

## Cerebrotendinous Xanthomatosis, A Rare Metabolic Disease

MAHMUDUR RAHMAN SIDDIQUI,<sup>1</sup> MD SHAHRIAR MAHBUB,<sup>1</sup> QUAZI TARIKUL ISLAM<sup>2</sup>

### Abstract:

*Cerebrotendinous xanthomatosis (CTX) is a rare genetic lipid storage disease. CTX is characterised by childhood-onset cataract, adolescent to young adult-onset tendon xanthomas and adult-onset progressive neurological dysfunction (dementia, psychiatric disturbances, pyramidal and/or cerebellar signs and seizures). A 32-year-old male patient presented to us with the features of this rare genetic metabolic disorder.*

**Keyword:** Cerebrotendinous xanthomatosis, tendon xanthoma, seizure, lipid storage disease.

### Introduction:

Cerebrotendinous xanthomatosis (CTX) is a rare genetic metabolic disorder of cholesterol and bile acid metabolism that results in systemic and neurologic abnormalities. The patient develops multiple tendon xanthomas, cataract and neuro-logical deficits (dementia, psychiatric disturbances, pyramidal and/or cerebellar signs and seizures).<sup>1,2</sup> The disease was first described in 1937 by Van Bogaert and colleagues.<sup>3</sup> More than 300 patients have been diagnosed worldwide, with an estimated prevalence of 1 case per 50,000 individuals in white populations.<sup>4</sup> It can present at any age with no sex differentiation. Early diagnosis during childhood helps early treatment that prevents progression of disease.

### Case Report:

A 32-year-old male patient presented with an illness that had started from his childhood with the development of multiple gradually enlarging painless skin swellings over knees,

ankles, elbows and dorsum of the feet. He did not complete his primary education because of learning difficulties. For last 2 years he had been suffering in recurrent seizure. On examination, the patient's IQ was below average. There were multiple subcutaneous swellings of different size and shape over the extensor surfaces of the knees, ankles, elbows, left great toe and dorsum of the right foot. They were firm, non-tender and fixed with underlying tendons. He also had bilateral cataract. The biochemical and haematological investigations, including the lipid profile were normal. CT scan of the head showed generalized mild cortical atrophy. Histopathological examinations of the tissue from xanthoma revealed Birefringent lipid crystals are surrounded by giant cells. With all of these findings he was diagnosed as a case of very rare lipid storage disease called Cerebrotendinous xanthomatosis (CTX).



**Fig-1:** Xanthoma over both tendoachilles, left great toe, dorsum of right foot.

1. Consultant, Medicine, The Medical Center
2. FCPS Medicine P-II Course, DMCH.
3. Professor of Medicine, Department of Medicine, DMCH.

**Correspondence:** Dr. Mahmudur Rahman Siddiqui, DMCH. E-mail: dr.mahmud99@yahoo.com



**Fig-2:** Xanthoma over both knees.

### Discussion:

Cerebrotendinous xanthomatosis is a rare autosomal recessive lipid-storage disease caused by mutations in the sterol 27-hydroxylase gene. Deficiency of the enzyme 27-hydroxylase causes an impairment of the metabolic pathway of bile acid synthesis from cholesterol, resulting in an excessive production of cholestanol, which then accumulates in many tissues (brain, tendon, muscle, blood vessels etc). The disease begins in infancy. Bilateral cataracts associated with chronic diarrhoea may be the earliest clinical manifestations. Xanthomata develop in the second and third decades of life. They are usually found on the Achilles tendon but may also be found on the patella, elbow, hand, and neck tendons. Significant neurological impairment also occurs; this often includes mental retardation, seizures, dementia and pyramidal and/or extra pyramidal dysfunction and typically begins in the third decade of life but the clinical presentations may vary considerably.<sup>1,2,5</sup>

High plasma and tissue cholestanol concentration with normal-to-low plasma cholesterol concentration and decreased chenodeoxycholic acid can easily differentiate it from other xanthomatous diseases (Familial hypercholesterolaemia, Sitosterolemia).<sup>1,2</sup> Bile acid production is reduced, although the activity of the rate-limiting enzyme of bile production is elevated.<sup>6</sup> MRI and CT scanning may revealed diffuse atrophy of the brain, as well as focal lesions (including demyelinating lesions and rarely, xanthomata) in the cerebellum, basal ganglia, and cerebrum.<sup>7</sup> Histopathology can be done from affected tissue which usually revealed spindle-shaped lipid crystal clefts, fibrosis, hemosiderin deposition surrounded by giant cells with foamy cytoplasm.<sup>8</sup>

Long term treatment with chenodeoxycholic acid (CDCA) effective in decreasing cholestanol concentration and improving clinical features.<sup>1,9</sup> If hypercholesterolemia is not controlled with CDCA treatment alone, 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase inhibitors may

be added.<sup>9</sup> This is a progressive and terminal disease if left untreated. Treated patients may have a normal lifespan.

**Conflict of Interest:** None

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