SOHC

SWISS ONCOLOGY & HEMATOLOGY CONGRESS

Compound *HFE*/*PIGA* Mutation as cause of hemochromatosis and neurological dysfunction: case report of a Swiss patient

Abstract category: Hemostasis, transfusion medicine, vascular, laboratory medicine

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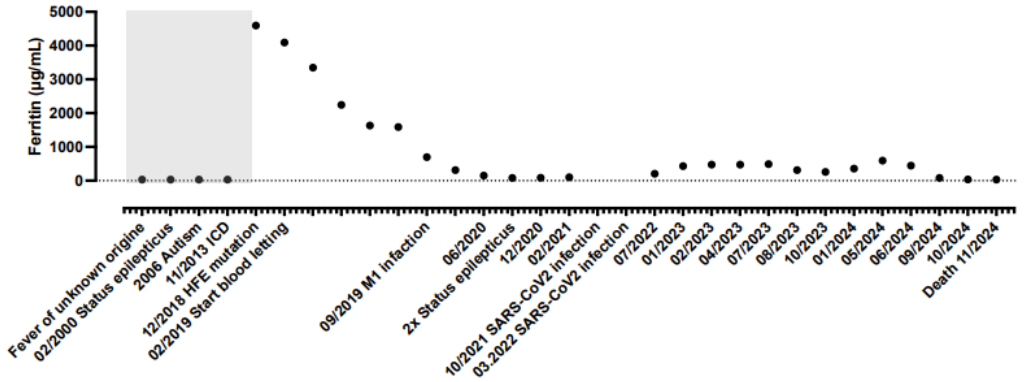
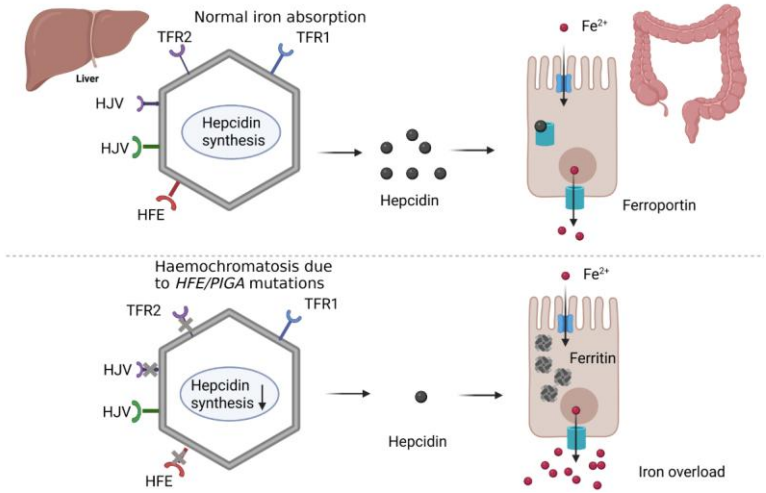
Introduction: Phosphatidylinositol glycan anchor biosynthesis class A (*PIGA*) mutations disrupt glycosylphosphatidylinositol (GPI) anchor synthesis, leading to a spectrum of congenital disorders characterized by neurological impairment, multisystem involvement, and systemic iron overload.

Methods: We describe the case report of a swiss patient affected by compound het. *HFE/PIGA* deficiency presenting since childhood with symptoms affecting the nervous system (autism, epilepsy and psychomotoric retardation); the cardiovascular system (dilatative cardiomyopathy); and the iron homeostasis (with overload in both liver and heart).





Results: The patient was referred at 22 y/o due to a hyperferritinemia (4592 ug/l). The MRI showed a severe iron overload of the heart and a moderate one of the liver. Genetic test for the *HFE* locus showed only a heterozygous C282Y mutation. Bloodletting was initiated; although a rapid normalization of the ferritin values was observed, the patient presented with repeated epileptic events after the procedures.

A genetic investigation of the *PIGA* gene was performed, leading to the identification of X-chromosomal hemizygous *PIGA*-missense Mutation c.242G>A. Iron chelation therapy was suggested; due to the numerous interactions with the antiepileptics of both deferoxamine and deferasirox, deferiprone was chosen as best therapy, leading to no neurological complication. Regardless of the optimal plasmatic iron values, the cardiac status of the patient turned for the worse.

The patient developed various serious complications. He expired after a fatal infectious complication.

Conclusions: *PIGA* catalyzes the first step of GPI anchor biosynthesis, a process that is important for the dynamics and cell membrane attachment of approximately 150 human proteins. As postulated before, iron overload in PIGA deficiencies could be caused by a failure to attach GPI anchors to HJV and a subsequent inability to appropriately induce hepcidin expression by hepatocytes. How this interacts with the heterozygous HFE C282Y mutation needs to be further investigated.

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