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CASE REPORT

Metabolic iron disorder after liver transplant: Hereditary hemochromatosis in a pediatric recipient of a pediatric donor with unknown HFE C282Y homozygous mutation

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Summary We report a case of an iron overload syndrome twenty years after a liver transplantation in a patient without feature for secondary iron overload. The diagnosis of hemochromatosis with homozygous mutationC282Y in the graft was made possible with liver biopsy, using real-time PCR technique with Light-Cycler 480. Our case suggests that in case of iron overload syndrome after liver transplantation we can perform a liver biopsy with real-time PCR technique that allows us to search for the mutation of the HFE.

Hereditary hemochromatosis (HH) is an autosomal recessive genetic disorder most common in Caucasiens [1]. C282Y homozygotes represent 80-85% of HH. It is characterized by an increased iron absorption by the intestine and deposition in solid organs [2]. We report here a case of a young patient who developed iron overload 26 years after liver transplantation from a deceased pediatric donor with HFE C282Y homozygous mutation, unknown at the time of organ harvesting.

A 26 year-old Caucasian woman was transplanted when she was 6 months old in 1990 for secondary biliary cirrhosis due to biliary atresia and failure of the Kasai procedure. The donor was a healthy three years old child. She required no

Abbreviations: HH, Hereditary Hemochromatosis; MRI, Magnetic resonance imaging; PCR, polymerase chain reaction.

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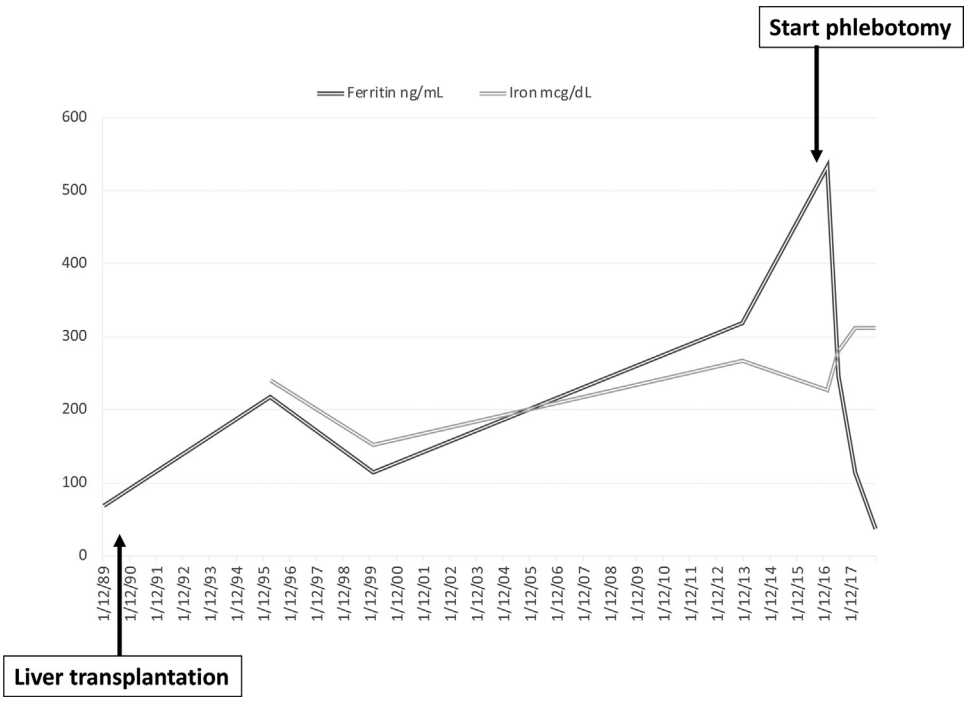

Figure 1 Graphical evolution of ferritin and iron level over time.

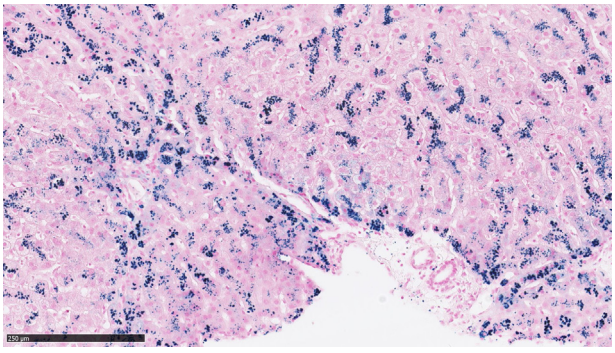

Figure 2 Peri-canalicular pattern of iron distribution is seen in the hepatocytes (Perls stain).

blood transfusion during the procedure. During the follow-up, she showed increased ferritin levels up to 719 μg/L (13-150 μg/L) in December 2016 with transferrin saturation above 80% (Fig. 1). There was no feature for secondary iron overload. Tacrolimus was her only medication. A hepatic MRI showed hepatomegaly with iron liver quantification increased to 160 μmol/g of liver (normal < 36 μmol/g) without iron overload in pancreas or spleen. She did not show the common HFE mutations (C282Y and H63D) in peripheral blood cells. In October 2017, a liver biopsy demonstrated peri-canalicular pattern of iron deposition in the hepatocytes, mainly in the periportal area. This aspect was highly suggestive of hemochromatosis (Scheuer grade 4) (Fig. 2). The C282Y mutation of the HFE gene was tested on the hepatocytes from a liver biopsy, using real-time PCR technique with Light-Cycler 480 (Roche). This confirmed that the young donor was homozygous for the C282Y mutation as the genetic of our patient was negative. As HFE gene mutation was present, we did not look for other rare hemochromatosis related mutation. A treatment by biweekly phlebotomies was started for four months (June to October 2017) allowing a decrease of ferritin level down to 164 μg/L (Fig. 1). The patient is now treated since then by phlebotomies every two months.

Our case suggests the immediate safety of transplanting a pediatric liver with HH. The delay of the diagnosis was due to normal ferritin measurements at the time of the ten years biopsy already showing iron deposition suggestive of HH. The absence of iron deposition in other organs and the absence of liver complications after more than twenty years of follow-up confirms the safety of transplantation with HFE mutated liver graft of young donors [3]. Other case reports have suggested earlier iron overload in patients transplanted with adult HFE mutated livers which should be used with more caution. Treatment of iron overload by phlebotomy was effective in decreasing ferritin levels [4]. The genetic research of HFE mutation on a liver biopsy should be done when discovering post-transplant iron overload without obvious secondary cause. Ferritin and transferrin saturation should be part of the follow-up [5].

Authors' contributions

Guarator of the article: Dr Monino.

Author contributions: Follow up patient (A); collecting data (B); Histological Analysis (C); Writing the manuscript (D); Reviewing the manuscript (E); Final revision (F).

Dr Monino: A, B, D, E, F; Pr Reding: A, E, F; Pr Komuta: C, E, F; Dr Dahlqvist: A, E, F.

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Disclosure of interest

The authors declare that they have no competing interest.

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