Cerebrotendinous Xanthomatosis Unmasked by Fine Needle Aspiration Cytology of Tendon Xanthomas.

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Abstract: Cerebrotendinous xanthomatosis (CTX) is a rare auto somal recessive lipid storage disorder caused by mutations in the *CYP27A1* gene, resulting in deficiency of sterol 27-hydroxylase, a key enzyme in bile acid synthesis. Impaired bile acid metabolism leads to accumulation of cholesterol and cholesterol in multiple tissues, particularly the brain, tendons, and eyes. We report a case of a 32-year-old male who presented with multiple symmetrical tendon swellings involving the Achilles tendons and elbows, along with progressive lower limb stiffness and a history of early-onset cataracts. Magnetic resonance imaging (MRI) of the brain demonstrated bilateral T2/FLAIR hyper intensities involving the cerebellar dentate nuclei and per ventricular white matter. Fine needle aspiration cytology (FNAC) from the tendon swellings revealed numerous foamy macrophages, multinucleated giant cells, and cholesterol clefts in a lipoidal background, consistent with xanthomatous pathology. Biochemical evaluation was suggestive of CTX. This case highlights the diagnostic value of FNAC as a simple and minimally invasive adjunct, particularly when correlated with clinical and radiological findings, and underscores its usefulness in resource-limited settings for early recognition of CTX.

Keywords: Cerebrotendinous xanthomatosis, tendon xanthoma, fine needle aspiration cytology, lipid storage disorder

Introduction

Cerebrotendinous xanthomatosis (CTX) is a rare but treatable autosomal recessive disorder of bile acid synthesis caused by mutations in the *CYP27A1* gene, leading to deficiency of sterol 27-hydroxylase. This enzymatic defect results in reduced synthesis of chenodeoxycholic acid and impaired feedback inhibition of cholesterol metabolism, causing excessive accumulation of cholestanol and related sterols in plasma and tissues[1].

The disease is characterized by deposition of these sterols in the central nervous system, tendons, and ocular tissues, producing a classical triad of early-onset cataracts, tendon xanthomas, and progressive neurological dysfunction[2]. Early diagnosis is crucial, as delayed recognition and treatment may result in irreversible neurological impairment. While biochemical assays, neuroimaging, and genetic confirmation are

central to diagnosis, cytological evaluation of tendon swellings can provide valuable early diagnostic clues, particularly in settings with limited access to advanced investigations.

Case Presentation

A 32-year-old male presented to the orthopaedic outpatient department with multiple painless, gradually progressive swellings over both elbows (Figure 1), bilateral Achilles tendons (Figure 2), dorsum of the left hand, and the upper part of the left tibia. He had a past history of bilateral cataracts, for which he underwent surgery ten years earlier, and a longstanding history of chronic diarrhea.

Plain radiographs of the right elbow showed globular soft tissue masses without underlying bony erosion (Figure 3). Radiographs of both ankle regions demonstrated fusiform to globular soft tissue swellings involving the Achilles tendons (Figure 4).

FNAC was performed from the swellings over the right elbow and Achilles tendon. The smears were moderately to highly cellular and revealed numerous multinucleated giant cells with abundant foamy, vacuolated cytoplasm. Scattered round to oval cells with centrally placed nuclei, consistent with foamy macrophages, were present in a blood-mixed lipoidal background. Cholesterol clefts were also identified (Figure 5). Based on these cytological findings, a diagnosis of xanthoma was suggested, with giant cell tumor of tendon sheath considered as a differential diagnosis.

MRI of the lower limbs demonstrated symmetrical fusiform enlargement of both Achilles tendons extending over approximately 14 cm. The tendons showed intermediate signal intensity on both T1- and T2-weighted images, with thickened tendon fibbers and loss of the normal fibrillary pattern. Hyperintense striations were seen interposed between the fibers (Figure 6).

MRI of the brain revealed bilateral T2/FLAIR hyperintensities involving the cerebellar dentate nuclei and periventricular white matter, characteristic of CTX (Figure 7). Bilateral pseudophakia was noted, along with a focus of chronic micro haemorrhage in the right dentate nucleus. Biochemical evaluation was suggestive of CTX. The patient was advised treatment with chenodeoxycholic acid; however, follow-up details were not available at the time of reporting.

