transplant.* 2021;36(3):413-25. doi: 10.1093/ndt/gfaa210.
4. Dursun F, Kirmizibekmez H. A case series of benign transient hyperphosphatasemia from a pediatric endocrinology reference health facility in Turkey. *Pan Afr Med J.* 2018;30:206. doi: 10.11604/pamj.2018.30.206.15754.
5. Huh SY, Feldman HA, Cox JE, Gordon CM. Prevalence of transient hyperphosphatasemia among healthy infants and toddlers. *Pediatrics.* 2009;124(2):703. doi: 10.1542/peds.2008-3093.
6. Ridfelt P, Gustafsson J, Aldrimer M, Hellberg D. Alkaline phosphatase in healthy children: reference intervals and prevalence of elevated levels. *Horm Res Paediatr.* 2014;82(6):399-404. doi: 10.1159/000369205.
7. Carroll AJ, Coakley JC. Transient hyperphosphatasemia: an important condition to recognize. *J Paediatr Child Health.* 2001;37(4):359-62. doi: 10.1046/j.1440-1754.2001.00686.x.
8. Griffiths J, Vernocchi A, Simoni E. Transient hyperphosphatasemia of infancy and childhood. A study of serum alkaline phosphatase by electrofocusing techniques. *Arch Pathol Lab Med* 1995;119(9):784-9. Available from: <https://europepmc.org/article/med/7668935>
9. Behúlová D, Bzdúch V, Holesová D, Vasilenková A, Ponec J. Transient hyperphosphatasemia of infancy and childhood: study of 194 cases. *Clin Chem.* 2000;46(11):1868-9. doi: 10.1093/clinchem/46.11.1868.
10. Bassrawi R, Alsabie N, Alsorani D, Amir B. Transient hyperphosphatasemia in children. *Sudan J Paediatr.* 2014;14(2):85-8. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4949803/pdf/sjp-14-85.pdf>