Rare disease

Cerebrotendinous xanthomatosis: a rare disorder with a rare presentation

N K Agrawal,¹ Sunny Garg²¹Department of Endocrinology and Metabolism, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India²Department of Internal Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India

Correspondence to Dr N K Agrawal, drnkavns@gmail.com

Summary

A young man was brought for mental retardation, frequent non-bloody diarrhoea and swellings at ankles and elbow. He became bed-ridden due to cataract, mental retardation and pain in the back and lower limb. There were repeated pathological fractures and vitamin D deficiency without renal dysfunction. There were low low-density lipoprotein and triglyceride levels. MRI of the brain revealed hypointense lesions in cerebellar white matter, heterogenous hyperintensity in dentate nucleus and adjacent white matter, right basal ganglia and in the periventricular region with diffuse cerebral atrophy. T1-weighted MRI (ankle region) revealed bilaterally thickened and irregular achilles tendons with hyperintense masses surrounded by patchy hypointensities. A similar xanthomatous lesion (cholesterol deposits) was also present in the sacral region. Vitamin D and calcium supplementation and chenodeoxycholic acid therapy improved pain at lower limbs and body weight. Cerebrotendinous xanthomatosis is a rare autosomal-recessive familial mutation of the sterol 27 hydroxylase causing lipid metabolic disease.

BACKGROUND

Cerebrotendinous xanthomatosis (CTX) is a rare autosomal-recessive familial lipid metabolic disease. It is caused by the mutations of the sterol 27 hydroxylase leading to elevated plasma levels of cholestanol and bile alcohols and increased urinary excretion of bile alcohol glucuronides with diminished concentrations of bile acids in the bile.¹⁻² The total and low-density lipoprotein (LDL) cholesterol and triglyceride levels are in low-to-normal range.² Bilateral juvenile cataracts and chronic diarrhoea are the earliest features of the disease.¹⁻³ The clinical features are highly suggestive but confirmation by elevated plasma cholestanol or mutations are advisable confirmatory steps even though the neurological manifestations discriminate this disorder from familial hypercholesterolaemia and phytosterolaemia.³

CASE PRESENTATION

A 38-year-old man, on his first visit to our clinic, presented with left ulnar fracture for 1 month. Developmental history revealed delayed language and motor milestones, and poor scholastic performance. Since 3 years of age, he had frequent diarrhoea without blood in stools. Five years later (at the age of 8 years), insidious onset of gradually progressive swellings appeared at both the ankles. After 3 years (ie, at the age of 11 years), similar swellings appeared at the right elbow and lower back (figure 1) with progressive diminution of vision, which was attributed to bilateral cataract. The increasing diminution of vision, profound mental retardation and lancinating pain in lower limbs and back progressively limited his walking; he was unable to walk independently for the last 2 years. The left eye was operated for cataract

Figure 1 Eruptions on foot, ankle and back.

Figure 2 MRI of the brain showing generalised atrophy, basal ganglia and cerebellar lesions.

1 year back. One month back, he developed a fracture of left ulna after trivial trauma. His elder sister had similar swellings on the tendoachilles and bilateral cataract since the age of 8 years; she expired at the age of 34 years due to some unknown illness.

On examination, the patient was lethargic and mentally retarded. There were firm, 3–5 cm, nodular, non-tender swellings fixed to bilateral achilles and right triceps tendons. A distinct swelling, 6 cm in diameter, was noted at lower lumbar vertebra level. Cataract was present in the right eye. Other general and systemic examinations were normal except for brisk tendon jerks, extensor planter response; motor and cerebellar signs could not be elicited due to fracture, mental retardation and pain.

INVESTIGATIONS

Serum calcium, phosphorus and vitamin D levels were low (6.8 mg/dl, 2.3 mg/dl and 2 ng/ml, respectively) whereas parathyroid hormone and alkaline phosphatase levels were raised (1772 pg/ml and 709 IU/l, respectively).

Renal function test was normal. Lipid profile revealed serum total cholesterol 167 mg/dl, serum triglyceride 88 mg/dl and serum LDL cholesterol 64.2 ng/dl. ECG showed QT interval (QTc) 0.5 s (normal <0.44). Ultrasonography of abdomen revealed left renal agenesis and normal right kidney. T1-weighted (T1W) MRI of brain images revealed hypointense lesions in cerebellar white matter with heterogenous hyperintensity in dentate nucleus and adjacent white matter, right basal ganglia and in the periventricular region (figure 2). Diffuse cerebral atrophy was present. T1W MRI of the ankle region revealed bilaterally thickened and irregular achilles tendons with hyperintense masses surrounded by patchy hypointensities (figure 3). A similar xanthomatous lesion was also present in the sacral region. A diagnosis of CTX with osteomalacia was made.

TREATMENT

Treatment with vitamin D and calcium supplementation and chenodeoxycholic acid (CDCA) improved pain at

Figure 3 MRI of foot and ankle showing tendon xanthomas.

lower limbs and body weight but without much improvement in the disease.

OUTCOME AND FOLLOW-UP

CDCA (750 mg/day) suppresses the synthesis of cholesterol, cholestanol, bile acid glucuronides, and bile acids and significantly alleviates clinical symptoms.^{4 5} Unfortunately, as in our case, the disease is usually diagnosed late when cholestanol has extensively got deposited in many tissues. This illustrates the need for an early diagnosis of the disease.

DISCUSSION

Osteoporosis and repeated fractures are also features of patients with CTX⁴ but have been rarely reported as the presenting complaint as in our case. Moreover, serum calcium and vitamin D levels are normal in those who suffer fractures, unlike in our case. An associated left renal agenesis has never been reported with CTX.

Learning points

- ▶ Cerebrotendinous xanthomatosis is a rare autosomal-recessive familial lipid metabolic disease.
- ▶ There are mutations of the sterol 27 hydroxylase leading to elevated plasma levels of cholestanol and bile alcohols and increased urinary excretion of bile alcohol glucuronides with diminished concentrations of bile acids in the bile.
- ▶ Bilateral juvenile cataracts and chronic diarrhoea are the earliest features of the disease.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Cali JJ**, Hsieh CL, Francke U, *et al*. Mutations in the bile acid biosynthetic enzyme sterol 27-hydroxylase underlie cerebrotendinous xanthomatosis. *J Biol Chem* 1991;**266**:7779–83.
2. **Koopman BJ**, Wolthers BG, van der Molen JC, *et al*. Cerebrotendinous xanthomatosis: a review of biochemical findings of the patient population in the Netherlands. *J Inherit Metab Dis* 1988;**11**:56–75.
3. **Cruysberg JR**, Wevers RA, Tolboom JJ. Juvenile cataract associated with chronic diarrhea in pediatric cerebrotendinous xanthomatosis. *Am J Ophthalmol* 1991;**112**:606–7.
4. **Federico A**, Dotti MT, Loré F, Nuti R. Cerebrotendinous xanthomatosis: pathophysiological study on bone metabolism. *J Neural Sci* 1993;**115**:67–70.
5. **Berginer VM**, Salen G, Shefer S. Long-term treatment of cerebrotendinous xanthomatosis with chenodeoxycholic acid. *N Engl J Med* 1984;**311**:1649–52.

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Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Agrawal NK, Garg S. Cerebrotendinous xanthomatosis: a rare disorder with a rare presentation. *BMJ Case Reports* 2012;10.1136/bcr-2012-006202, Published XXX

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