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Case Report

Achilles swelling and ataxia in an adolescent: A case report of cerebrotendinous xanthomatosis*

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ABSTRACT

Cerebrotendinous xanthomatosis (CTX) is a rare hereditary disease characterized by a bile acid metabolic problem that causes cholesterol metabolites to accumulate in various organs. There are 2 types of CTX: traditional and spinal. The imaging characteristics are usual and allow for diagnosis confirmation. The brain's magnetic resonance imaging (MRI) reveals bilateral dentate nucleus lesions as well as modest white matter abnormalities. Tendon xanthomas (typically in the Achilles tendons on both sides) are a common finding. Cerebrotendinous xanthomatosis is a multidisciplinary diagnosis that must be made early to avoid neurologic injury and worsening. We show a CTX instance that has typical imaging and biology features.

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Introduction

CTX (cerebrotendinous xanthomatosis) is a rare autosomal-recessive bile acid metabolism condition caused by a sterol 27-hydroxylase enzyme deficiency [1,2]. Lack of it causes bile acid synthesis to be hampered, as well as an increase in the creation of cholesterol metabolites such cholestanol, which then accumulate in the brain, tendons, eyes, bones, and arteries [3]. The disease's most noticeable characteristics are juvenile cataract, mental retardation, and tendons swelling with cerebellar ataxia [4]. A mix of neurological, ocular, and musculoskeletal aspects, as well as neuroimaging and biochemical results, are used to make the diagnosis [5]. Early diagnosis is

critical in order to benefit from chenodeoxycholic acid therapy and thereby prevent the condition from progressing [4].

Case report

An 18-year-old woman came in with swelling in her ankles and a cognitive decline. The patient was well until she was 7 years old, when she experienced bilateral increasing ankle edema. From the age of ten years old, her parents noted frequent stumbles and difficulty walking, followed by ataxia. The patient's knees swelled a few years later, when he was 12 years old. In addition, she had previously experienced sight issues.

CTX, cerebrotendinous xanthomatosis.

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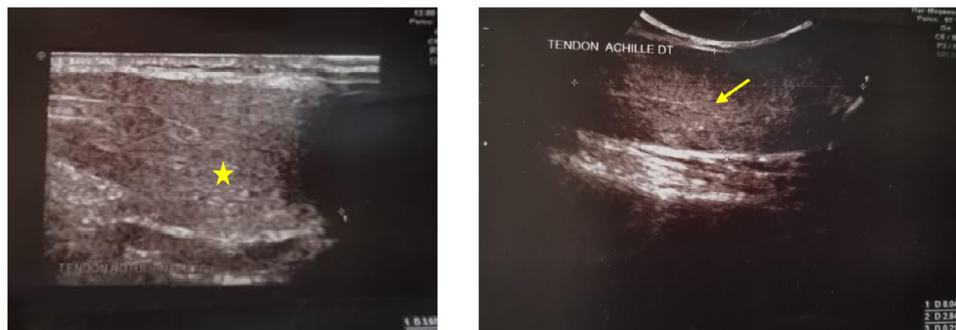


Fig. 1 – US of ankle and knee swelling revealing a well-defined, homogenous, hyperechoic mass completely replacing the Achilles (arrow) and patellar tendons (star)

Over all Achilles, quadriceps, and patellar tendons, the osteo-myo-articular examination revealed bilateral painless and non-fistulized masses. Spastic paraparesis, rapid deep reflexes, and extensor plantar responses were discovered during a neurological examination. The Romberg test resulted in a positive result with 1 eye closed.

A bilateral thick cataract with impaired vision was discovered during the ophthalmic examination.

Total cholesterol, LDL, HDL, and triglyceride levels were all within normal limits. Otherwise, the amounts of cholestanol and bile alcohol in the bile and urine were high.

An ultrasound of the ankles and knees revealed well-defined, homogeneous, hyperechoic masses that had nearly completely replaced the tendons (Achilles, quadriceps and patellar tendons) (Fig. 1).

The Achilles tendons had a fusiform expansion with a convex anterior border and were isointense to muscle on MRI of the ankles. The axial image revealed low signal intensity patches strewn over the muscle, giving it the distinctive speckled look (Fig. 2)

On T2 weighted and FLAIR sequences, MRI of the brain revealed hyperintensity of the dentate nuclei (with a hypointensity on susceptibility weighted imaging corresponding to calcification deposits) (Fig. 3).

