ATP6V0A2-CDG

(Morava et al., EJHG, 2005, Kornak et al, Nature Genetics, 2008)

ATP6V0A2-CDG is a CDG syndrome with an estimated prevalence of one to nine in one million people, which makes it a rare disorder. One of the major and most notable features in these patients is generalized cutis laxa (lax skin). Their skin is wrinkly, abundant and loose. Because of these skin problems children may look old, especially when the facial skin is affected as well. The cutis laxa is already present at birth, but skin manifestations become less pronounced and may disappear completely with age. Young children have a large fontanel, which closes later than normal. Patients do have characteristic facial features: a small head, down-slanting palpebral fissures, a broad flat nasal bridge and a short nose with anteverted nostrils, large ears and a small mouth with a large space between nose and upper lip. The most common ocular anomalies are squinting and near-sight. Increased joint laxity is very common, as is congenital hip dislocation. Inguinal and umbilical hernias are frequent. Many patients have decreased bone density. Patients may have low muscle tone. Developmental (speech, motor) delay is observed in the majority of patients. Intellectual deficit and seizures have been reported in older patients. Pre- and postnatal growth delay is common.

Etiology

ATP6V0A2 CDG is caused by a double change in the genetic material of the patient. The disease-causing gene is: ATP6V0A2. Changes in this gene cause a certain cellular pump (the so-called V-ATPase) to malfunction. This pump is used in cells to optimize conditions for the connection between glycans and proteins. If the function of this pump is insufficient, cells are unable to connect the glycans to the proteins properly: a glycosylation disorder (CDG).

Establishing the diagnosis

In cutis laxa a skin biopsy is often performed. A very small piece of numbed skin (around 3 mm) is collected for microscopical examinations of the different skin components. Skin of cutis laxa patients often shows a decreased number of faulty build elastin fibers. Elastin is responsible for the elasticity in normal skin. Glycosylation is evaluated in a blood test. Often additional
metabolic evaluation is performed as well. The final diagnosis of ATP6V0A2 CDG is made by genetic evaluation in white blood cells.

**Inheritance**

Every cell in the human body contains genetic material in the form of DNA, in which lay many genes coding for certain traits. Every gene has two copies; one inherited from mother, one from father. The inheritance pattern of ATP6V0A2 CDG is autosomal recessive. This means you will only get the disease, if you do have two ‘faulty’ copies of the involved gene. If you have only one changed copy of the gene, you don’t have the disease; you are a carrier. If both parents have one changed gene (and thus are healthy carriers) they have a 25% percent chance to have a child that inherits two changed copies and has the disease. So, it is possible that your sick child has healthy brothers and sisters. They did at least inherit one ‘normal’ gene from one of their parents. The chance that a new baby also has the disease is 25%.

**Treatment/Care**

There is no effective treatment for ATP6V0A2 CDG is, neither for the other CDG syndromes (except for PM1-CDG). However, we are able to treat certain symptoms, recognize certain problems early on and provide the proper care for these problems. For example, many patients have in addition to the cutis laxa very dry skin, which can be treated with hydrating creams. Eye problems may be corrected with glasses and hernias can be surgically corrected. Children with learning difficulties could be properly supported.

**Prognosis**

The prognosis for patients is variable: life expectancy is generally not reduced. Although the skin manifestations improve with age, cognitive decline has been reported in some older patients.