Case Report

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Tetraparesis as an initial manifestation of biotinidase deficiency: a case report

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Introduction and importance: Biotinidase deficiency (BTD) is an autosomal recessive disorder and causes the deficiency of four biotin-containing carboxylases. The prevalence is estimated at 1 in 60 000 births. BTD is associated with a wide spectrum of clinical manifestations, including abnormalities of the neurological, dermatological, immunological, and ophthalmological systems. Spinal cord demyelination as a manifestation of BTD has been infrequently described.

Case presentation: The authors present a case of 2.5-year-old boy complained of progressive weakness in all four limbs, with difficulties in breathing.

Clinical discussion: Abdominal examination revealed hepatomegaly and splenomegaly. Also, her parents were first-degree cousins. Therefore, tandem mass spectroscopy and urine organic acid analysis were planned to exclude metabolic disorders. Urinary organic acid analysis revealed elevated levels of methylmalonic acid and 3-hydroxyisovaleric acid. Serum biotinidase activity was found to be 3.9 nmol/min/ml. Oral biotin at a dose of 1 mg/kg daily was initiated. A marked improvement of his neurological deficit was noted over a period of 15 days after treatment and cutaneous manifestations resolved within 3 weeks.

Conclusion: Myelopathy due to BTD is a challenging diagnosis. Spinal cord impairment is a rare complication of this disease and is frequently unrecognized. BTD should be included in the differential diagnosis of children presenting with demyelinating spinal cord disease.

Keywords: biotinidase deficiency, spinal cord demyelination, tetraparesis

Introduction

Biotinidase deficiency (BTD) is an autosomal recessive disorder and causes the deficiency of four biotin-containing carboxylases. The prevalence is estimated at 1 in 60 000 births[1–3].

Wolf and colleagues[1,2] first described BTD in the 1980s.

BTD is associated with a broad-ranging of clinical manifestations, including abnormalities of the neurological, dermatological, immunological, and ophthalmological systems[2,4].

Perioral or facial rash, eczema, glossitis, blepharoconjunctivitis, keratoconjunctivitis, and alopecia are common cutaneous lesions[2,3]. Initial neurological symptoms may consist of seizures, ataxia, or psychomotor regression[2,5,6].

Spinal cord demyelination as a manifestation of BTD has been infrequently described.

HIGHLIGHTS

- Biotinidase deficiency (BTD) is an autosomal recessive disorder and causes the deficiency of four biotin-containing carboxylases.
- Spinal cord demyelination as a manifestation of BTD has been infrequently described.
- Myelopathy due to BTD is a challenging diagnosis.

We present a case of a 2.5-year-old boy who complained of tetraparesis and difficulties in breathing due to BTD.

This work has been reported in line with the Surgical CAse REport (SCARE) Criteria[7].

Case presentation

A 2.5-year-old boy presented at our pediatric neurology clinic with progressive weakness in all four limbs and difficulties in breathing.

His complaints had begun 2 months earlier, with frequent falls and intermittent sighing respirations.

His birth and developmental history were unremarkable. He was born of a nonconsanguineous union.

On admission, she was afebrile, pulse rate 140 /min, her blood pressure 9/6, respiratory rate 30 /min and oxygen saturation of 95% on room air. Initial neurological examination revealed intact cranial nerves, Physical examination results showed full eye movements.

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Facial movements were symmetric with normal strength.

She had upper and lower limbs weakness with medical research council score of 2/5 in proximal and distal. Ankle clonus and Babinski sign were positive.

The skin showed an erythematous maculopapular rash in the upper and lower limbs. (Fig. 1) He had alopecia, conjunctivitis, and seborrheic dermatitis involving the scalp.

Abdominal examination revealed hepatomegaly 3 cm below the left costal margin and splenomegaly 2 cm below the right costal margin.

Routine laboratory test results, including blood erythrocyte sedimentation rate, gas, ammonia, antinuclear antibody, and C-reactive protein were normal. The serum lactate level was slightly elevated, while the pyruvate concentration was normal. Blood and cerebrospinal fluid cultures were negative.

The cranial computed tomography scan and MRI results were normal. The spinal sagittal and axial T2-weighted MRI revealed diffuse edema and an abnormal signal between the medulla and the fifth cervical vertebra. Figure 2.

