AMINO ACID DISORDERS | Tyrosinemia Type I

What is Tyrosinemia Type I (Hepatorenal tyrosinemia)?

Tyrosinemia is also known as hepatorenal tyrosinemia, tyrosinemia type 1, tyrosinosis or hereditary tyrosinemia.[1] The deficient enzyme is fumarylacetoacetase.[2]

CLINICAL MANIFESTATIONS

Tyrosine-I is usually asymptomatic in newborns, but if left untreated it affects liver, kidney, bone, and peripheral nerves.[3] Two patterns are reported: an acute or chronic form. The acute form presents with acute hepatic decompensation where infants are noted to have jaundice, abdominal distention, failure to thrive, ascites and hepatomegaly, renal disease is also prominent and a "boiled cabbage" odor in urine is observed; the chronic liver disease feature is that of hepatic cirrhosis.[4] Some affected patients can present with a neurologic crisis.

PATHOPHYSIOLOGY

The deficient enzyme, fumarylacetoacetase catalyzes the last step in tyrosine degradation.[2] The increased concentrations of tyrosine and its metabolites is postulated to inhibit many transport functions and enzymatic activities.[3]

Inheritance: autosomal recessive[2]

CONFIRMATORY TESTING

Confirmation can be done through plasma amino acid levels (increased tyrosine) and urine metabolic screening (increased succinylacetone).[2] Further confirmatory testing may be required after referral to a metabolic specialist.

Overview of Disease Management

Treatment options for tyrosinemia include dietary therapy (restriction of phenylalanine and tyrosine), and use of the pharmacologic agent 2(2-nitro-4-trifluoro-methylbenzoyl)-1,3-cyclohexanedione or NTBC (1mg/kg).[3] Initiation of management should be done in consultation with an attending physician/metabolic specialist.

Prognosis

If untreated, death from liver failure may occur in the first year of life.[4]

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state, correct the acidosis and prevent essential amino acid deficiency.

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WHAT TO DO

If unwell and cannot tolerate oral intake:

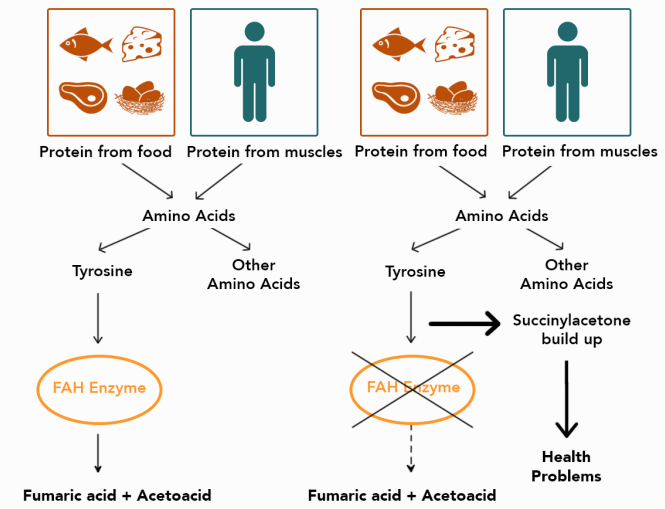
- Nothing per orem except medications
- Ensure patient's airway is secure
- Insert IV access. Collect samples for blood glucose, plasma amino acids, liver function tests, coagulation studies, bloodspot for blood succinylacetone, and urine succinylacetone. May request for investigations (i.e. CBC, blood gas, etc.) as needed.
- May give fluid boluses if patient requires.
- Start D12.5% 0.3NaCl at full maintenance. Assess patient clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5x the maintenance.
- Start nitisinone (2mg/kg) per orem
- Monitor input and output strictly (q6 hours).

If unwell and can tolerate oral intake:

- Insert oro- or nasogatric tube and start continuous feeding with TYR milk formula or protein free formula at maintenance rate
- Insert IV access. Collect samples for blood glucose, plasma amino acids, liver function tests, coagulation studies and urine succinylacetone. May request for investigations (i.e. CBC, blood gas, etc.) as needed
- Start D12.5% 0.3NaCl at 5-10 cc/hr.
- Start nitisinone (2mg/kg) per orem
- Monitor input and output strictly (q6 hours)

**Children should not be protein restricted for longer than necessary (24-48 hours)*
**Inform the metabolic doctor on call for further guidance regarding on-going management*
**If the patient is well, coordinate with a metabolic specialist regarding further management*

Normal breakdown of protein vs Tyrosinemia Type 1 patient's breakdown of protein



[1] *Nyhan WL, Barshop BA and Ozand P. Chapter 26: Hepatorenal tyrosinemia. Atlas of Metabolic Diseases 2nd ed. Great Britain:Oxford University Press, 2005 pp 175-179.*
[2] *Schulze A, Matern D, Hoffmann GF. Chapter 2: Newborn screening in Sarafoglou K, Hoffman GF and Roth KS (eds). Pediatric Endocrinology and Inborn Errors of Metabolism. New York:McGraw Hill, 2009 pp 17-32.*
[3] *Nyhan WL, Barshop BA and Ozand P. Chapter 26: Hepatorenal tyrosinemia. Atlas of Metabolic Diseases 2nd ed. Great Britain:Oxford University Press, 2005 pp 175-179.*
[4] *Pass Ka and Morrissey M. Enhancing newborn screening for tyrosinemia type I. Clin Chem 2008;54(4):627-629.*