Non-syndromic congenital sideroblastic anemia (CSA).
X-linked CSA (XLSA). Defects in ALAS2.

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). X-linked CSA is due to mutations of the erythroid-specific enzyme ALAS2, the first enzyme of the heme biosynthetic pathway.

What causes the disease and how common is it?

Non-syndromic CSA is a rare genetic disease, being the most common form the X-linked form. X-linkled sideroblastic anemia (XLSA) is due to mutations of the aminolevulinic acid synthase 2 (ALAS2) gene, encoding the ALAS2 enzyme involved in the first step of heme synthesis. These mutations lead to a reduced ALAS2 activity and a reduction of heme and hemoglobin formation. Gain-of-function mutations in the ALAS2 gene give rise to another disease called X-linked dominant Erythropoietic protoporphyria.
Other forms of non-syndromic CSA are due to mutations of the SLC25A38 and GLRX5 genes.
XLSA is a rare disorder with fewer than 100 unrelated probands described in the literature. Estimated prevalence is 1-9 / 1 000 000.

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

Deficiency of heme synthesis causes microcytic hypochromic anemia with mitochondria iron accumulation in the erythroid cells and formation of excessive “ring sideroblasts” in the bone marrow. Iron overload may develop in the liver and other organs. Affected subjects are usually males, but also females may be affected because of inactivation of the normal X chromosome (lyonization) or in cases of autosomal recessive forms.

Which treatment must I follow if I have the disease?

X-linked sideroblastic anaemia may respond to treatment with vitamin B6 (pyridoxine) and folic acid. In unresponsive cases with severe anemia supportive measures such as red cell transfusions are needed. Iron overload is treated with chelation therapy.

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

XLSA is an X-linked recessive disease. In case of X linked forms, there are different parental combinations that may lead to an affected child, as following:

Parents	Children
Mother: Healthy carrier Father: Healthy	Female: 50% Healthy /50% Healthy carrier Male: 50% Healthy/ 50% Affected
Mother: Healthy Father: Affected	Female: 50% Healthy /50% Healthy carrier Male: 100% Healthy
Mother: Healthy carrier Father: Affected	Female: 50% Healthy carrier/50% Affected Male: 50% Healthy/ 50% Affected
Mother: Affected Father: Affected	Female: 100% Affected Male: 100% Affected

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