According to clinical and laboratory findings, transverse myelitis was diagnosed.

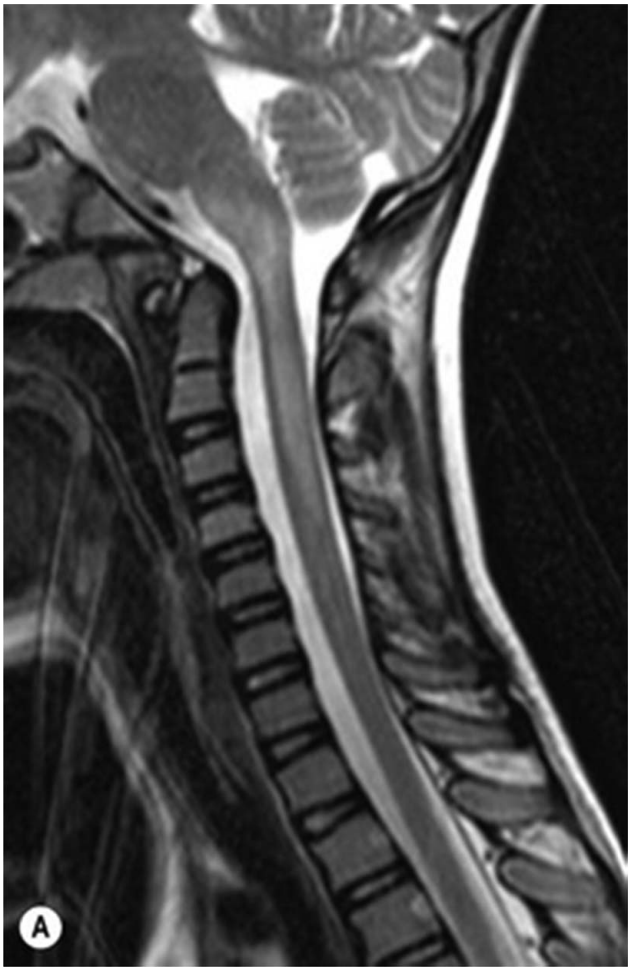

Figure 1. Erythematous and scaly rash with erosions involving the limbs.

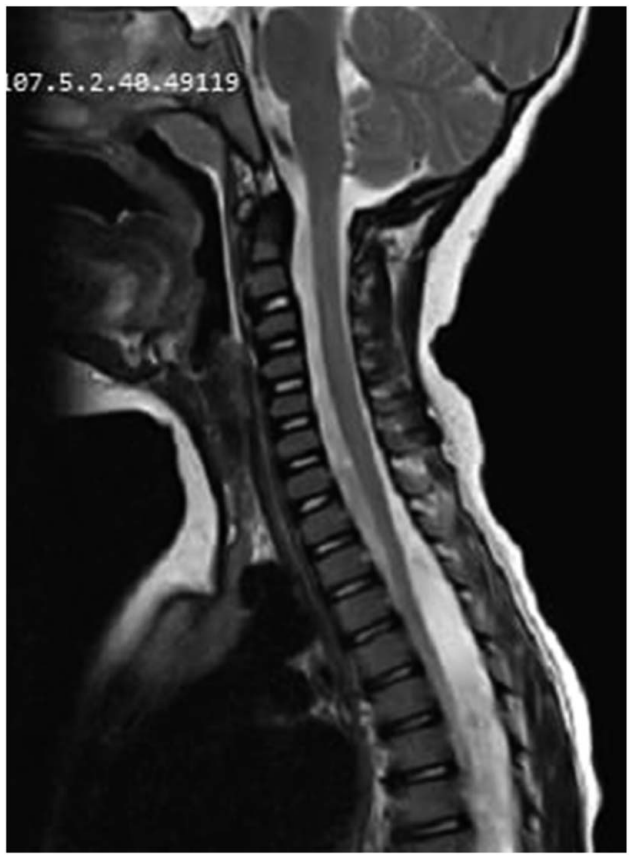

Figure 2. Sagittal T2-weighted MRI reveals diffuse edema and abnormal signal between the medulla and the fifth cervical vertebra.

After obtaining the patient's informed consent, treatment was planned by a consultant neurologist

She was given pulse doses of IV methylprednisolone (30 mg/kg). Then intravenous immunoglobulin 1 gr/kg was given daily for 2 days to the patient. Unfortunately, her clinical findings did not show any improvement.