Discussion

Cerebrotendinous xanthomatosis is a rare inherited neurometabolic disorder first described in 1937. It is characterized by abnormal accumulation of cholestanol and cholesterol in various tissues due to impaired bile acid synthesis. If left untreated, CTX follows a progressive course leading to significant neurological disability[3].

Clinical manifestations include chronic diarrhea, tendon xanthomas, early-onset bilateral cataracts, and a wide spectrum of neurological features such as cerebellar ataxia, peripheral neuropathy, seizures, pyramidal and extrapyramidal signs, cognitive decline, and behavioral disturbances[4]. Additional associations such as premature atherosclerosis and osteoporosis have also been reported.

Diagnosis of CTX is based on a combination of clinical features, biochemical findings, characteristic neuroimaging, and genetic confirmation. MRI of the brain plays a pivotal role, with typical involvement of the cerebellar dentate nuclei and surrounding white matter on T2-weighted and FLAIR sequences[7].

There is limited literature describing the cytological features of tendon xanthomas in CTX. FNAC findings typically include foamy macrophages, multinucleated giant cells, and cholesterol clefts within a lipid-rich background. Previous reports have highlighted the role of cytology in raising suspicion of CTX in clinically suspected cases, including those with associated gouty infiltration of the Achilles tendon[8–10].

Although molecular confirmation remains the definitive diagnostic modality, cytology serves as a useful adjunct by providing early diagnostic clues and guiding further investigations, particularly in resource-limited settings. Early recognition is essential, as treatment with chenodeoxycholic acid has been shown to halt disease progression and prevent irreversible neurological damage.

Conclusion

This case underscores the importance of integrating clinical presentation, radiological findings, and cytological assessment in the diagnosis of cerebrotendinous xanthomatosis. FNAC, as a simple and minimally invasive procedure, can provide valuable diagnostic clues and facilitate early recognition of this rare but treatable disorder. Timely diagnosis and initiation of appropriate therapy remain crucial for improving long-term outcomes.

Declarations

Patient Consent:

Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

Ethics Approval:

Ethics committee approval was not required for this single case report.

Conflict of Interest:

The authors declare no conflict of interest.

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Figures:

Figure 1: Multiple globular soft tissue masses over the right elbow joint.

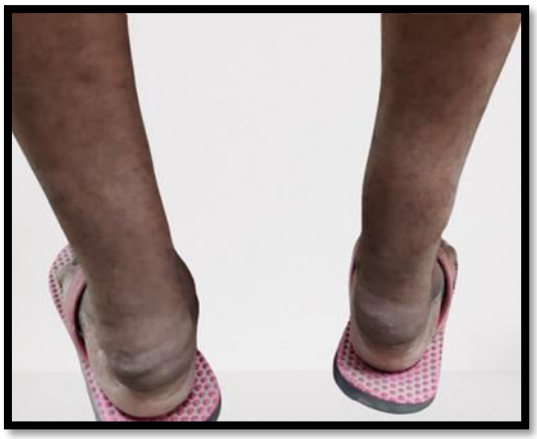

Figure 2: Fusiform to globular swelling involving both Achilles tendon regions.

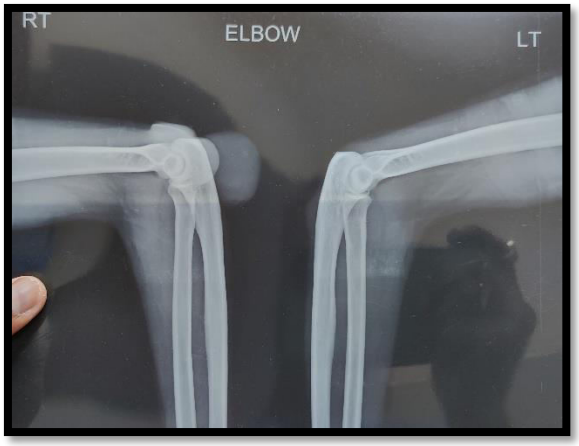

Figure 3: Lateral plain radiograph of the right elbow joint showing globular soft tissue masses.

