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Benign transient hyperphosphatasemia in children

Бенигна пролазна хиперфосфатаземија код деце

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Бенигна пролазна хиперфосфатаземија код деце

SUMMARY

Introduction/Objective Benign transient hyperphosphatasemia (BTH) is a pathogenetic insufficiently clear clinical entity that is mostly seen in infants and young children.

The aim of this paper is to present our experience regarding the age of occurrence, the conditions of the discovery, and the length of duration of BTH in children.

Methods The study was realized on a sample of 18 children, 9 boys and 9 girls, aged 10–42 (21.06 ± 9.35) months with BTH. The diagnosis of BTH is based on the absence of bone and hepatobiliary diseases, and its spontaneous disappearance over the course of several months.

Results One patient was in the first year, 13 in the second, 3 in the third and one in the fourth. Isolated high activity of serum alkaline phosphatase (ALP), which was 2.04–21.9 (8.05 ± 5.31) times above the upper reference value for the corresponding age, in 14 cases it was found during the acute diarrhea and in 4 with acute rhinopharyngitis, of which in 2 complicated with otitis media. The cause of diarrhea in 6 cases was Rotavirus, in 2 Campylobacter and in one Adenovirus, and otitis media in one case was Streptococcus pneumoniae, while in other etiologic factors of infection it was not identified. Spontaneous normalization of serum ALP activity was recorded between 1 and 3 months.

Conclusion BTH is a harmless biochemical disorder that spontaneously subsides within 3 months after initial observation. It is found randomly as a routine laboratory finding most often within the treatment of acute gastrointestinal and respiratory infections.

Keywords: benign transient hyperphosphatasemia; diagnostics; children

САЖЕТАК

Увод/Циљ Бенигна пролазна хиперфосфатаземија (БПХФ) представља патогенетски недовољно јасан клинички ентитет који се претежно виђа код одојчади и мале деце.

Циљ рада је да се изнесу наша искуства везана за узраст јављања, околности откривања и дужину трајања БПХФ код деце.

Методе Рад је реализован на узорку од 18 деце, девет дечака и девет девојчица, узраста 10–42 (21,06 ± 9,35) месеци са БПХФ. Дијагноза БПХФ је базирана на одсуству коштаних и хепатобилираних обољења, као и њеном спонтаном ишчезавању током неколико наредних месеци.

Резултати Једно дете је било у првој години, 13 у другој, три у трећој и једно у четвртој. Изолована висока активност серумске алкалне фосфатазе (АЛФ), која је била 2,04–21,9 (8,05 ± 5,31) пута изнад горње референтне вредности за одговарајућу старост, у 14 случајева је нађена у оквиру акутне дијареје и код четири са акутним ринофарингитисом, од чега код два компликованим оптитисом медиа. Узрок дијареје у шест случајева био је ротавирус, у два *Campylobacter* и у једном аденовирус, а отитиса медиа у једном случају *Streptococcus pneumoniae*, док код осталих етиолошки чинилац инфекције није идентификован. Спонтана нормализација серумске активности АЛФ регистрована је између једног и три месеца.

Закључак БПХФ представља безазлен биохемијски поремећај који се спонтано повлачи унутар три месеца након иницијалне опсервације. Открива се случајно као рутински лабораторијски налаз најчешће у склопу третмана акутних гастроинтестиналних и респираторних инфекција.

Кључне речи: бенигна пролазна хиперфосфатаземија; дијагностика; деца

INTRODUCTION

Benign transient hyperphosphatasemia (BTH) is a complex and pathogenetic vague clinical entity expressed by transiently increased serum activity of alkaline phosphatase (ALP) [1–7]. It occurs in the absence of skeletal, liver and other diseases characterized by the increase in ALP [2, 3, 5–9]. It is detected by accident either during routine health check or by examining one of the diseases [2, 3, 5–10]. It is most commonly found in children under 5

years of age, especially in infants, and rarely later [2–12]. Although rare, BTH is also occurrening in adults [13]. Return to normal ALP levels usually occurs within four months, and sometimes a little later [4, 9–12]. The most common circumstance of its occurrence is various infections, usually viral, and rarely other pathological conditions [1, 3, 10, 14]. Bearing in mind the absence of any negative consequences, BTH is considered a benign biochemical disorder and does not require extensive investigations nor the use of vitamin D or other therapeutic procedures [3, 4, 8].

We present our experiences regarding age of occurrence, detection conditions, diagnostic mode and duration of BTH in children.

METHODS

The study included a sample of 18 children, 9 boys and 9 girls, aged 10–42 (21.06 ± 9.35) months with BTH. The diagnosis of BTH is based on the absence of bone and hepatobiliary diseases, and its spontaneous disappearance over the next few months. The study protocol was approved by the local ethics committee.

Apart from current infections in which isolated elevated serum ALP levels have been identified, medical history, clinical findings and routine laboratory analyzes have indicated that they are healthy, optimally developed and adequately nourished children.

