Effectiveness of Cholic acid treatment in CTX

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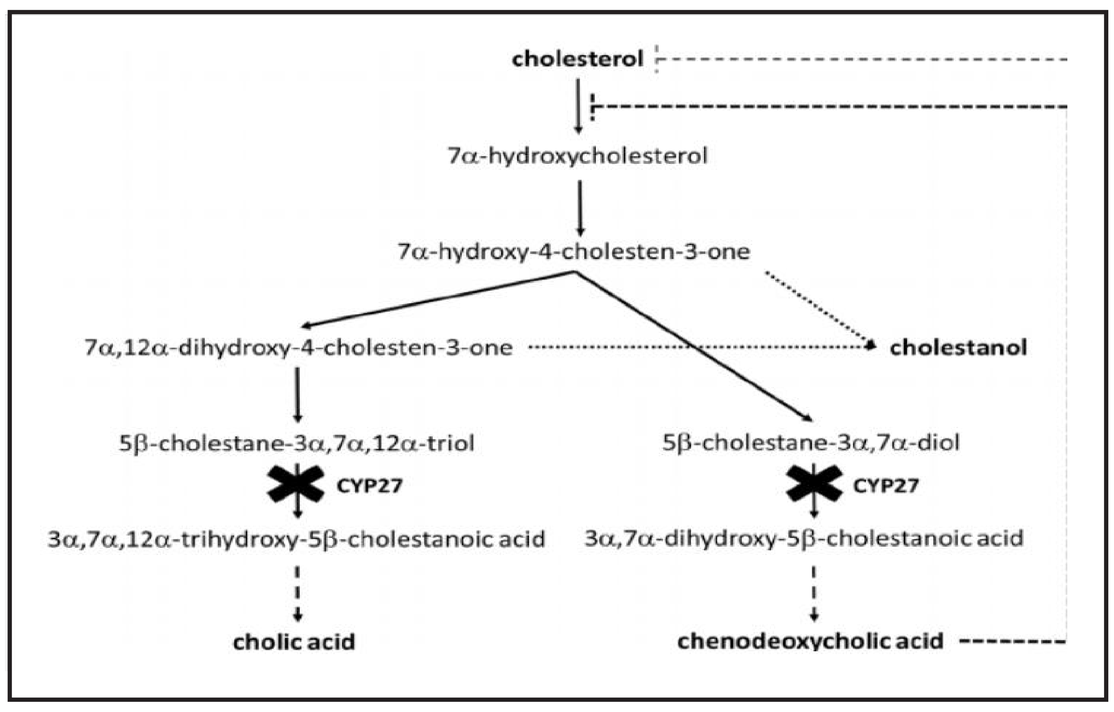
Introduction: Cerebrotendinous Xanthomatosis (OMIM # 213700) is an autosomal recessive disorder of bile acids synthesis characterized by development of bilateral cataracts, tendon xanthomas, chronic diarrhea during childhood and progressive neurological deterioration which may include cognitive decline and motor disorders[1]. Plasma cholestanol is used as a diagnostic marker of CTX, and also to monitor the response to the treatment. Current treatment for CTX is **chenodeoxycholic acid (CDCA)**, which was reported to improve and/or stabilize clinical status and decrease levels of plasma cholestanol. However, CDCA is not easily available in India. Some reports have also suggested a potential efficacy of **cholic acid (CA)** in patients with CTX. Here we present a case of CTX treated with Cholic acid alone and report its usefulness.

