CEREBRO TENDINOUS XANTHOMATOSIS (CTX)
Author : GEETHA G
Department of Radio Diagnosis, MADRAS MEDICAL COLLEGE AND GOVERNMENT GENERAL HOSPITAL

Abstract: Cerebrotendinous xanthomatosis (CTX) is a rare autosomal recessive lipid storage disorder characterized by accumulation of cholesterol and cholestanol in various tissues, predominantly the central nervous system (CNS), tendons, lungs, liver, and kidneys. Juvenile cataract, childhood diarrhea, mental retardation, and cerebellar ataxia, along with tendon xanthomas, are the most prominent features of this disease. Early diagnosis is extremely important as patients benefit from therapy with chenodeoxycholic acid and further progression of the disease can be prevented. We present and discuss the clinical, radiological, 33-year-old male patient, 1st child of non consanguineous marriage presented with progressive unsteadiness while walking and frequent falls from 10 years of age, slurring of speech, swelling over both ankle.

Keyword: Cerebrotendinous xanthomatosis, cholestanol, chenodeoxycholic acid

CASE REPORT:
33 year old male patient, 1st child of non consanguineous marriage presented with progressive unsteadiness while walking and frequent falls – from 10 years of age, slurring of speech, swelling over both ankle. No H/o seizure/sensory disturbance. No similar illness in the family.

CLINICAL EXAMINATION:
Cerebellar signs like slurring of speech, frequent falls and unsteadiness of gait. B/L immature cataract. Swelling over both achilles tendon and generalized wasting of muscles.

BIOCHEMICAL PARAMETERS:
Lipid profile:
Total Cholesterol -- 147mg/dl
Total Triglyceride -- 90mg/dl
HDL -- 44mg/dl
Complete hemogram : NORMAL
ECHO: NORMAL
Liver function test: NORMAL
Thyroid function test: NORMAL
MINI MENTAL SCORE 19/30

CLINICAL PICTURE:

Enlarged and bulky Achilles tendon and triceps tendon in elbow

ULTASOUND:
USG: Thickening and smooth symmetric homogenous hypoechoic infiltration of Achilles tendon

COMPUTED TOMOGRAPHY ANKLE:
CT: shows thickened Achilles tendon
MRI ANKLE:
MRI: shows thickened Achilles tendon with few linear hyperintense strands due to edema. Hypointensity is due to accumulation of cholesterol and cholestenol

MRI ELBOW:
Xanthoma in Triceps Muscle causing hypointense thickening of the muscle and tendon
CT BRAIN: Bilateral Symmetrical Hypodensities in Cerebral peduncle, medial thalamus, cerebellar white matter and dentate nucleus.

MRI BRAIN: AXIAL.

MRI BRAIN: CORONAL.

MRI BRAIN: AXIAL.

MRI: Bilateral symmetric T2, FLAIR Hyperintensities in thalamus, cerebral peduncle, periventricular white matter, cerebellar white matter and dentate nucleus.

High ADC values and few foci of blooming in gradient either due to calcification and haemorrhage.

DIAGNOSIS: CEREBRO TENDINOUS XANTHOMATOSIS (CTX)

TREATMENT:
The patient has been put on chenodeoxy cholic acid and and HMG-CoA reductase. Biopsy is not mandatory. The cholestrol level is not available in India hence not done. It is mostly a clinical and radiological diagnosis and literature also insist the same. The patient is under follow up.

DISCUSSION:
CTX is a rare autosomal recessive condition caused by a deficiency of the mitochondrial enzyme sterol 27 hydroxylase, which normally catalyses the oxidation of cholesterol to bile acids. Absence of this enzyme results in an accumulation of cholesterol and cholestanol in all tissues, giving rise to tendon xanthomas.

