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Case Report Of Cerebrotendinous Xanthomatosis- A Rare Entity With Spectrum Of Clinical And Imaging Findings

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I. INTRODUCTION

Cerebrotendinous Xanthomatosis – An uncommon lipid deposition disorder, due to defective metabolisation of cholestanol-cholesterol metabolite accumulation in various tissues.[1,2]

It is inherited in an autosomal recessive manner, and is characterized by a mutated sterol 27-hydroxylase gene (CYP27A1). This enzyme is responsible for converting cholesterol and cholestenol into bile acids (cholic and chenodeoxycholic acid).[3,4]

When this enzyme is non-functional, these cholestanol compounds aggregate in soft tissues leading to clinical manifestations such as tendon xanthomas, reduced vision due to early cataract formation, early atherosclerotic changes. [5,6]

Various neurological manifestations are also seen including progressive intellectual impairment, gait abnormalities due to cerebellar dysfunction and neuropathy.[5,6]

Radiological imaging, metabolic tests, and the presence of the typical neurological and musculoskeletal symptoms, all contribute to the diagnosis..[7,8]

Early diagnosis is essential as the progress of the disease, including the intellectual impairment and cerebellar symptoms, can be halted with early treatment.[9,10]

II. CASE HISTORY:

A woman in her mid-thirties presented to Sharda Hospital , Greater Noida, India, with complains of difficulty in walking and gradually growing swelling on both lower legs and ankles posteriorly.

She had history of deterioration in scholastic performance, beginning at around the age of 13.

On clinical examination, the patient had signs of cerebellar ataxia, dysdiadochokinesia, immature cataract and diffuse, non-tender, firm swelling on the posterior aspect of bilateral ankles and lower legs.

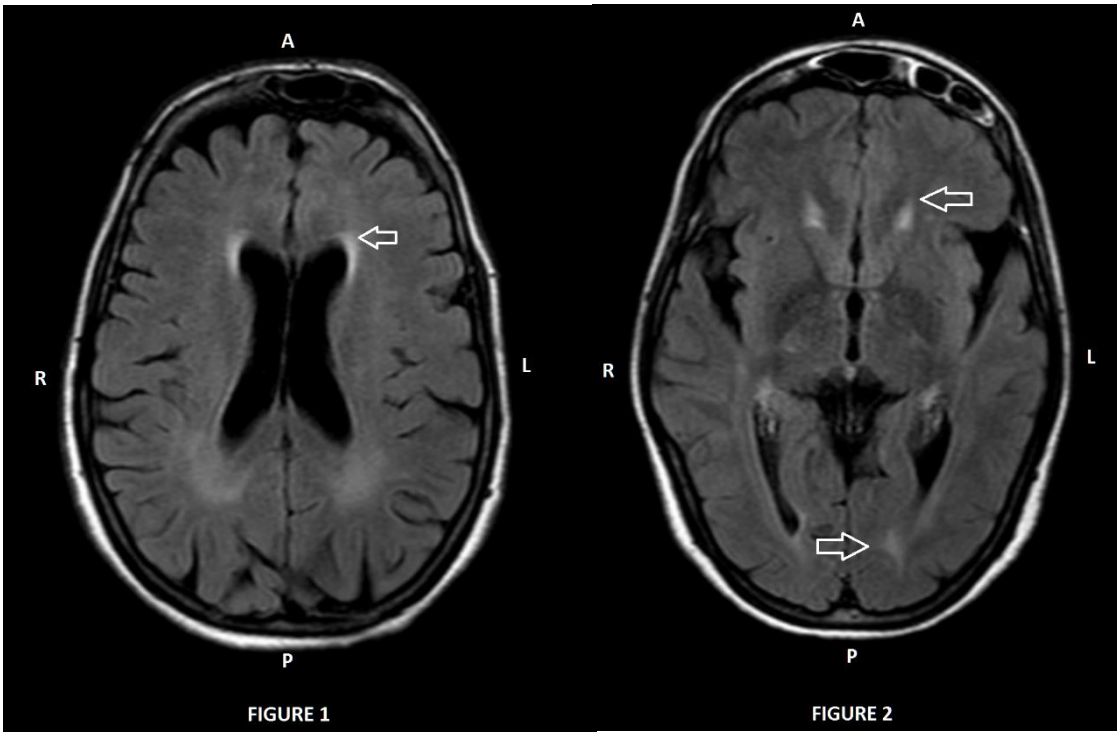
Mental status examination revealed mild intellectual disability.

Lipid profile revealed total cholesterol of 380 mg/dl and triglycerides of 523 mg/dl. Rest of the blood investigations were relatively normal.