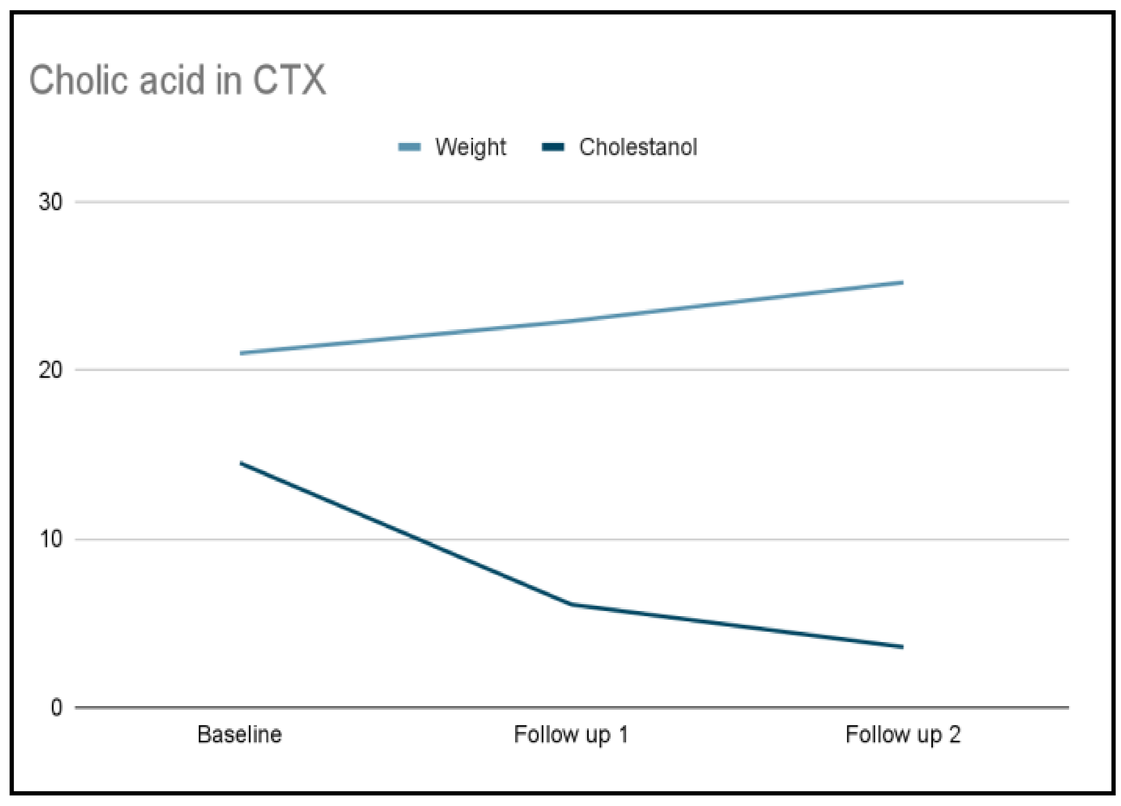


Objective: To evaluate the effectiveness of cholic acid treatment in CTX

Case study: Patient CA born full term by LSCS to 2nd degree consanguineously married couple, presented at 9 years of age with blurred vision and was reported to have bilateral developmental cataracts by ophthalmological examination. There was no significant family history or neonatal symptoms. At 9 years he had normal mental milestones, no history of seizures and no history of jaundice. However he had frequent complaints of loose motions, difficulty in walking and climbing stairs. On examination we found him to have myopia, bilateral cataracts, low weight (21 kg) and ataxic gait. Whole exome sequencing was done and a **homozygous frame shift truncation pathogenic variant: c.526del; p.Asp176Metfs*6; rs765512351 was identified in CYP27A1 gene**, confirming the diagnosis of CTX. Parents were found to have this mutation in heterozygous state confirming the carrier status.

The baseline cholestanol levels were analyzed and found to be significantly elevated (14.49 umol/L). Although the expected normal range of cholestanol in literature is 3.01 – 6.73 uMol, we have observed lower levels of cholestanol in our population by our method (<2.85 uMol, n=30). He was started on treatment with Cholic acid due to the unavailability of chenodeoxycholic acid (CDCA) in the dose of 200 mg/day. Follow up studies including clinical evaluation, cholestanol levels and lipid profile was done for the following 6 months. We observed significant improvement in vision and gait along with increase in weight (4.2 kg). Loose motions have stopped. His walking, running and ability to climb stairs also improved. Levels of cholestanol have significantly improved over last 6 months with cholic acid treatment. At 3 months his lipid profile showed mild increase in cholesterol and hence Rosuvastatin was added, in the dose of 5 mg/day and a low-fat diet was also recommended. No adverse reaction was observed till the date of writing this manuscript.

Discussion: Currently, the standard of care for CTX is oral bile acid supplementation with CDCA[2]. However some reports have reported elevated transaminases with use of CDCA. Very few studies have shown effectiveness of Cholic acid as a treatment for CTX deficiency[3]. In our country CDCA is not readily available and hence CA can be used instead. Here we report the effects of Cholic acid treatment in a symptomatic patient diagnosed at 9 years of age. Our patient has shown significant improvement in cholestanol levels within 3 months of initiation of treatment. There is also clinical improvement in the form of weight gain, improvement in vision, ataxia and disappearance of cataracts. There was however some increase in blood cholesterol levels and hence statins were added.



Follow up visit	Weight	Cholesterol	Cholestanol
	kg	<200 mg%	<2.85 uMol
Baseline	21	173	14.49
Follow up 1: 3 months	22.9	204	6.07
Follow up 2: 6 months	25.2	144	3.58

Conclusion:

We found that treatment with CA alone significantly reduced cholestanol levels in our patient over a period of 6 months. Additionally clinical improvement in the form of weight gain and improved vision was observed. No adverse effects were reported in our patient. In conclusion, these findings suggest that CA may be a suitable alternative treatment for CTX.

Conflict of Interest : None

References:

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