Bearing in mind the fact that skeletal and hepatobiliary diseases are the most frequent cause of increased serum activity of ALP, initial diagnostic procedures have been primarily targeted in this direction. In this sense, ultrasonographic examination of the abdomen and radiography of he wrist was done in all patients. A key laboratory parameter for the absence of a hepatobiliary disease as the cause of hyperphosphataemia was the normal serum activity of gamma glutamyl transferase, while the elimination of bone disease was based on values of laboratory parameters sveral laboratory parameters, such as normal serum calcium, phosphorus, 25(OH)D, parathyroid hormone, creatinine, as well as blood acid-base status and urinary calcium/creatinine ratio. After skeletal and hepatobiliary disorders were excluded, the follow up of the patients included check-up of ALP every 2-4 weeks, untill normalization of values.

RESULTS

One patient was in the first year, 13 in the second, 3 in the third and one in the fourth.

In all patients, BTH was reported accidentally within a routine laboratory blood test, in 14 with acute diarrhea and in 4 with acute rhinopharyngitis, two of which complicated by otitis media. The cause of diarrhea in 6 cases was Rotavirus, in 2 Campylobacter and in one Adenovirus, and otitis media in one case was Streptococcus pneumoniae, while in other etiologic factors of infection it was not identified.

The initial value of serum ALP was 2.04–21.9 (8.05 ± 5.31) times above the upper reference value for the corresponding age, while its spontaneous normalization was registered after 1 to 3 months of follow-up, respectively, in 10 patients within 1 month, and 4 within.5 months, and in 4 within after 3 months.

DISCUSSION

ALP is an omnipresent cell membraneous zinc-containing metalloenzyme that catalyzes the hydrolysis of phosphate monoesters at basic pH values [15, 16]. According to the origin, human APHs are divided into four isozymes that are intestinal, placental, germ cell and tissue nonspecific or liver/bone/kidney [2, 15, 16]. Except for the bone ALP, which has role in skeletal mineralization, the exact physiological function of other isoenzymes both in the physiological and pathological conditions is not clear [16–19]. In circulation it is an inactive enzyme. The half-life in the blood of the liver isoenzyme is 3 days and the bone isoenzyme is 1–2 days [20, 21]. The serum level of ALP in children is normally 2 to 3 times higher than in adults due to physiologically higher osteoblast activity [2]. For the same reason in healthy children, bone isoenzyme contributes 85% to ALP activity and liver isoenzyme contributes only 15% [2]. Due to placental isoenzyme, the serum ALP level is physiologically elevated during pregnancy, while in all other conditions, with the exception of BTH, it represents a significant marker of the presence of various diseases, primarily skeletal and hepatobiliary [3, 3].

BTH represents a harmless biochemical abnormality that spontaneously disappears within a few months [1–9]. It is most commonly found in children under 5 years of age usually as an incidental finding during laboratory testing for routine health care, or as part of an evaluation for a specific complaint [2, 3, 5, 10]. When it comes to children, the most common illnesses accompanied by BTH are various infections, usually viral, and rarely other pathological conditions [1–5, 10, 11, 14, 22, 23, 24]. Also, BTH occurs as part of the use of some drugs, such as sulfamethoxazole / trimethoprim, cyclosporine, methotrexate and 6-mercaptopurine, as well as after renal and liver transplantation [25–28]. Described are the rare cases of benign familial hyperphosphatasemia [29, 30].

Our patients demonstrate the classic features of children with BTH. Apart from current infections in which isolated elevation of serum ALP levels were identified, all were healthy, optimally developed and adequately nourished children. They all belonged to the children of the youngest age, of whom 13 were in the second and third year, one in the first and one in the fourth. Smilar to most other authors, BTH was found in our patients as an incidental finding during routine laboratory testing as part of an evaluation of intercurent infections. In 14 of our patients, BTH was identified during acute infectious diarrhea and in 4 during acute upper respiratory infection, in two of them 2 complicated by otitis media. The cause of diarrhea in 6 patients was Rotavirus, in 2 Campylobacter and in one Adenovirus, and otitis media in one patient was Streptococcus pneumoniae, while in other etiologic factors of infection it was not identified. The period of spontaneous normalization of serum ALP activity occurred after 1–3 months, so none of them, except initial exclusion of bone and hepatobiliary disease, did not require additional examination.

CONCLUSION

BTH represents a harmless biochemical disorder. Its diagnosis is based on the absence of bone and hepatobiliary diseases, and its spontaneous disappearance over the next few months. According to our findings, it is happening in children within the first 4 years as a random finding during routine laboratory testing as part of evaluation of intercurrent gastrointestinal and respiratory infections. If bone and hepatobiliary disorders are excluded and thereafter a spontaneous fall in the serum ALP activity followed, no additional examination is required.

Conflict of interest: None declared.

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