Tandem mass spectroscopy and urine organic acid analysis were planned to exclude metabolic disorders.

Urinary organic acid analysis revealed elevated levels of methylmalonic acid and 3-hydroxyisovaleric acid. By clinical and laboratory findings, BTD was diagnosed, and serum biotinidase activity was found to be 3.9 nmol/min/ml (4.4 to 10 nmol/min/ml) by the colorimetric assay.

The management was done by a consultant neurologist.

After obtaining the patient's informed consent, treatment was planned.

Oral biotin at a dose of 1 mg/kg daily was initiated.

A marked improvement of his neurological deficit was noted over a period of 15 days after treatment, and cutaneous manifestations resolved within 3 weeks.

A spinal cord MRI performed after 4 months showed complete regression of the white-matter changes. Figure 3.

Discussion

Biotinidase (EC 3.5.1.12) is the enzyme that cleaves the vitamin, biotin, from the biocytin and from the dietary protein-bound

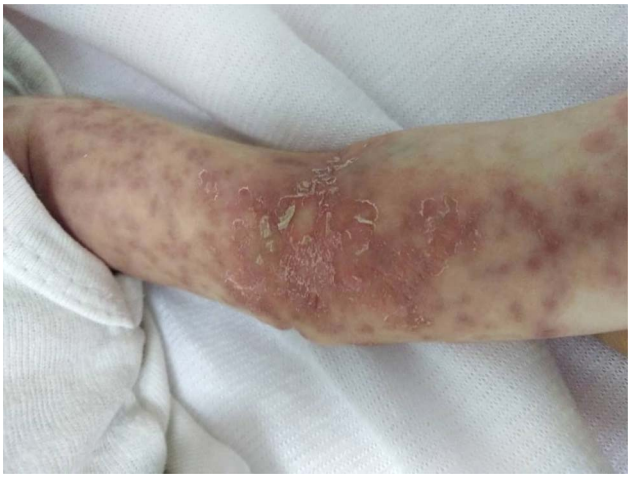

Figure 3. Sagittal T2-weighted MRI shows complete regression of the white-matter changes.

sources, thereby recycling the biotin[1]. Free biotin can directly enter the biotin pool and is used by four carboxylases to convert their active forms. Biotin is the coenzyme for four carboxylases that have roles in gluconeogenesis, the catabolism of several branch-chain amino acids, and fatty acidsynthesis[8,9].

BTD is an autosomal recessive inherited neurocutaneous disorder[1,10].

Spinal cord impairment is a rare complication of BTD and is often difficult to recognize.

Multiple individuals who have exhibited spastic para- or tetraplegia, ranging in age from 19 months to 22 years of age at the time of diagnosis, have since been reported[11,12]

The following are disorders commonly considered in the differential diagnosis of acute inflammatory myelitis, multiple sclerosis, transverse myelitis, myasthenia gravis, Leigh syndrome, Leber hereditary optic atrophy, neuromyelitis optica, brainstem encephalitis, and Weinicke encephalopathy.

Fortunately, the disorder can be effectively treated by administering these individuals' pharmacological doses of oral biotin. Although the symptoms can markedly improve, some, such as optic atrophy, hearing loss, and some aspects of cognitive disabilities, may be irreversible[13].

The findings indicate that BTD should be considered in the differential diagnosis of unexplained spinal cord demyelination because prompt diagnosis and treatment with biotin may enable an excellent recovery[14,15].

Conclusion

Myelopathy due to BTD is a challenging diagnosis. Spinal cord impairment is a rare complication of this disease and is frequently unrecognized.

BTD should be included in the differential diagnosis of children presenting with demyelinating spinal cord disease.

Ethical approval

This study was not applicable for ethical approval.

Consent for publication

Written informed consent was obtained from the patient's parents for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

M.B.: first author, data collection, writing the paper; F.A.: writing the paper; A.H.: writing the paper; S.B.: treatment and examination of the patient, writing the paper.

Conflicts of interest disclosure

All authors declared no conflict of interest.

Research registration unique identifying number (UIN)

The case report at hand is not a first-in-man case report of a novel technology or surgical technique, therefore a registration of these case reports according to Declaration of Helsinki 2013 is not required.

Guarantor

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