Cerebrotendinous xanthomatosis: a rare cause of spinocerebellar syndrome

Żółtakowatość mózgowo-ścięgnista: rzadka przyczyna zespołu rdzeniowo-móżdżkowego

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Abstract

A 34-year-old patient demonstrating pyramidal and cerebellar signs, accompanied by epilepsy, peripheral neuropathy, mental retardation and bilateral cataract was diagnosed with cerebrotendinous xanthomatosis based on the clinical picture, magnetic resonance imaging of the brain and serum sterol analysis. Tendon xanthomas were not observed in this case. After establishing the diagnosis, treatment with chenodeoxycholic acid and statin was introduced. During the next two years of the follow-up, serum cholestanol and 7α-hydroxycholesterol levels decreased in response to the therapy, but this was not reflected in the patient's neurological condition, which was slowly progressing. Treatment effectiveness in cerebrotendinous xanthomatosis is variable, notably better in patients who had started therapy before the injury to the nervous system took place. The present case report points to cerebrotendinous xanthomatosis as a rare cause of spinocerebellar syndrome, which might be treatable if diagnosed in early life.

Key words: cerebrotendinous xanthomatosis, spinocerebellar syndrome, treatment.

Streszczenie

U 34-letniego chorego z objawami piramidowymi i móżdż - kowymi, padaczką, neuropatią obwodową, upośledzeniem umysłowym oraz obustronną zaćmą na podstawie obrazu klinicznego, badania rezonansu magnetycznego mózgu i oznaczenia stężenia steroli w surowicy rozpoznano żółtakowatość mózgowo-ścięgnistą. Nie obserwowano u tego chorego żółtaków ścięgien. Do leczenia włączono kwas chenodeoksycholowy oraz statynę. Chociaż podczas kolejnych dwóch lat obserwacji stwierdzono zmniejszenie stężenia cholestanolu i 7α-hydroksycholesterolu w surowicy chorego w odpowiedzi na leczenie, jego stan neurologiczny stopniowo się pogarszał. Odpowiedź na leczenie żółtakowatości mózgowo-ścięgnistej jest zróżnicowana; lepsza u chorych, u których leczenie rozpoczęto, zanim wystąpiły zmiany w ośrodkowym układzie nerwowym. Przedstawiany opis przypadku zwraca uwagę na żółtakowatość mózgowo-ścięgnistą jako rzadką przyczynę zespołu rdzeniowo-móżdżkowego, który mógłby być uleczalny, jeśli zostałby rozpoznany na wczesnym etapie życia.

Słowa kluczowe: żółtakowatość mózgowo-ścięgnista, zespół rdzeniowo-móżdżkowy, leczenie.

Introduction

Cerebrotendinous xanthomatosis (CTX) is an autosomal recessive lipid storage disorder caused by deficiency in a mitochondrial enzyme – 27-sterol hydroxylase (CYP 27), which is involved in the conversion of cholesterol into bile acids. Impairment of this metabolic pathway leads to excessive formation of cholestanol, a poorly soluble compound that later accumulates in the tissues, predominantly in the brain, tendons, lenses and lungs [1].

Clinical manifestations of CTX include progressive neurological dysfunction (pyramidal and cerebellar signs, epilepsy, mental retardation, extrapyramidal features, polyneuropathy), bilateral cataract, tendon xanthomas, and

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diarrhoea. Due to varying occurrence of these signs and symptoms, the diagnosis may not be straightforward. Cerebrotendinous xanthomatosis is potentially treatable. Administration of chenodeoxycholic acid inhibits the synthesis of cholestanol and bile alcohols and thus can stop the progression of clinical symptoms. However, treatment is most efficient if started at early stages, before irreversible brain lesions take place.

We describe a patient with spinocerebellar ataxia as the major symptom, who was diagnosed with CTX. The patient has been treated with chenodeoxycholic acid and statin, but his condition failed to improve during two-year follow-up.

Case report

A 34-year-old male was admitted with progressive gait impairment and concomitant slurred speech, that had been present for several months. There were behavioural problems reported by the patient's family: he became more impulsive, irritable and had lost his interests during the preceding months. His medical history also revealed bilateral cataract developed in his childhood, mild mental retardation and epilepsy, which started when he was 17. The family history was not remarkable.

