Test Definition: CTXBS

Cerebrotendinous Xanthomatosis, Blood Spot

Overview

Useful For

Evaluating patients with a clinical suspicion of cerebrotendinous xanthomatosis *(*CTX) using dried blood spot specimens

Monitoring 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
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Blood Spot Collection Instructions

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 HSMBS / Hepatosplenomegaly Panel, Blood Spot. If this test (CTXBS) is ordered with either GPSY / Glucopsychosine, Blood Spot or OXYBS / Oxysterols, Blood Spot, the individual tests will be canceled and HSMBS ordered.

Specimen Required

Supplies:

-Card-Blood Spot Collection (Filter Paper) (T493)

-Card-Postmortem Screening (Filter Paper) (T525)

Container/Tube:

Preferred: Blood Spot Collection Card (Filter Paper)
Acceptable: Whatman Protein Saver 903 filter paper, PerkinElmer 226 filter paper, Munktell filter paper, Postmortem Screening Card or collected with EDTA, sodium heparin, lithium heparin, or ACD B-containing devices
Specimen Volume: 2 Blood spots
Collection Instructions:
1. Let blood dry completely on filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
2. At least 1 spot should be complete (ie, unpunched).
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry.
Additional Information:
1. For collection instructions, see Blood Spot Collection Instructions
2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777)
3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800)

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

1 Blood spot

Reject Due To

Blood spot showing serum rings Insufficient specimen Layering Multiple applications	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Refrigerated (preferred)	10 days	FILTER PAPER
	Ambient	10 days	FILTER PAPER
	Frozen	59 days	FILTER PAPER

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 [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 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 (7aC4) 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 November 29, 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
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
Normal: 2 months; Abnormal: 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
CTXBS	Cerebrotendinous Xanthomatosis, BS	92739-2

Result ID	Test Result Name	Result LOINC® Value
BA4361	Interpretation (CTXBS)	59462-2
BA4359	7a-hydroxy-4-cholesten-3-one	92763-2
BA4360	7a,12a-dihydroxycholest-4-en-3-one	92760-8
BA4362	Reviewed By	18771-6