Test Definition: CTXWB

Cerebrotendinous Xanthomatosis, Blood

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.

Special Instructions

- Biochemical Genetics Patient Information

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

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

This test is also available as a part of a panel; see HSMWB / Hepatosplenomegaly Panel, Blood. If this test (CTXWB) is ordered with either GPSYW / Glucopsychosine, Blood or OXYWB / Oxysterols, Blood, the individual tests will be canceled and HSMWB ordered.

Specimen Required

Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: Green top (sodium heparin, lithium heparin), yellow top (ACD B)
Specimen Volume: 1 mL
Collection Instructions: Send whole blood in original vial. **Do not aliquot.**

Forms

1. Biochemical Genetics Patient Information (T602)
2. If not ordering electronically, complete, print, and send a Biochemical Genetics 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 & 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 is an important enzyme in both the alternative and classic bile acid synthesis pathways. Consequently, patients with CTX will experience increased storage of the sterol, cholestenol, and ketosterol bile acid precursors (7-alpha-hydroxy-4-cholesten-3-one [7aC4] 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 disease-causing 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 can be substantial. Some heterozygous carriers may experience a higher incidence of cardiac disorders or gallstones; however, carriers are typically asymptomatic. Treatment with CDCA has been shown to improve both biochemical and clinical outcomes in patients with CTX. Supplementation with beta-hydroxy beta-methylglutaryl-CoA (HMG-CoA) reductase inhibitors can be used as alternative treatment alone or in combination with CDCA. Cholic acid treatment has been used in few patients showing a decrease in cholestanol levels and improvement in neurologic symptoms. The availability of effective therapy makes early diagnosis and treatment of patients with CTX essential.

The diagnostic evaluation of patients with suspected CTX may reveal abnormalities on brain magnetic resonance imaging

(eg, 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 CHLGP / Cholestasis Gene Panel, Varies; or order CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies and indicate the gene to be assessed).

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) or 7-alpha,12-alpha-dihydroxycholest-4-en-3-one (7a12aC4) or both 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(1):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(1):146-154
4. Federico A, Gallus GN. Cerebrotendinous xanthomatosis. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2003. Updated November 14, 2024. Accessed December 2, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK1409/
5. Lutjohann D, Stellaard F, Bjorkhem I. Levels of 7alpha-hydroxycholesterol and/or 7alpha-hydroxy-4-cholest-3-one are the optimal biochemical markers for the evaluation of treatment of cerebrotendinous xanthomatosis. J Neurol. 2020;267(2):572-573. doi:10.1007/s00415-019-09650-0
6. Mandia D, Chaussenot A, Besson G, et al. Cholic acid as a treatment for cerebrotendinous xanthomatosis in adults. J Neurol. 2019;266(8):2043-2050. doi:10.1007/s00415-019-09377-y
7. Nobrega PR, Bernardes AM, Ribeiro RM, et al. Cerebrotendinous xanthomatosis: A practice review of pathophysiology, diagnosis, and treatment. Front Neurol. 2022;13:1049850. Published 2022 Dec 23. doi:10.3389/fneur.2022.1049850

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 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 determined by the LC-MS/MS is used to calculate the concentration of in the sample.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Tuesday, Thursday

Report Available
3 to 7 days

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

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & 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 account representative. 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. It has not been cleared or approved by the US 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