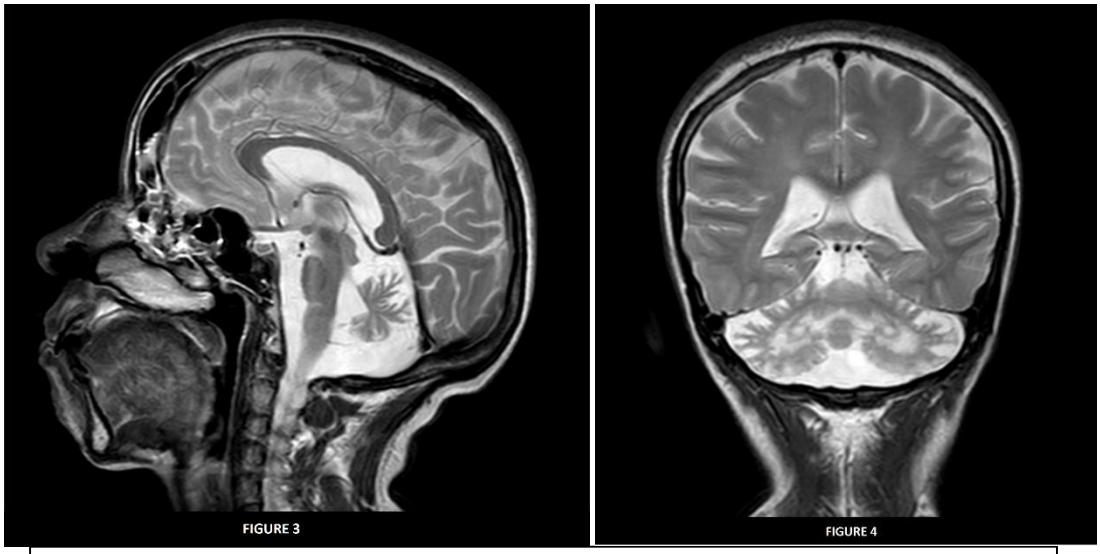
No other previous investigations were available.

MRI Brain revealed diffuse premature atrophy of bilateral cerebellar hemispheres manifesting as marked dilation of sulcal spaces and ventricular systems along with hyperintensity involving the deep white matter of both cerebellar hemispheres in symmetrical fashion.

Additionally T2 weighted hyperintensities were seen in bilateral periventricular regions.



T2_FLAIR axial (Fig 1) and (Fig 2) images show periventricular hyperintensities.



T2W sag(Fig 3) and T2W Coronal (Fig 4)images show severe diffuse atrophy of bilateral cerebellar hemispheres.

Additionally MRI of the ankle joint revealed ovoid to elliptical, well-encapsulated, soft tissue mass completely replacing the Achilles tendon and measuring approximately~ 14 cm in length, ~ 4.5 cm in width and ~3.3 cm in depth.

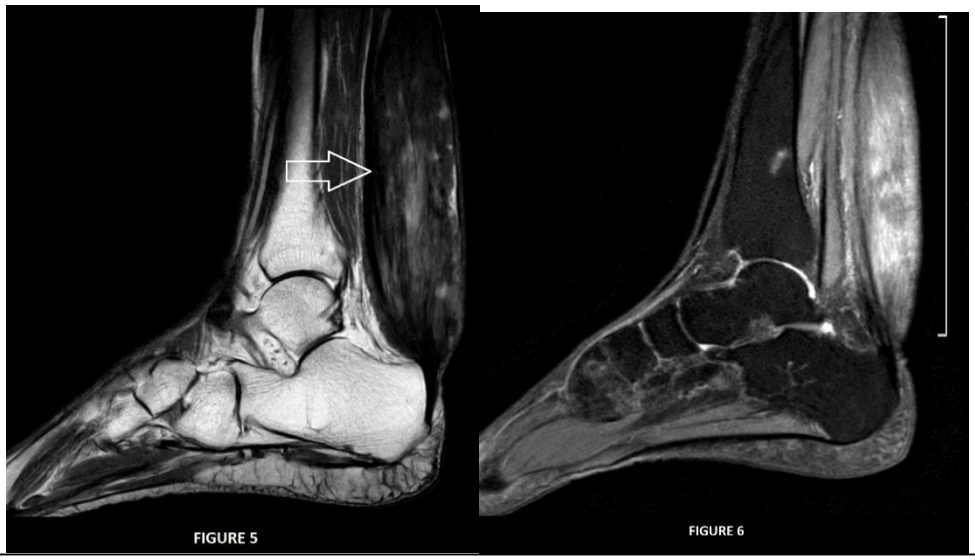
The mass comprises of heterogenous mixed intensity largely as T1W hypointense signal intensity, with few foci of T1W hyperintensities in the centre.

These central T1W hypointensities appear hyperintense on T2W images.