Neurological examination on admission revealed spastic paraparesis with bilateral extensor plantar responses, cerebellar ataxia, pes cavus and slight, predominantly distal wasting of lower limbs. The tendons were not enlarged. The patient's score on the Mini-Mental State Examination (MMSE) was 24. Neuropsychological assessment indicated frontal and subcortical dysfunction.

Electroencephalography demonstrated slight slowing of background rhythm and groups of delta waves in centro-parietal leads. Nerve conduction study and electromyography were suggestive of chronic, primary demyelinating, sensorimotor polyneuropathy.

Magnetic resonance imaging (MRI) of the brain revealed hyperintense areas in T2-weighted images and FLAIR sequences in periventricular white matter and dorsal parts of the centrum semiovale, along corticospinal tracts in posterior limbs of the internal capsules, cerebral peduncles, pons, anterior part of the medulla oblongata and in dentate nuclei bilaterally, where they were accompanied by fluid signal areas. None of those areas showed contrast enhancement (Fig. 1).

Differential diagnosis in this case included autosomal dominant spinocerebellar ataxias, Marinesco-Sjögren syndrome, Friedreich's ataxia, mitochondrial diseases, abetalipoproteinaemia, multiple sclerosis (MS), leukodystrophy and CTX. The diagnosis of autosomal dominant spinocerebellar ataxia was questionable due to negative family history and hyperintensities on MRI. Nevertheless, genetic tests for spinocerebellar ataxia type 1, 2 and 3 were performed and were negative. Magnetic resonance imaging findings were incompatible with the diagnosis

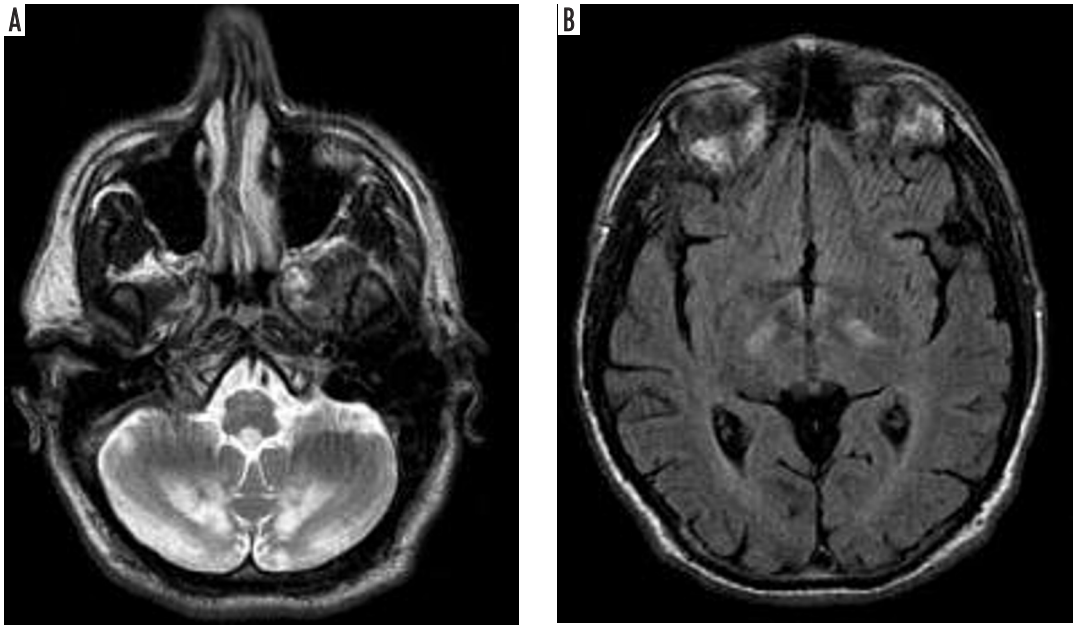

Fig. 1. Hyperintense areas in dentate nuclei of cerebellum bilaterally on axial T2-weighted magnetic resonance imaging (A) and in posterior limbs of both internal capsules on FLAIR sequences (B)