© Pediatr Med Rodz 2018, 14 (4), p. 428–430
DOI: 10.15557/PiMR.2018.0058

Received: 08.06.2018
Accepted: 19.09.2018
Published: 31.12.2018

Cigdem Alkan[1], Makbule Neslişah Tan[2], Vildan Mevsim[2]

Attention to biotinidase deficiency in children! A case report

Uwaga na niedobór biotynidazy u dzieci! Opis przypadku

[1] Karaburun State Hospital, Izmir, Turkey
[2] Department of Family Medicine, Faculty of Medicine, Dokuz Eylul University, Izmir, Turkey
Correspondence: Makbule Neslişah Tan, Dokuz Eylul Universitesi Tıp Fakultesi Aile Hekimligi AD, 35340 Balcova Izmir, Turkey, tel.: +90 505 5669019, fax: +90 232 4124956, ORCID: 0000-0002-3262-7815, e-mail: drnesli293@hotmail.com

Abstract

Biotinidase deficiency is an autosomal recessive metabolic disease that causes biotin deficiency. The exact diagnosis of the lack of biotinidase is made by demonstrating the absence of enzyme activity in the serum. Biotinidase deficiency is treated with oral biotin taken for lifetime. Early diagnosis and treatment are very important and prevent a number of complications. In this case report, a newborn baby was referred for periodic healthcare assessments to a family medicine centre, where biotinidase deficiency was diagnosed. Screening performed as part of periodic health assessment in the primary care setting is important for the detection of certain diseases, as many disease-related disabilities can be prevented with early diagnosis. In family practice, "shared decision-making," which represents one of the elements of the patient-centred clinical method, is very effective, provided that patients and their relatives adapt to preventive healthcare.

Keywords: biotinidase deficiency, newborn screening, primary care

Streszczenie

Niedobór biotynidazy jest autosomalnym recesywnym zaburzeniem metabolicznym powodującym niedobór biotyny. Rozpoznanie niedoboru biotynidazy ustala się na podstawie braku aktywności enzymatycznej w surowicy, a jego leczenie polega na doustnym przyjmowaniu biotyny przez całe życie. Wczesne rozpoznanie i leczenie mają bardzo istotne znaczenie i pozwalają zapobiec licznym powikłaniom. W opisanym przypadku niedobór biotynidazy został rozpoznany u noworodka w ośrodku medycyny rodzinnej, gdzie został on skierowany w celu przeprowadzenia okresowej oceny stanu zdrowia. Badania przesiewowe wykonywane w ramach okresowej kontroli w placówkach podstawowej opieki zdrowotnej odgrywają ważną rolę w wykrywaniu niektórych chorób. W praktyce lekarza rodzinnego „wspólne podejmowanie decyzji", które stanowi jeden z elementów klinicznej metody zorientowanej na pacjenta, jest skuteczne o tyle, o ile pacjenci i ich krewni potrafią dostosować się do wymogów profilaktycznej opieki zdrowotnej.

Słowa kluczowe: niedobór biotynidazy, badania przesiewowe u noworodków, podstawowa opieka zdrowotna

INTRODUCTION

Biotinidase deficiency is an autosomal recessive metabolic disease causing the deficiency of biotin which acts as a cofactor for carboxylases including propionyl-CoA carboxylase, methylcrotonyl-CoA carboxylase, pyruvate carboxylase, and acetyl-CoA carboxylase[1–4]. The exact diagnosis of the lack of biotinidase is made by demonstrating the absence of enzyme activity in the serum. The lack of biotin causes multiple carboxylase deficiency resulting in lactic acidosis and organic aciduria[2]. If untreated, individuals with biotinidase deficiency usually develop skin rash, alopecia, ataxia, seizures, respiratory problems, fungal infections, developmental delay, hypotonia and also hearing loss and visual problems such as optic atrophy[3–5]. The disease may also lead to death from lactic acidosis[2]. The reported age at presentation is from the second week of life in neonates[2], but the typical age of presentation ranges from 3 to 12 months[4].

Fortunately, early diagnosis and treatment with pharmacological doses of oral biotin can prevent all symptoms if treatment is initiated at birth or before the symptoms develop; but the hearing loss, visual abnormalities and neurological sequelae do not appear to be reversible once they occur – even with biotin therapy[3–5]. Turkey is one of the world's countries with the highest prevalence of biotinidase deficiency. The frequency of occurrence in Turkey is 1:11,000 in newborns, and it is approximately eight times the combined worldwide incidence[6,7]. After the detailed characterisation of biotinidase deficiency in 1983, a rapid colorimetric method for measuring biotinidase activity on dried blood spots was developed. This resulted in the first neonatal screening for biotinidase deficiency in 1985[3]. Neonatal screening for biotinidase deficiency is conducted in many countries[8]. In Turkey, biotinidase deficiency screening based on heel blood samples has been performed since 2007, and it is legally mandated as part of routine child care.

CASE REPORT

The baby described in the case report was born weighing 3,250 g, at 39 weeks, of G2 P2 A0 (gravida/para/abortus) mother after normal spontaneous vaginal birth, and was discharged on the 2nd postnatal day, as there were no health problems in the postnatal period.

