

Case Report

Haemochromatosis in end-stage renal disease: when waste is a treatment option

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Abstract

For patients with end-stage renal disease and hereditary haemochromatosis, prevention and treatment of anaemia differ from usual nephrologic guidelines. Monitoring of individual disease progression and ferritin levels is crucial. We describe a case of a young haemodialysis patient with early-stage organ dysfunction caused by hereditary haemochromatosis, in whom iron stores have successfully been depleted with phlebotomy and supplemental erythropoietin over 22 months. Target ferritin levels could finally be reached without severe, persisting or symptomatic anaemia.

Keywords: haemochromatosis; haemodialysis; phlebotomy

Background

Patients with end-stage renal disease usually need iron and erythropoietin substitution to prevent renal anaemia [1]. In our centre, target haemoglobin level is 110–130 g/l and target ferritin level is usually >200 ng/ml, according to international guidelines. However, in patients with iron storage diseases such as hereditary haemochromatosis (HH), iron substitution is contra-indicated and ferritin levels, in general, should be <50 ng/ml to prevent secondary organ damage [2]. In long-term haemodialysis patients with HH, it might be challenging to achieve constant and sustained iron depletion without inducing anaemia. Here, we describe a case of a young haemodialysis patient in whom iron depletion (phlebotomy) and iron mobilization (erythropoietin) halted progression of newly diagnosed HH. Ferritin levels according to hepatologic guidelines could be achieved without severe, persisting or symptomatic anaemia.

Case report

In June 2005, a 29-year-old Mexican tennis coach started haemodialysis treatment at our hospital. Continuous ambulant peritoneal dialysis (CAPD) had been initiated in his home country in September 2000 when he first presented with newly diagnosed end-stage renal disease. Chronic glomerulonephritis was suspected, but no kidney biopsy was performed and the cause of his renal failure remained unknown. He had an otherwise uneventful medical history, with no significant illnesses reported in his family. In February 2001, he was switched to haemodialysis after repeated Tenckhoff catheter dysfunction. In Mexico, he was treated for renal anaemia with regular iron substitution (iron dextran 100 mg after each haemodialysis) and weekly epoetin beta 8000 IU injections.

Blood tests in Switzerland in June 2005 revealed slightly elevated liver enzymes (ASAT 48 U/l, ALAT 86 U/l) and high levels of ferritin and transferrin saturation (4714 ng/ml, normal range 30–300 ng/ml and 91%, normal range 16–45%, respectively), raising suspicions of iron overload syndrome. Iron and erythropoietin substitution were therefore discontinued. Nevertheless, ferritin levels remained inappropriately high during the following months (Figure 1). Further diagnostic investigations in June 2006 led to the diagnosis of HH: liver biopsy revealed severe siderosis (stage IV) and mild portal fibrosis; MRI of the heart and the liver showed a reduced cardiac ejection fraction (53%, normal range 56–78%) and a highly elevated hepatic iron concentration (HIC, 16 mg/g dry liver, normal range <1.4 mg/g dry liver, iron overload syndromes ≥ 4.0 mg/g dry liver) [3]. Genotyping ruled out the most common HFE mutations (C282Y, H63D, S65C). No other complications of HH (e.g. diabetes mellitus, secondary hypogonadism) were found. According to hepatologic guidelines for HH, a target ferritin level of <50 ng/ml was defined [2].

Initially, phlebotomy was performed twice weekly, achieved by discarding the circulating extracorporeal blood volume of ~150 ml rather than retransfusing it at the end of haemodialysis sessions. In addition, haematopoiesis and iron utilization were stimulated with high-dose erythropoietin substitution: darbepoetin alpha, 40–100 μ g i.v. was

