

Disease Name:

ARGININOSUCCINIC ACIDURIA

(ARGININOSUCCINASE DEFICIENCY; ARGININOSUCCINATE LYASE DEFICIENCY; ASL DEFICIENCY; ARGININOSUCCINIC ACID LYASE DEFICIENCY)

Classification: Urea cycle defect

Genetic **Inheritance:** Autosomal recessive

Information: **Population Incidence:** 1: 70,000 live births

Ethnic Incidence: No known population at increased risk

Gene & Location: Gene is ASL on 7cen-q11.2

Common Mutation: None, more than 25 mutations detected

OMIM # *207900

Disease **Symptom Onset:** Severe neonatal; infancy or childhood; rare reports of asymptomatic
Information: individuals.

Symptoms: Neonatal onset presents in the first 2-3 days of life with vomiting, lethargy, respiratory alkalosis, and hypothermia progressing to hyperammonemic encephalopathy, cerebral edema, hepatomegaly, and death. There is a high mortality rate. Late onset patients may present with non-specific mental retardation, seizures, hepatomegaly, and/or skin and hair abnormalities, between a few months to years of age. There is usually a history of episodic coma or seizures and often patients will self select a low protein diet. Hyperammonemia is not severe and symptoms are non-specific.

Physical Findings: No particular dysmorphisms. Older undiagnosed patients may have hepatomegaly, microcephaly and/or coarse, brittle hair consistent with trichorrhexis nodosa or skin lesions due to arginine deficiency.

Treatment: Treatment consists of a low protein diet, arginine supplementation to help complete the urea cycle, ammonia scavenging drugs in some cases and supplement carnitine if the patients have a secondary deficiency. Liver transplant offers a partial correction of the enzyme deficiency and improved metabolic status. Patients must avoid fasting and during stressors, like illness, need to supplement with high carbohydrates, non-protein calories to avoid catabolism. In metabolic emergency, acute hemodialysis may be necessary to lower ammonia levels.

Natural History without treatment: Episodes of hyperammonemia, coma and possibly death. Patients who survive the hyperammonemia episodes will have mental retardation and neurological dysfunction. Some adults have developed liver failure.

Natural History with treatment: There is a direct correlation between the length of time a patient is in hyperammonemic coma as a neonate and IQ. While early diagnosis and treatment may be lifesaving, neurologic damage is not usually prevented. Despite optimum treatment, patients are prone to periodic bouts of hyperammonemia, which can be life threatening and damaging. In some patients, chronic hepatic dysfunction results in cirrhosis and liver failure, and a liver transplant is indicated despite adequate treatment and metabolic control. Parents should be counseled as to the considerable burden of care these patients represent.

Metabolic Information:

Missing Enzyme & Location: The missing enzyme is argininosuccinic lyase; it cleaves argininosuccinate to arginine and fumarate as part of the urea cycle.

MS/MS profile: Citrulline –elevated
Arginine- low
May have argininosuccinic acid peak

Prenatal testing: Prenatal diagnosis is possible with enzyme assay of CVS or amniocytes. ASA levels can be measured in amniotic fluid, but can be normal in affected cases.

Miscellaneous Information:

Prepared for the NW Regional Newborn Screening Program by Sara Copeland MD, Judith Tuerck RN MS and Lorinda Paradise at OHSU in Portland, OR.

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