Cerebrotendinous Xanthomatosis: A Moroccan Case Report and Review of Literature

Dear Editor,

Cerebrotendinous xanthomatosis is a rare autosomal recessive disease, classified within the group of normolipemic xanthomatosis.\[1\] It’s the result of sterol 27-hydroxylase deficiency. This enzyme is part of the cytochrome P-450 family, which is required for side-chain oxidation of cholesterol to bile acids. As a result, the synthesis of bile acids is reduced.

The absence of the negative feedback mechanism of cholic acid on 7α-hydroxylase, which is a rate-limiting enzyme of bile acid synthesis, increases this enzyme activity and leads to the accumulation of bile precursors, such as cholestanol in plasma and tissues and bile alcohols that are excreted in urine.\[2\]

The age at onset of cerebrotendinous xanthomatosis is variable, although most clinical presentations appear in the first or second decade of life. Clinical features are insidious and unpredictable. Cataracts and diarrhea are seen in adolescence but are not always present. These lesions appear in infancy as nodules usually located on the Achilles tendons, although the tibia tuberosities, the extensor tendons of the fingers, and the triceps may also be involved. A high incidence of coronary artery disease can be seen because of premature atherosclerosis.\[3,4\]

Our case is a 29-year-old Moroccan woman who was admitted to the department of rheumatology with a slow progressive enlargement of both ankles and the back side of the third and the fourth fingers of the left hand and tumors in the elbow of the right arm and the lateral side of the left foot [Figure 1] since she was 10-year-old and which have become painful in the previous year. Her parents are not related. Her one older and one younger siblings were normal, while one older sibling was mentally subnormal with less intense symptoms as his sister, declining a visit to the hospital for medical care.

Physical examination revealed firm, rounded and subcutaneous tumors of noninflammatory nature, over the Achilles, extensor digitatarum longus in the base of the fifth metatarsal, finger extensor of the third and fourth fingers of the left hand and common extensor in the right arm tendons, xanthomas were not found. Neurologic examination showed ataxia and mental retardation. Ophthalmologic examination was normal.

The results of laboratory studies of our patient, including cholesterol and triglycerides levels were normal. Blood cell count and protein electrophoresis, conducted to exclude malignant hemopathies in front of the normality of lipid tests, were also normal.

X-ray revealed soft tissue density in bilateral Achilles tendons. The MRI including T1 and T2 sequences of sagittal and axial sections of both ankles showed infiltration of the Achilles tendons [Figure 2]. Electroencephalogram showed diffuse slow activity. Brain MRI demonstrated slight cerebral atrophy and hypersignal in bilateral dentate nuclei [Figure 3]. Otherwise a chronic pansinusitis was found.

Surgical removal of xanthomas of the extensor digitatarum longus in the base of the fifth metatarsal, finger extensor of the third and the fourth fingers of the left hand and common extensor in the right arm tendons was performed, [Figure 4] with good recovery after the surgery. The histological examination of the biopsy specimen revealed fibrocollagenous tendinous tissue with many ill-defined aggregates of foamy histiocytes, which confirms the diagnosis of tendinous xanthoma.
Life style recommendations, along with close and regular follow-ups, and genetic counseling, were proposed to the patient.

Cerebrotendinous xanthomatosis is a rare lipid storage disease characterized by tendon xanthomatosis and progressive neurologic dysfunction. The diagnosis is confirmed by biochemical blood tests that include measurement of b-cholestanol, in parallel with an abnormal sterol profile characteristic of cerebrotendinous xanthomatosis, or by measurement of urinary bile alcohols by gas chromatography in tandem with mass spectrometry that is not a common analysis, or by histological study of the biopsy specimen which can reveal an aggregate of foamy cells separated.\(^{[2,5]}\) Genetic study of family members can lead to an early diagnosis in presymptomatic homozygotes and detect heterozygotes.\(^{[2]}\)

Magnetic resonance imaging shows cerebral and cerebellar atrophy and typically includes a bilateral and almost symmetric increase of the signal intensity on the T2-weighted images in the cerebellar and periventricular white matter, the basal ganglia, the dentate nuclei, and the brain stem. The electroencephalogram might show diffuse slow activity or mild neuronal dysfunction.\(^{[6‑8]}\)

The impact assessment including ECG, echocardiography, supraaortic trunks ultrasound and lower limb Doppler ultrasound were normal.

The treatment is based on administering the bile acids that are lacking. Chenodesoxycholic acid (CDCA) is used as standard therapy. It appears that prolonged use could stop or, less likely, cause a regression of the disease, without any significant adverse effects. Recent studies propose the addition of Hydroxymethylglutaryl Coenzyme A reductase inhibitors (atorvastatin or simvastatin) to lower cholesterol.

**Figure 1:** Clinical appearance of tendons xanthomas

**Figure 2:** The MRI of sagittal and axial sections of both ankles showed infiltration of the Achilles tendons and a xanthome in the extensor digitarum longus in the base of the fifth metatarsal of the left foot

**Figure 3:** Brain MRI shows hyperintense signals in the bilateral cerebellar dentate nuclei

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concentrations that might increase with administration of CDCA.[9] The neurological damage is irreversible. The treatment should be initiated at the onset of symptoms (cataracts, diarrhea, and mild neurologic abnormalities). If xanthomas have developed, it is usually too late to obtain satisfactory results.[10]

However, this treatment is not available in many countries, including Morocco.

Also a surgical removal of disturbing xanthomas can be proposed.

Between the fourth and sixth Decades, death usually occurs as a consequence of progressive neurologic deterioration, pseudobulbar paralysis, or acute myocardial infarction.[11]

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There are no conflicts of interest.