Molecular genetic analysis has revealed that this disease is associated with a mutation of the CYP 27 gene. Van Bogaert et al. described the first CTX phenotype in 1937. Subsequent work established several additional symptoms of CTX, including cholestanol accumulation in several tissues and the absence of chenodeoxy cholic acid in the bile. These symptoms were determined to be the result of a disorder of hepatic conversion of cholesterol to cholic acid and chenodeoxycholic acid. In 1975, Salen et al. reported that administration of chenodeoxy cholic acid dramatically reduced cholestanol synthesis in CTX patients. In 1984, Berginer et al. demonstrated that one year of chenodeoxy cholic oral supplementation treatment at 750 mg/day was sufficient to produce a significant improvement in neurological symptoms, normalization of EEG readings, and a reduction in serum cholestanol in CTX patients. In 1991, Cali et al. identified a defect in the gene encoding the 27-hydroxylase enzyme in CTX patients. More than fifty different mutations of this gene have been found worldwide, and molecular analysis has enabled diagnosis during the pre-symptomatic period. In a recent study, Berginer et al. demonstrated that early diagnosis and initiation of Chenodeoxy cholic acid treatment during the pre-clinical and initial phases of CTX may prevent the development of clinical manifestations of CTX. These authors suggest that the following three steps are fundamental to prevent irreversible damage in patients with CTX:

1) recognition of early symptoms, including chronic diarrhea and juvenile cataracts, by pediatricians.
2) confirmation of the diagnosis through biochemical and genetic analysis, and
3) immediate Chenodeoxy cholic acid treatment to prevent the CTX phenotype.

These patients present with diarrhea, cataracts, and psychomotor retardation (in infancy/childhood) followed by development of xanthomas after the second decade. Xanthomas involves achilles tendons, the quadriceps, triceps, and finger extensor tendons. Patients presents with cerebellar ataxia, spinal cord paresis, and peripheral neuropathy. T2W and FLAIR images reveal bilateral symmetrical hyperintensities involving the dentate nuclei and the deep cerebellar white matter. The basal ganglia and thalami may also be involved. A few hypointense foci are sometimes seen within the hyperintensities and are presumed to be due to hemorrhage/calcification. Achilles tendon xanthomas are classically hypointense on T1W and T2W images due to the deposition of free cholesterol and cholestanol rather than triglycerides and fatty acids (which are responsible for the normal hyperintense fat signal on T1W images). The MRI may reveal a reticular/speckled appearance due to interspersed areas of slightly high signal intensity, which are presumably due to secondary edema/inflammation. USG is as sensitive as MRI in depicting the number and extent of intratendinous lesions.

CT scan and USG have been used to monitor the response to treatment as both are equally good in assessing the anteroposterior diameter of the tendons, the reduction of which is a parameter for measuring the success of treatment.

Diagnosis is based on the typical clinical history and radiological findings, and the presence of normal or low cholesterol in association with raised cholestanol levels, and the characteristic MRI appearance. biopsy is seldom necessary in the presence of all these features.

Clinically, CTX resembles the Marinisco-Sjogren syndrome, an autosomal recessive disorder characterized by the triad of cerebellar ataxia, congenital cataract, and mental retardation. The presence of tendon xanthomas helps differentiate CTX from this condition. This differentiation...
important as CTX is a treatable condition. Conservative management with chenodeoxycholic acid and HMG-CoA reductase inhibitors must be started in these patients. Clinical improvement takes time and the patient must be advised long-term follow-up and periodic evaluation. Furthermore, the clinical improvement correlated with a reduction in cholestanol serum levels. Timing of treatment is very important because treatment initiated at a late stage did not result in a functional cure of CTX. However, the treatment did promote a significant improvement in quality of life and, more importantly, prevented progression of the disease.

CONCLUSION:
Early recognition of this condition is essential because cholic and chenodeoxycholic acid replacement therapy can prevent Cerebrotendinous xanthomatosis-induced brain damage, which leads to severe neurological dysfunction and death. But as said earlier timing and early recognition is important. The response of this patient is awaited and the patient is under follow up. High clinical suspicion and immediate radiological work up is needed for early diagnosis.

REFERENCE