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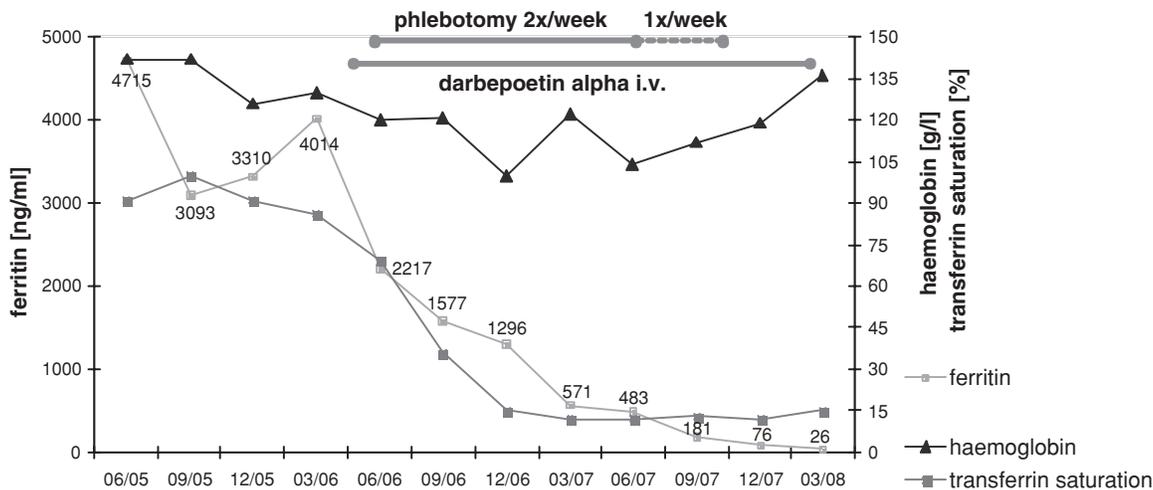


Fig. 1. Haemoglobin, ferritin and transferrin saturation before and during treatment.

given weekly (Figure 1). With few exceptions, haemoglobin levels remained between 110 and 130 g/l despite continuously decreasing ferritin levels (Figure 1). An MRI of the heart and the liver in April 2007 showed a normalized ejection fraction of the heart and a reduced HIC as compared to the first imaging (14 mg/g dry tissue). The frequency of phlebotomy was reduced to once weekly and finally stopped in March this year when ferritin levels reached the target range (Figure 1). Two months later, a cadaveric kidney transplant was successfully performed, and the follow-up is uneventful so far.

Discussion

Little is known about specific demands of supplemental iron and erythropoietin for long-term haemodialysis patients with HH [4,5]. There seems to be a reduced need of erythropoietin substitution in patients with a heterozygous C282Y mutation [6], but guidelines are lacking.

In this young Mexican patient, we diagnosed HH with early-stage organ dysfunction related to characteristic iron deposition in liver and heart that could be visualized and measured by MRI. The missing family history and the negative genetic testing was not surprising as the Hispanic race in general has a much lesser prevalence for the most frequent mutation, that is C282Y homozygosity (0.03% compared to 0.44% in Whites) [7]. We assume that this patient has a genetically unknown type of HH (non-HFE haemochromatosis), which affects roughly 3–10% of all HH patients [8], because the histological picture with a porto-central gradient of siderosis is typical for a genetically determined haemochromatosis. Other less probable iron overload syndromes with increased iron absorption are juvenile haemochromatosis, which occurs in childhood and in which severe liver pathology is uncommon [9], and diseases with ineffective erythropoiesis such as sideroblastic anaemias, severe thalassaemia and myelodysplastic syndrome. In our case, the latter are unlikely as there was no anaemia and a ferritin level above expected levels in those entities (2000–4000 ng/ml) [10]. Porphyria cutanea

tarda could be excluded as a cause of excess iron accumulation, as could chronic liver disease, and transfusional overload was unlikely because of a persistently high ferritin level several months after cessation of iron substitution (Figure 1).

From a practical point of view, this patient would have needed about 44 therapeutic phlebotomy units according to the following equation: phlebotomy units = $(\text{HIC} - 1.4) \times 3$. These additional interventions could be spared and blood withdrawal could be performed by simple and safe means during haemodialysis sessions as described above. Concerning the use of erythropoietin, it is known that in iron overload syndromes due to ineffective erythropoiesis such as hereditary sideroblastic anaemias or severe alpha and beta thalassaemia, administration of erythropoietin should be used to force mobilization of iron and to treat anaemia.

We conclude that, in haemodialysis patients who present with renal anaemia and concomitant HH, phlebotomy and the additional use of erythropoietin might well accelerate the complete removal of iron stores and prevent irreversible secondary organ damage and severe or symptomatic anaemia.

Conflict of interest statement. None declared.

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