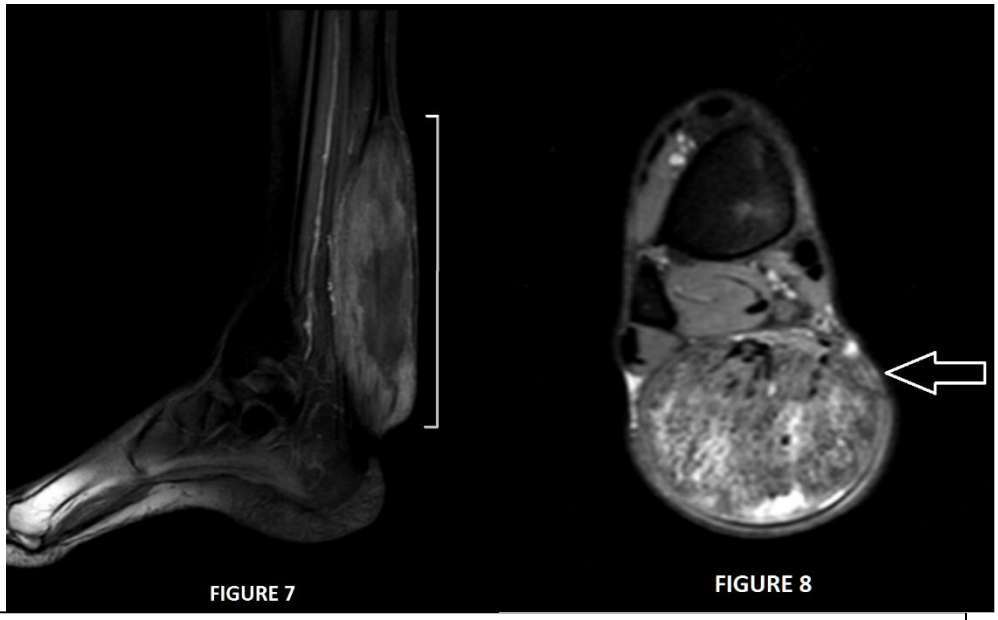
The PD_SPAIR sequences show multiple foci of linear and nodular hyperintensity.

The mass shows mild to moderate heterogenous enhancement on post contrast images with the capsule remaining hypointense. There is no evidence of skin ulceration or encasement of underlying vascular structures. Rest of the bones and muscles showed normal signal intensity.

These findings suggested lipomatous pseudotumor in bilateral Achilles tendon.



The above images Figure 5(Sagittal T2 Weighted image) and Figure 6(sagittal PD fat saturated) reveal lipomatous pseudotumor in Achilles Tendon



The above images (fig 7 sagittal PD fat saturated) and (fig 8 Axial PD Fat saturated) images reveal lipomatous pseudotumor in Achilles tendon.

III. DISCUSSION:

CTX (Van Bogaert-Scherer-Epstein disease)was first described in 1937 as a "cholestérinose généralisée". They had described neurological and ocular manifestation in these patients[1].

Cerebrotendinous Xanthomatosis is an uncommon disorder with approximately 300 cases reported[2] . It is known to have equal male and female predilection, with average age of presentation at 10 to 20 years.

Cerebrotendinous Xanthomatosis is an autosomal recessive disorder is characterized by aberrant cholesterol and cholestanol deposition in a variety of soft tissues resultant of impaired bile acid production. It is due to CYP27 gene mutation. This gene encodes sterol 27-hydroxylase. Sterol 27-hydroxylase, an enzyme needed for the conversion of cholesterol to the primary bile acids cholic and chenodeoxycholic acid [3]. The absence of conversion into these acids there is upregulation in the production of bile acid percussor cholestanol. This gets accumulated in various tissues and gives signs and symptoms [4].

Patients with CTX exhibit a wide variety of symptoms, including multi-organ involvement, neurological and non-neurological symptoms. For instance, psychomotor impairment and persistent infantile-onset diarrhoea are frequent concomitant clinical symptoms of CTX. In individuals with CTX, the average age of symptom start is 19 years, whereas the average age at diagnosis is 23–44 years , resulting in a delay of 15 to 20 years in diagnosis. [5,6].

Laboratory tests reveal elevated amounts of bile alcohols and related glycoconjugates in bile, urine, and plasma, as well as high plasma and tissue cholestanol levels, normal to low plasma cholesterol concentrations, and high levels of bile alcohols. Additionally, higher levels of brain and serum lactate were seen along with elevated cholestanol and apolipoprotein B concentrations in the cerebrospinal fluid.[7]

Brain imaging shows cerebral and cerebellar atrophy with MR spectroscopy showing lactate peak[8].

Our patient 37 year old female presented with progressive swelling in posterior aspect of bilateral legs. She had deterioration in the scholastic performance, mild mental retardation. She also presented with the recent onset of cerebellar symptoms, including difficulty in walking and dysdiadochokinesia. Ophthalmological examination revealed bilateral mature cataract. These features signify multisystemic involvement. Furthermore, the radiological features were similar to those documented in previously reported texts.

Chenodeoxycholic acid (CDCA), used as the mainstay treatment, is known to decrease plasma cholestanol levels. Early intervention is known to provide better prognosis[9,10]. Few studies have also suggested efficacy of cholic acid (CA) in patients with CTX[9,10].

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