ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

ACT Sheet

Newborn Screening ACT Sheet

[Increased Tyrosine]
Tyrosinemia

Differential Diagnosis: Tyrosinemia type I (hepatorenal); tyrosinemia type II (oculocutaneous); tyrosinemia type III; transient tyrosinemia of the neonate (TTN); liver disease; prematurity.

Condition Description: Elevated tyrosine can be caused by inherited defects in tyrosine metabolism, the pathway that converts tyrosine (from dietary protein) to other compounds integral to metabolism. Tyrosinemia type I (fumarylacetoacetate hydrolase deficiency) is accompanied by elevated succinylacetone and other toxic byproducts that damage the liver and kidneys. Tyrosinemia types II and III (tyrosine aminotransferase deficiency and 4-hydroxyphenylpyruvate dioxygenase deficiency, respectively) both have elevated plasma tyrosine, but do not have the toxic tyrosine byproducts seen in tyrosinemia type I.

You Should Take the Following Actions:

- Inform family of newborn screening result.
- Ascertain clinical status (diarrhea, vomiting, liver disease, failure to thrive).
- Consult with pediatric metabolic specialist.
- Evaluate the newborn for signs of jaundice, failure to thrive, diarrhea, vomiting.
- Initiate confirmatory/diagnostic testing and management, as recommended by the specialist.
- Provide the family with basic information about tyrosinemia and its management.

- Report final diagnostic outcome to newborn screening program.

Diagnostic Evaluation: Plasma amino acids: Tyrosine is elevated in all forms of tyrosinemia. Urine organic acids or quantitative succinylacetone: Tyrosine metabolites are elevated in all forms of tyrosinemia. Succinylacetone is elevated only in tyrosinemia type I. Because succinylacetone is included in many state NBS panels, review of the initial NBS results can help differentiate tyrosinemia type I from types II or III. Additional molecular genetic testing may be required.

Clinical Considerations: Tyrosinemia type I is the most severe form but is usually asymptomatic in the neonate. If untreated, it will cause failure to thrive, liver disease, and renal failure in the first year of life. Nitisinone (NTBC) treatment along with the dietary restriction of phenylalanine and tyrosine usually prevents these features. Tyrosinemia type II is asymptomatic in the neonate but can cause hyperkeratosis of the skin, corneal ulcers, and in some cases, developmental delay in the absence of dietary restriction. Tyrosinemia type III is extremely rare and may present similarly to tyrosinemia type II. Some newborns have transient tyrosinemia (TTN) that resolves within several weeks.

Additional Information:

How to Communicate Newborn Screening Results
Gene Reviews
Medline Plus
Condition Information for Families- HRSA Newborn Screening Clearinghouse
Tyrosinemia Type I
Tyrosinemia Type II
Tyrosinemia Type III

Referral (local, state, regional, and national):

Find a Genetics Clinic Directory
Genetic Testing Registry
Tyrosinemia Type I
Tyrosinemia Type II
Tyrosinemia Type IIIa

Local Resources *(Insert Local Website Links)*

State Resource Site (Insert Website Information)

Name	
URL	
Comments	

Local Resource Site (Insert Website Information)

Name	
URL	
Comments	

Appendix *(Resources with Full URL Addresses)*

Additional Information

How to Communicate Newborn Screening Results

- https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/Resources/achdnc-communication-guide-newborn.pdf

Gene Reviews

- https://www.ncbi.nlm.nih.gov/books/NBK1319/

Medline Plus

- https://medlineplus.gov/genetics/condition/tyrosinemia/

Condition Information for Families- HRSA Newborn Screening Clearinghouse

- https://newbornscreening.hrsa.gov/conditions/tyrosinemia-type-i
- https://newbornscreening.hrsa.gov/conditions/tyrosinemia-type-ii
- https://newbornscreening.hrsa.gov/conditions/tyrosinemia-type-iii

Referral (local, state, regional and national)

Find a Genetics Clinic Directory

- https://clinics.acmg.net

Genetic Testing Registry

- https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268490/
- https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268487/
- https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268623/

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