Non-syndromic congenital sideroblastic anemia (CSA):
GLRX5-related CSA.

Non-syndromic congenital sideroblastic anemia (CSA) is characterized by anemia and iron overload of erythroid precursors and other organs and it is due to mutations of at least 3 genes (ALAS2, SLC25A38 and GLRX5). GLRX5-related CSA is an autosomal recessive sideroblastic anemia due to mutations of the mitochondrial enzyme GLRX5.

What causes the disease and how common is it?

Non-syndromic CSA is a rare genetic disease. This disease can be due to mutations in the GLRX5 gene encoding glutaredoxin 5, a mitochondrial enzyme with an essential role in the iron/sulphur (Fe/S) cluster synthesis. The impairment of the Fe/S cluster synthesis leads to the activation of the IRP1 RNA binding activity, blocking ALAS2 translation what cause anemia.

GRLX5-related CSA is a very rare disorder only described so far in one patient. Estimated prevalence it is not known. Other most frequent forms of non-syndromic CSA are due to mutations of the ALAS2 (XLSA) or the SLC25A38 genes.

What are the most frequent symptoms if I have the disease?

Deficiency of the mitochondrial GLRX5 enzyme in the only patients described for this disease causes mild microcytic hypochromic anemia with liver iron overload and type 2 diabetes. Liver and spleen were enlarged and low number of ringed sideroblasts was detected in bone marrow (12-28%).

Which treatment must I follow if I have the disease?

GLRX5-related CSA do not respond to treatment with vitamin B6 (pyridoxine) and folic acid. Surprisingly, in this patient the anemia worsened by blood transfusion but improved by iron chelation.

What is the risk of passing the condition on to my children?

GLRX5-related CSA is an autosomal recessive disease. An individual can be heterozygous for the disorder (healthy carrier) when only one of the GLRX5 allelel is mutated, or homozygous or compound heterozygous (affected individual) when two GLRX5 allelels are mutated.

A couple who carries each one a mutated GLRX5 allele have a 25 percent risk of having a child affected by the disorder at each pregnancy. The risk of having a child who is a healthy carrier of the disorder is 50 percent at each pregnancy, and the risk that a child will not have the disorder and will not be a carrier is 25 percent. Ask for genetic counselling to get a complete explanation.

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