CASE REPORT

Biotinidase deficiency mimicking primary immune deficiencies

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SUMMARY

Biotinidase deficiency (BD) is an inborn metabolic disorder inherited in an autosomal recessive manner. Partially due to high consanguinity rates in Turkey, BD incidence is high in Turkey. If left untreated, neurological abnormalities including seizures, hypotonia, sensorineural deafness, alopecia, egzamatous skin rash and candidiasis may occur. Three-years-old girl was admitted to hospital with recurrent infections, candidiasis and egzamatous skin rash. Immunological evaluation was normal. Associated deafness and consanguinity of the parents suggested BD which has been proven by enzyme activity measurement. With this report, we want to emphasise that BD can be the underlying cause of recurrent infections and candidiasis.

BACKGROUND

Biotinidase deficiency (BD) is an inborn metabolic disorder caused by low enzyme activity giving rise to impaired biotin release from dietary proteins. The enzyme activity is within 10–30% in partial type and <10% in severe forms.[1] Although the worldwide prevalence is known as 1:60 000, it is reported as high as 1:11 614 in Turkey partially due to high consanguinity rates.[1 2] The gene encoding biotinidase enzyme has been found in chromosome 3p25. Biotin deficiency can give rise to sensorineural deafness, optic atrophy, seizures, hypotonia, mental retardation, alopecia, dermatitis and ataxia. The first symptoms may be seen at first week following birth until 1 year of age. The delay in diagnosis and treatment may cause irreversible neurological damage, growth retardation and autistic behaviours. The goal of the therapy is to increase biotin bioavailability by daily 5–20 mg lifelong biotin replacement.[3 4]

CASE PRESENTATION

Three-year-old girl born to consanguineous parents, admitted to paediatric immunology clinic with oral moniliasis resistant to oral antifungal therapy, recurrent upper respiratory tract infections, recurrent diaper dermatitis, folliculosis and erythematous skin rash. Physical examination revealed oral moniliasis, skin dryness and peroral erythematous rash. BCG scar and tonsils were present. She had no onychomycosis and was using hearing device. Neurological examination was normal except for sensorineural deafness. Complete blood cell count showed hypochromic microcytic anaemia with normal absolute lymphocyte and neutrophil counts. Immunoglobulin levels and lymphocyte subset analysis were within normal range. Candidin skin test showed no induration. Iron replacement therapy and oral antifungal therapies were started with no improvement in her symptoms.

BD was considered due to the consanguinity, sensorineural hearing loss, recurrent infections and dermatitis. She was born before the nationwide biotinidase newborn screening programme. Enzyme assay for biotinidase revealed low activities 1.6 IU/L (normal ranges >3.5 IU/L). Urinary organic acid analysis was normal. Molecular analysis was performed for BD and she was found heterozygote for the mutation of R157H. Oral biotin replacement was started in a dose of 5 mg/day which dramatically improved her symptoms besides hearing loss.

DISCUSSION

Biotinidase is an enzyme giving source to biotin with releasing it from dietary proteins. The biotin is then utilised by carboxylase enzyme class involved in fatty acid synthesis, amino acid catabolism and gluconeogenesis.[4] Impaired biotin bioavailability causes multiple carboxylase deficiency and thus, secondary ketoacidosis, hyperammonaemia and organic aciduria. Various neurocutaneous symptoms like seizures, motor mental retardation, hypotonia, spastic paraparesis, ataxia, sensorineural deafness, optic atrophy, egzamatous dermatitis and alopecia are associated with the classical disease.[5]

The diagnosis is made with detection of low enzyme activity and genetic mutation analysis besides clinical suspicion. The enzyme activity is <10% in severe form whereas between 10% and 30% in partial deficiency. Biotin replacement therapy may improve symptoms, although the hearing loss cannot be reversed.[5–8] The newborn screening programme provides early diagnosis with appropriate therapy before onset of the neurological symptoms.[5] Partial BD may be less serious despite our patient with severe deafness. The vulnerability to *Candida* infections seen in those patients is not clear, but further functional assessments may elicit the relation between biotin and recurrent infections. The unresponsiveness to candidin skin test in our case suggests an impaired T lymphocyte function to *Candida* antigen. BD should be suspected in patients with recurrent infections, persistent candidiasis, deafness and growth retardation which in this case misleaded us by mimicking primary immune deficiencies. We reported this case to increase awareness and to emphasise the importance of early diagnosis.

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Learning points

- Biotinidase deficiency should be investigated in patients with unexplained recurrent infections, candidiasis and dermatitis.
- Biotinidase deficiency can cause negative candidin test.
- Replacement therapy can reverse the clinical findings except sensorineural deafness.

Contributors EK serves as the guarantor for the article. He accepts full responsibility for the work and/or the conduct of the study, had access to the data and controlled the decision to publish. He has been involved in conception, design, analysis and interpretation of the data and also drafting the article. AK has been involved in conception, design, analysis and interpretation of the data. MSC has been involved in analysis and interpretation of the data. CAAZ has been involved in conception, design, interpretation of the data, revising the article critically for important intellectual content.

Competing interests None declared.

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