



Available online at

ScienceDirect
www.sciencedirect.com

Elsevier Masson France

EM|consulte
www.em-consulte.com/en



CASE REPORT

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

Laurent Monino^{a,*}, Raymond Reding^b, Mina Komuta^c,
Géraldine Dahlqvist^{a,b}

^a Service d'Hépatogastroentérologie adulte, Cliniques universitaires Saint-Luc, avenue Hippocrate 10, Bruxelles, Belgique

^b Service de Chirurgie et Transplantation abdominale, Cliniques universitaires Saint-Luc, Bruxelles, Belgique

^c Service d'anatomopathologie, Cliniques universitaires Saint-Luc, Bruxelles, Belgique

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 mutation C282Y 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.

© 2020 L'Auteur(s). Publié par Elsevier Masson SAS. Cet article est publié en Open Access sous licence CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Hereditary hemochromatosis (HH) is an autosomal recessive genetic disorder most common in Caucasians [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 blood transfusion during the procedure. During the follow-up, she showed increased ferritin levels up to 719 µg/L

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

* Corresponding author.

Adresses e-mail : laurent.monino@uclouvain.be,
monino.laurent@hotmail.fr (L. Monino).

<https://doi.org/10.1016/j.clinre.2020.04.009>

2210-7401/© 2020 The Author(s). Published by Elsevier Masson SAS. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Pour citer cet article : Monino L, et al. Metabolic iron disorder after liver transplant: Hereditary hemochromatosis in a pediatric recipient of a pediatric donor with unknown HFE C282Y homozygous mutation. Clin Res Hepatol Gastroenterol (2020), <https://doi.org/10.1016/j.clinre.2020.04.009>

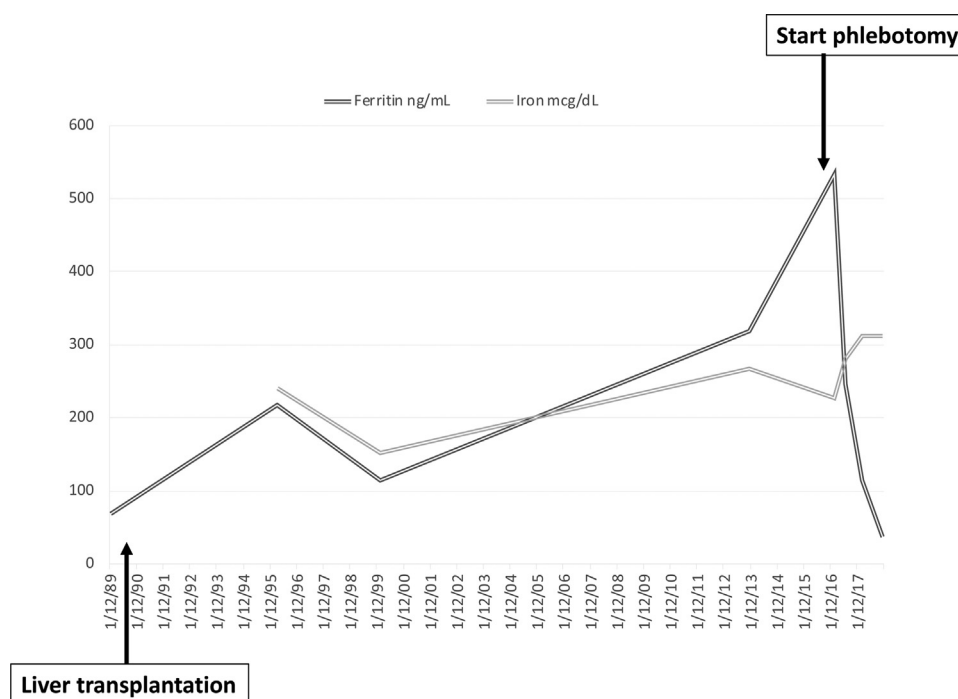


Figure 1 Graphical evolution of ferritin and iron level over time.

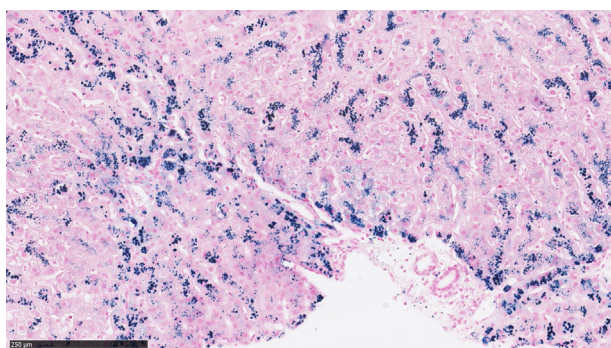


Figure 2 Peri-canalicular pattern of iron distribution is seen in the hepatocytes (Perls stain).

(13-150 $\mu\text{g/L}$) 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 $\mu\text{mol/g}$ of liver (normal < 36 $\mu\text{mol/g}$) 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 $\mu\text{g/L}$ (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.

Funding

The authors declare no funding was received for this study.

Disclosure of interest

The authors declare that they have no competing interest.

Acknowledgements

We acknowledge the patient that gave informed consent to publish her medical history and bioclinical data.

Références

- [1] Bacon BR, Adams PC, Kowdley KV, Powell LW, Tavill AS. Diagnosis and management of hemochromatosis: 2011 practice guideline by the American Association for the Study of Liver Diseases. *Hepatology* 2011;54(1):328–43.
- [2] Powell LW, Seckington RC, Deugnier Y. Haemochromatosis. *Lancet* 2016;388(10045):706–16.
- [3] Tan A, Florman SS, Schiano TD. Genetic, hematological, and immunological disorders transmissible with liver transplantation. *Liver Transpl* 2017;23(5):663–78.
- [4] Palmer WC, Vishnu P, Sanchez W, et al. Diagnosis and Management of Genetic Iron Overload Disorders. *J Gen Intern Med* 2018;33(12):2230–6.
- [5] Dwyer JP, Sarwar S, Egan B, Nolan N, Hegarty J. Hepatic iron overload following liver transplantation of a C282y homozygous allograft: a case report and literature review. *Liver International* 2011;31(10):1589–92.