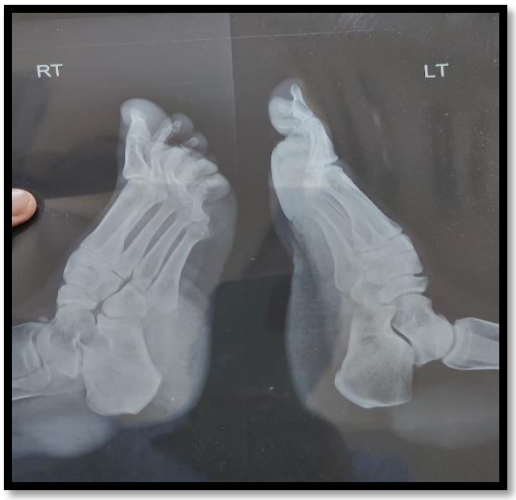

Figure 4: X-ray of both ankle regions showing fusiform to globular swelling involving both Achilles tendons.

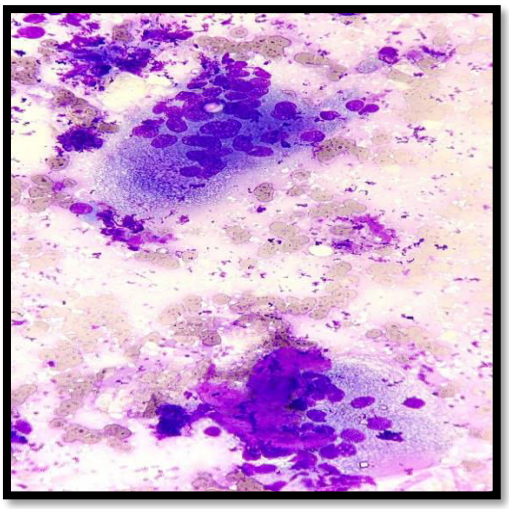

Figure 5: Fine needle aspiration cytology smear showing a multinucleated giant cell with foamy, vacuolated cytoplasm and scattered round to oval cells in the background.

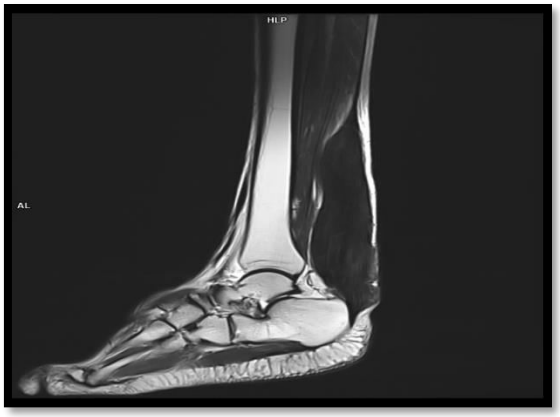

Figure 6: MRI of the leg showing fusiform thickening with loss of normal fibrillar appearance of the Achilles tendons with increased signal-intensity striations between the fibers.

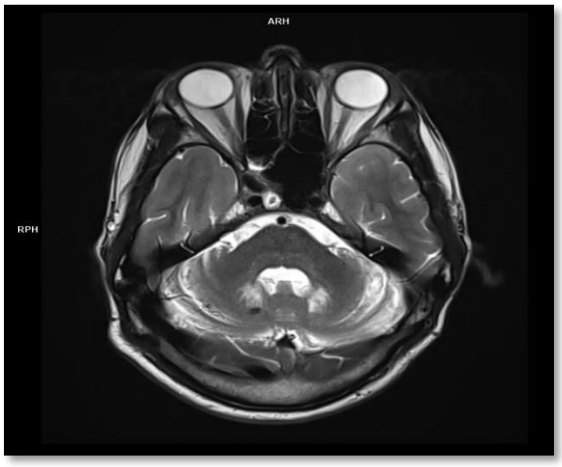

Figure 7: Axial T2-weighted MRI brain shows bilateral symmetrical hyperintensities involving the cerebellar dentate nuclei, characteristic of Cerebrotendinous xanthomatosis (CTX)