A biopsy at the level of Achilles tumefaction showed an aspect of tendinous xanthoma made of fibroblastic tissue remodelled by a dense inflammatory granuloma rich in cholesterol crystals. In contact with these crystals, numerous multinucleated giant cells were observed, associated with numerous foamy histiocytes.

All of these clinical, biological, radiological, and histological data supported the CTX diagnosis.

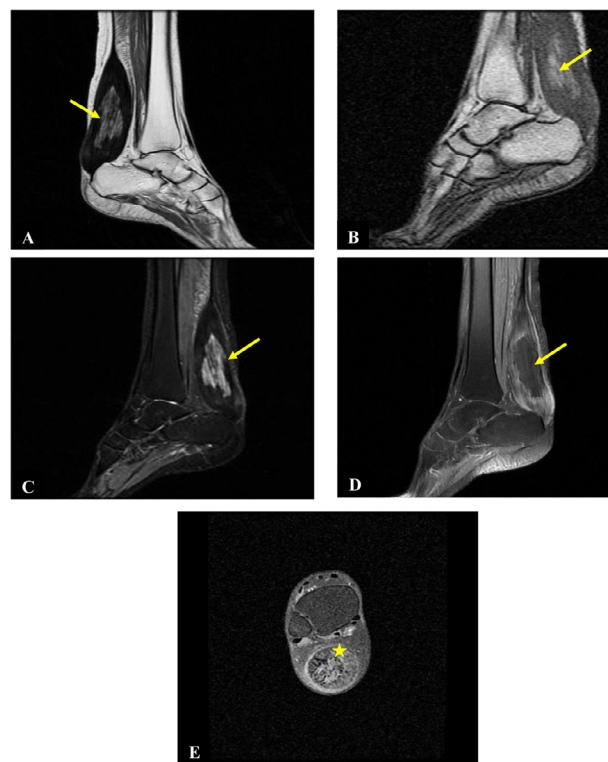


Fig. 2 – Sagittal proton density image (A), T1-weighted image (B), fat suppression on short tau inversion recovery (STIR) (C), T1-fat-saturated-weighted image following contrast agent injection (D), T1-weighted image with fat saturation (E) demonstrating a fusiform enlargement of the Achilles tendon, which has a convex anterior border and is isointense to muscle (arrows), with widely spaced tendon fibers interposed with fat (speckled appearance) (star)

Discussion

CTX, also known as Van Bogaert-Scherer-Epstein disease, is an extremely rare genetic illness that was originally described in 1937 [6,7]. Setoguchi et al. found in 1974 that faulty side chain oxidation causes reduced bile acid production in patients with cholesterol CTX [1]. Mutations in the CYP27A1 gene on chromosome 2q33-qter cause this condition [1]. Despite the fact that 54 distinct mutations have been identified, no established

link between genotype and phenotype has been discovered [7]. The mitochondrial enzyme sterol 27-hydroxylase is encoded by this gene. This enzyme is involved in the conversion of cholesterol to cholic acid and chenodeoxycholic acid, which are the major bile acids [1,8]. The bile acid synthesis route, cholesterol 7-hydroxylase, is hampered by the paucity of these acids [8].

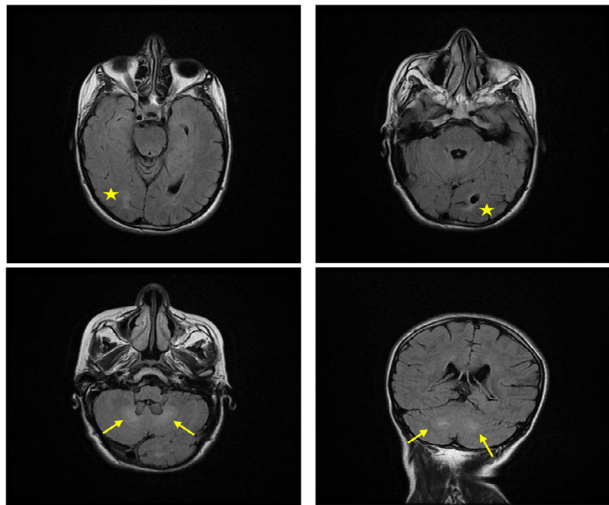


Fig. 3 – Axial and coronal FLAIR images showing hyperintensities of dentate nuclei (arrows) and periventricular white matter (stars)

Increased serum cholestanol levels and increased bile alcohol levels in urine are used to make a biochemical diagnosis of CTX [8]. 33030 g/dL plasma cholestanol concentration, 8.483.67 nmol/L bile alcohol concentration, and 14 0003 500 nmol/L urine bile alcohol concentration [1]. High plasma cholestanol concentration, normal-to-low plasma cholesterol concentration, decreased CDCA level, and higher levels of cholestanol and apolipoprotein B in cerebral fluid distinguish CTX from other disorders with xanthomas [1]. 5- α -cholestanol is a CTX biomarker [1].

