Test Definition: CTXWB

Cerebrotendinous Xanthomatosis, B

Overview

Useful For

Evaluating patients with a clinical suspicion of cerebrotendinous xanthomatosis (CTX)

Monitoring of individuals with CTX on chenodeoxycholic acid (CDCA) therapy

This test is **not useful for** the identification of carriers

This test is **not useful for** the evaluation of bile acid malabsorption

Method Name

Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Advisory Information

For assessment of bile acid malabsorption in patients with irritable bowel syndrome-diarrhea, order 7AC4 / 7AC4, Bile Acid Synthesis, Serum.

Specimen Required

Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Green top (sodium heparin, lithium heparin), yellow top (ACD B)

Specimen Volume: 1 mL

Forms

If not ordering electronically, complete, print, and send an Inborn Errors of Metabolism Test Request (T798) with the specimen.

Specimen Minimum Volume

0.25 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Refrigerated (preferred)	72 hours	
	Ambient	48 hours	

Clinical and Interpretive

Clinical Information

Cerebrotendinous xanthomatosis (CTX) is an autosomal recessive disorder of bile acid synthesis resulting from the deficiency of the mitochondrial enzyme, sterol 27-hydrolase. Sterol 27-hydrolase facilitates the first step of sterol degradation in the formation of bile acids; consequently patients with CTX will experience increased storage of the sterol, cholestenol, and ketosterol bile acid precursors (7-alpha-hydroxy-4-cholesten-3-one [7a-C4] and 7-alpha,12-alpha-dihydroxycholest-4-en-3-one [7a12aC4]) in multiple tissues throughout the body with a resulting deficiency of the bile acid, chenodeoxycholic acid (CDCA). CTX is caused by variants in the *CYP27A1* gene.

Patients with CTX can present with a constellation of findings including infantile onset diarrhea, childhood onset cataracts, development of tendon/cerebral xanthomas in adolescence and early adulthood, early onset osteoporosis, as well as a broad array of neuropsychological manifestations such as intellectual disability, dementia, psychiatric symptoms, ataxia, pyramidal signs, dystonia, and muscle weakness. Patients may occasionally present with cholestatic liver disease, which may present as jaundice, poor growth, and hepatosplenomegaly. Intrafamilial variability exists, and some heterozygous carriers may experience a higher incidence of cardiac disorders or gallstones. Treatment with CDCA normalizes bile acid synthesis and suppresses cholestenol biosynthesis, with improvement of clinical symptoms and arrest of disease progression. Supplementation with beta-hydroxy beta-methylglutaryl-CoA (HMG-CoA) inhibitors and coenzyme Q10 has been proposed. The availability of effective therapy makes early diagnosis and treatment of patients with CTX essential.

The estimated incidence of CTX is 1 in 50,000 individuals of Northern European ancestry and as high as 1 in 440 in the Druze population of Israel.

The diagnostic evaluation of patients with suspected CTX may reveal abnormalities on brain magnetic resonance imaging (such as cerebellar atrophy, decrease in volume of grey and white matter, and abnormal white matter signal) in addition to the biochemical and clinical abnormalities. The biochemical diagnosis of CTX can be confirmed by molecular genetic analysis of the *CYP27A1* gene (included in: NPPAN / Peripheral Neuropathy Genetic Panels by Next-Generation Sequencing [NGS], Blood).

Reference Values

7-ALPHA-HYDROXY-4-CHOLESTEN-3-ONE (7a-C4)

Cutoff: < or =0.750 nmol/mL

7-ALPHA,12-ALPHA-DIHYDROXYCHOLEST-4-en-3-ONE (7a12aC4)

Cutoff: < or =0.250 nmol/mL

Interpretation

An elevation of 7-alpha-hydroxy-4-cholesten-3-one (7a-C4) and 7-alpha,12-alpha-dihydroxycholest-4-en-3-one

(7a12aC4) is strongly suggestive of cerebrotendinous xanthomatosis.

Cautions

Patients with bile acid malabsorption or ileal resection may have elevations of 7-alpha-hydroxy-4-cholesten-3-one (7aC4).

Clinical Reference

1. Mignarri A, Magni A, Del Puppo M, et al: Evaluation of cholesterol metabolism in cerebrotendinous xanthomatosis. J Inherit Metab Dis. 2016:39:75-83

2. Nie S, Chen G, Cao X, Zhang Y: Cerebrotendinous xanthomatosis: a comprehensive review of pathogenesis, clinical manifestations, diagnosis, and management. Orphanet J Rare Dis. 2014:9:179

3. DeBarber AE, Luo J, Star-Weinstock M, et al: A blood test for cerebrotendinous xanthomatosis with potential for disease detection in newborns. J. Lipid Res. 2014:55:146-154

4. Federico A, Dotti MT, Gallus GN: Cerebrotendinous xanthomatosis. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2003. Updated April 14, 2016. Accessed November 20, 2020. Available at www.ncbi.nlm.nih.gov/books/NBK1409/

Performance

Method Description

Whole blood is spotted on filter paper and dried overnight. A 3-mm dried blood spot is extracted with internal standard. The extract is subjected to liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis. The MS/MS is operated in the multiple reaction monitoring (MRM) positive mode to follow the precursor to product species transitions for each analyte and internal standard. The ratio of the extracted peak areas to internal standard is determined by LC-MS/MS is used to calculate the concentration of in the sample.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Specimens received Monday through Saturday; 4 p.m.; Sunday 1 p.m. will be prepared same day.

Testing performed Tuesday; 8 a.m.

Analytic Time

2 days (not reported on Saturday or Sunday)

Maximum Laboratory Time

8 days

Specimen Retention Time

Whole blood: 7 days; Dried Blood Spot: Normal results: 2 months; Abnormal results: Indefinitely

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

82542

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
CTXWB	Cerebrotendinous Xanthomatosis, B	92737-6

Result ID	Test Result Name	Result LOINC Value
BA4365	Interpretation (CTXWB)	59462-2
BA4363	7a-hydroxy-4-cholesten-3-one	92762-4
BA4364	7a,12a-dihydroxycholest-4-en-3-one	92759-0
BA4366	Reviewed By	18771-6