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Cerebrotendinous xanthomatosis: Heterogeneity of clinical phenotype with evidence of previously undescribed ophthalmological findings

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Summary: Cerebrontendinous xanthomatosis (CTX) is a rare autosomal recessive neurometabolic disease involving lipid metabolism. The classical phenotype is characterized by neurological dysfunction, tendon xanthomas and juvenile cataracts. Other ophthalmological findings have occasionally been reported. To gain more insight into the type and frequency of ophthalmological alterations in this multisystem metabolic disorder, we examined 13 CTX patients. Besides cataracts, found in all cases, the second most frequent ocular abnormality was paleness of the optic disk, which was found in 6 patients and was probably previously underestimated. Signs of premature retinal senescence were also observed. We discuss the possible relation between these ocular manifestations and the metabolic defect.

Cerebrotendinous xanthomatosis (CTX), first described by van Bogaert in 1937 (van Bogaert et al 1937), is a rare recessive inherited disorder caused by a deficiency of the mitochondrial sterol 27-hydroxylase. In the last few years, different mutations of the sterol 27-hydroxylase gene (*CYP27*) have been described (Cali and Russel 1991; Cali et al 1991; Dotti et al 2000; Federico et al 1995; Garuti et al 1996a,b 1997). The metabolic defect causes reduced bile acid synthesis and increased plasma and tissue cholestanol levels (Bjorkhem and Boberg 1995; Salen et al 1985, 1991). Therapy with chenodeoxycholic acid (CDCA) alone or in association with HMG-CoA inhibitors reverses the metabolic abnormalities and significantly improves clinical and laboratory parameters (Berginer et al 1993; Federico and Dotti 1994; Nakamura et al 1991; Verrips et al 1999). Early diagnosis is therefore crucial to