Before leaving the hospital, the baby's family were advised that they should report to their registered family physician, and the baby's health checks and follow-ups should be continued by the family physician. The baby was taken by the family to the primary care facility on the 5th postnatal day. The physical examination performed by the family physician revealed no abnormalities. There was no remarkable family history. A heel blood sample, which is legally required to be examined in the primary care setting, was taken and the family was advised to continue periodic examinations as part of routine child care, and report the results of laboratory tests. The baby's repeated heel blood colorimetric measurement found the biotin value to be 16.3 (normal reference range: 62–143 nkat/L). The result was evaluated as low by the family physician who suggested repeating the test. The parents indicated that a heel blood sample had already been taken at the hospital where the child was born, and therefore they were opposed to taking a sample of heel blood for the third time in order to verify the result. The mother and father said that the first child, aged 6 years, was healthy and so their newborn infant did not have any disease. For this reason, they declared that they would not allow the blood tests to be repeated. The family physician gave explanatory information about the disease prevalence and the screening programme, and encouraged the parents to share their reasons and concerns related to the refusal. The parents stated that having a baby diagnosed with an unknown disease made them experience anxiety and fear. The family, who had been registered at the family healthcare centre for approximately one year, was informed by the family physician that if the diagnosis is made early on, the necessary treatment can be started without delay and it is possible to avoid many complications. After this conversation between the family doctor and the physician, the family consented to the repetition of the heel blood sample test.

While waiting for the results of the repeated test, the baby became ill and was referred with respiratory distress to the paediatrician, and ultimately admitted to the secondary referral healthcare institution with the diagnosis of paediatric pneumonia. The expected biotin value at this time was 16.7 nkat/L (normal reference range: 62–143 nkat/L). The paediatrician was notified by the family physician, and the baby was admitted to the healthcare facility where the university paediatric neurology unit is located in order to continue examinations and undergo treatment of both respiratory distress and biotinidase deficiency. The paediatric neurology unit confirmed the diagnosis of biotinidase deficiency and started treatment both for the current health problems and the underlying biotinidase deficiency.

Therapeutic compliance, participation in follow-up examinations and changes in drug dosage were closely monitored by the family healthcare centre throughout this process, and psychological support and medical consulting services were provided to the family in the primary care setting.

DISCUSSION

The patient-centred approach refers to a two-way interaction between the patient and the clinician; discovering patient values and preferences, helping patients and their relatives in the clinical decision-making phase, facilitating appropriate care access, and establishing grounds for the development of behavioural changes that are difficult or necessary for the patient in the interest of protecting and promoting health. The "shared decision-making" principle

 DOI: 10.15557/PiMR.2018.0058

is one of the fundamental competencies in the discipline of family medicine.

The baby's family members were initially opposed to the repeat test after a low biotinidase value was detected, so a biopsychosocial approach was adopted by the family physician in search of the common ground. While trying to understand the reason for the family's opposition, it was found that the family experienced increasing levels of anxiety and concern about not knowing whether their baby had a disorder. It was understood that the family members did not want to accept this situation. The mother, father and sister had no disease, which also reinforced their belief that there was no evidence for an autosomal recessive disorder, and hence the baby was disease-free.

Patient advocacy is defined as "helping the patient to participate effectively in the clinical decision-making process and work with the authorities to ensure that services are equally distributed to all the people in the community at the highest level." Here, the family physician is a cost-effective function by providing services from the secondary or tertiary healthcare systems and managing contacts with the services. Advocacy is the basic task of the discipline, aimed at protecting patients from harm that might be caused by unnecessary screening, testing and treatment, and guiding them in the complexity of the healthcare system[9].

CONCLUSION

It is necessary to emphasize the importance of periodic health screening by the family physicians, based on mutual confidence and communication, biopsychosocial approach, finding common ground with the patient, demonstrating advocacy of the patient, and active involvement in the management of resources.

Conflict of interest

There was no financial support for our work or potential conflicts of interest.

References

1. Rezvani I, Rosenblatt DS: Valine, leucine, isoleucine, and related organic acidemias. In: Behrman RE, Kliegman RM, Jenson HB (eds.): Nelson Textbook of Pediatrics. 17th ed., W.B. Saunders, Philadelphia 2004: 409–418.
2. Haagerup A, Andersen JB, Blichfeldt S et al.: Biotinidase deficiency: two cases of very early presentation. Dev Med Child Neurol 1997; 39: 832–835.
3. Porta F, Pagliardini V, Celestino I et al.: Neonatal screening for biotinidase deficiency: a 30-year single center experience. Mol Genet Metab Rep 2017; 13: 80–82.
4. Hoffman TL, Simon EM, Ficicioglu C: Biotinidase deficiency: the importance of adequate follow-up for an inconclusive newborn screening result. Eur J Pediatr 2005; 164: 298–301.
5. Wolf B: Biotinidase: its role in biotinidase deficiency and biotin metabolism. J Nutr Biochem 2005; 16: 441–445.
6. Baykal T, Hüner G, Sarbat G et al.: Incidence of biotinidase deficiency in Turkish newborns. Acta Paediatr 1998; 87: 1102–1103.
7. Pomponio RJ, Coskun T, Demirkol M et al.: Novel mutations cause biotinidase deficiency in Turkish children. J Inherit Metab Dis 2000; 23: 120–128.
8. Therrell BL, Padilla CD, Loeber JG et al.: Current status of newborn screening worldwide: 2015. Semin Perinatol 2015; 39: 171–187.
9. Allen J, Gay B, Crebolder H et al.: The European definition of general practice/family medicine. In: Evans P (ed.): WONCA Europe 3rd ed.; 2011. Available from: http://www.woncaeurope.org/gp-definitions.

DOI: 10.15557/PiMR.2018.0058