CTX manifests itself in a variety of ways. Bilateral cataracts and diarrhea appear in children, followed by progressive cerebellar and pyramidal symptoms, cognitive difficulties, seizures, and the development of tendon xanthomas in late adolescence or early adulthood [10]. Slowly progressing myelopathy, including pyramidal and dorsal column symptoms, characterizes the spinal type of CTX [10].

Cerebellar atrophy, white matter signal changes, bilateral and symmetrical hyperintensities in the dentate nuclei, globus pallidus, substantia nigra, and inferior olive are among the most prevalent neuroimaging findings in CTX patients [8,7] (Fig. 3). The pathogenic process of rarefaction and neuronal death corresponds to FLAIR hyperintensity and enhanced diffusivity [8]. Necrosis and consequent calcium deposits are responsible for the reduced signal on all sequences [11]. The demyelinated areas, caused by the xanthomas, appear hyperintense on T2-weighted images with a peripheral rim in T2 hyposignal [11]. The Xanthomas are sometimes seen in the choroid plexus [11].

In hypointense FLAIR lesions, magnetic resonance spectroscopy (MRS) tests revealed raised lactate and lipid peaks, as well as a diffusely reduced N-acetyl-aspartate (NAA) peak [1]. Before and after treatment, SPECT imaging reveals variations in regional cerebral blood flow (rCBF) in different cerebral lobes, enabling for treatment response monitoring in CTX patients [1].

Tendon xanthomas are most commonly found on the Achilles tendon in adults [4]. The accumulation of xanthoma cells and many, distributed lipid crystal clefts in tendon blocks can be seen histopathologically [1].

The scanner allows us to assess the tendon's size and density. The density of the tendon is reduced when cholesterol builds up in it [12]. The degenerative or inflammatory process of the tendon fibers could increase the density, thereby compensating for the effect of cholesterol accumulation [12], but this situation is not widely noted in the literature.

Xanthomas that seem hypoechoic or hyperechoic can be distinguished from normal tendon that appears isoechoic with a fibrillar structure using ultrasound [12] (Fig. 1). Calcifications can be detected by conventional radiology [12].

A hypointense signal on MRI indicates tendon hypertrophy. On T1 and T2 weighted sequences, soft tissue xanthomas also look hypointense [5] (Fig. 2).

The spinal type of CTX is characterized by white matter abnormalities in the lateral and gracile corticospinal pathways [10].

CTX has a wide range of differential diagnoses, most of which are related to lipid storage disorders such as familial hypercholesterolemia and sitosterolemia [8,9]. The absence of neurological symptoms and cataract formation distinguishes CTX from sitosterolemia.

The absence of neurological symptoms and the growth of cataracts distinguish Sitosterolemia from CTX. Hypercholesterolemia is indicated by the development of xanthomas with high cholesterol levels but normal cholestanol levels [5]. Marinesco-Sjogren syndrome, an autosomal recessive disease characterized by the triad of cerebellar ataxia, congenital cataract, and mental retardation, is also a differential diagnosis, but the presence of scoliosis, short bones of the hand and foot, and the absence of tendon xanthomas distinguish this disease from CTX [5,6].

Disorders with hyperintensity of dentate nuclei on T2W images must be distinguished from CTX on neuroimaging [5]. Metronidazole toxicity, acutely decompensated maple syrup urine illness, and Langerhan cell histiocytosis are just a few of them [5,8].

The treatment is based on chenodeoxycholic acid, which stops cholestanol from forming [5]. This therapy avoids neurological injury and degeneration when started early [8].

Conclusion

CTX is a lipid metabolic illness that has distinct clinical and radiologic characteristics. Imaging studies serve an important role in early diagnosis. It's a diagnosis that shouldn't be overlooked, especially since it may be treated with CDCA substitution therapy to avoid negative neurological repercussions.

Patient consent

Written informed consent for publication was obtained from patient.

Author's contributions

All authors contributed to this work. All authors have read and approved the final version of the manuscript.

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