Aicardi-Goutieres Syndrome

National Institute of Neurological Disorders and Stroke (NINDS)

Source

National Institute of Neurological Disorders and Stroke (NINDS). Aicardi-Goutieres Syndrome Information Page.

Aicardi-Goutieres syndrome (AGS) is an inherited encephalopathy that affects newborn infants and usually results in severe mental and physical handicap. There are two forms of the syndrome: an early-onset form that is severe, and a late-onset form that has less impact upon neurological function. The early-onset form affects about 20 percent of all babies who have AGS. These infants are born with neurological and liver abnormalities, such as enlargement of the liver and spleen and elevated liver enzymes. Their jittery behavior and poor feeding ability mimic congenital viral infection.

Babies with later-onset AGS begin having symptoms after the first weeks or months of normal development, which appear as a progressive decline in head growth, weak or stiffened muscles (spasticity), and cognitive and developmental delays that range from moderate to severe. Symptoms last for several months, and include irritability, inconsolable crying, intermittent fever, seizures, and loss of developmental skills. Children may also have puffy swelling on the fingers, toes, and ears that resemble chilblains. A number of children have a noticeable startle reaction to sudden noise. For babies with the later-onset form, as symptoms lessen, there is no further worsening of the disease.

AGS is difficult to diagnose since many of the symptoms are similar to those of other disorders. Diagnosis is made based on the clinical symptoms of the disease, as well as characteristic brain abnormalities that can be seen in an MRI brain scan. Cerebrospinal fluid (CSF), taken using a "spinal tap," can also be tested for increased levels of a specific immune system cell (a lymphocyte), which indicates a condition known as chronic lymphocytosis. These cells are normally only elevated during infection, so that lymphocytosis without evidence of infection can be used as an indicator of AGS. CSF may also be tested for elevated levels of a substance known as interferon-gamma, which can also support a diagnosis of AGS.

The mutations of four different genes are associated with AGS:

- **Aicardi-Goutieres syndrome-1 (AGS1)** and AGS5 (an autosomal dominant form) are caused by a mutation in the TREX1 gene,
- **AGS2** is caused by a mutation in the RNASEH2B gene,
- **AGS3** is caused by a mutation in the RNASEH2C gene,
- **AGS4** is caused by a mutation in the RNASEH2A gene.

Most cases of AGS are inherited in an autosomal recessive manner, which means that both parents of a child with AGS must carry a single copy of the defective gene responsible for the disease. Parents do not have any symptoms of disease, but with every child they have together, there is a one in four chance that the baby will receive two copies of the defective gene and inherit AGS.

NOTE: AGS is distinct from the similarly named Aicardi syndrome (characterized by absence of a brain structure (corpus callosum), and spinal, skeletal, and eye abnormalities).