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Cholestanol Serum, Gas Chromatography Mass Spectrometry

Useful for: Diagnosis of Cerebrotendinous xanthomatosis (CTX). Additionally, follow-up of cholestanol levels can be useful for therapy dose adjustment.

Methodology: Gas Chromatography mass spectrometry (GC-MS)

Necessary Information: Reason for referral and relevant clinical presentation description are required.

Specimen Required: Serum: isolated from blood samples obtained by venipuncture and collected in tubes; prepared by centrifugation (10 min, 1600 × *g*) at room temperature following a clotting period for at least 1 h at room temperature; storage at – 18º C or lower (stable for 1 year). Send it protected from light and frozen.
Specimen Volume: 1 ml.
Turnaround Time: 45 working days

Clinical Information: Cerebrotendinous Xanthomatosis (CTX) is an autosomal recessive inherited disorder of bile acid synthesis, in which cholestanol, a product of altered cholesterol and bile acid metabolism, accumulates in the body. Several genetic studies have shown mutations in the sterol 27-hydroxylase gene (CYP 27 gene) resulting in markedly diminished activity of the enzyme sterol 27-hydroxylase in CTX patients. Patients with CTX present diverse manifestations with multi-organ involvement and a broad range of neurological and non-neurological symptoms. CTX is characterized by infantile-onset diarrhea, childhood-onset cataract, adolescent-to young adult-onset tendon xanthomas, and progressive neurologic dysfunction. Some patients present early with cholestatic jaundice, which resolves. The neurologic dysfunction can include dementia, psychiatric disturbances, pyramidal and/or cerebellar signs, and seizures. Xanthomas appear in the second or third decade of life and can occur in the Achilles tendon, the extensor tendons of the elbow and hand, the patellar tendon, and the neck tendons. Some individuals may demonstrate mental impairment from early infancy while others have normal or subnormal intellectual function until puberty. Neuropsychiatric symptoms may include behavioral changes, hallucinations, agitation, aggression, depression, and suicide attempts.

Interpretation: Elevated plasma concentration of cholestanol is highly suggestive of a biochemical diagnosis of Cerebrotendinous xanthomatosis (CTX). A diagnosis of CTX should be confirmed by gene mutation. Mildly increased cholestanol is also found in patients with familial hypercholesterolaemia. Exposure to light may cause degradation of sterols.

Reference Values:
Serum: Normal Controls: 0 -6.0 µg/ml
CTX patients: 13.0 -150.0µg/ml

Ministry of Health code: 83918

Reference:
1. Bjorkhem I, Boberg K, Leitersdorf E. Inborn errors in bile acid biosynthesis and storage of sterols other than cholesterol. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA. eds. The Online Metabolic and Molecular Bases of Inherited Disease. 2019
2. Kelley RI. Diagnosis of Smith-Lemli-Opitz syndrome by gas chromatography/mass spectrometry of 7-dehydrocholesterol in plasma, amniotic fluid, and cultured skin fibroblasts. Clin Chim Acta 1995; 236:45-58
3. Nie S, Chen G, Cao X, Zhang Y. Cerebrotendinous xanthomatosis: a comprehensive review of pathogenesis, clinical manifestations, diagnosis, and management. Orphanet J Rare Dis. 2014 Nov 26; 9(1):179