Iron Overload After Pediatric Liver Transplantation: A Case Report

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ABSTRACT

Iron is an essential nutrient for living cells; however, an excessive accumulation of iron leads to organ damage and directly affects systemic immunity. Iron overload is clinically classified as hereditary or secondary. Most of secondary iron overload is caused by frequent blood transfusions because there is no active mechanism to excrete iron from the body. As recommended in various guidelines, chelation therapy is effective for reducing iron burden and improving organ function. There have been few reports on iron overload through blood transfusion during the perioperative period of liver transplantation. This report presents a case of iron overload due to repeated transfusions after pediatric liver transplantation managed by chelation therapy. The patient, an 11-month-old female with biliary atresia, underwent living donor liver transplantation. She revealed refractory anemia and required frequent blood transfusion. Both serum ferritin and transferrin saturation tended to increase after repeated transfusions, leading to secondary iron overload. Iron chelation therapy was started to prevent progression to organ failure and infection due to iron overload, and yielded a favorable outcome. It is crucial to consider the possibility of secondary iron overload and to achieve early detection and treatment to avoid progression to irreversible organ damage.

IRON is an essential nutrient for living cells because of its role as a cofactor for enzymes in the mitochondrial respiration chain, in the citric acid cycle or DNA synthesis, as well as being the central molecule for binding and transport of oxygen by hemoglobin and myoglobin. The total amount of body iron is approximately 3 to 4 g, two-thirds of which is red blood cell (RBC) iron and recycled iron by RBC destruction; the remainder is stored in ferritin/hemosiderin, whereas only 1 to 2 mg of iron are absorbed in the intestinal tract and circulated in the blood [1]. Meanwhile, excessive accumulation of iron leads to saturation of transferrin and the circulation of non–transferrin-bound iron, which produces reactive oxygen species in serum [2]. Iron overload induces organ damage in the liver, heart, pancreas, thyroid, and the central nervous system. The main cause of this organ damage is due to the overproduction of reactive oxygen species in the presence of excess iron [3–7].

There is no active mechanism to excrete iron from the body, thus a progressive accumulation of body iron easily occurs as a result of long-term repeated transfusions in patients with anemia due genetic disorders such as thalassemia, and of bone-marrow failure such as aplastic anemia and myelodysplastic syndrome [8]. Chelation therapy has recently been adopted as a treatment for iron overload after repeated transfusions, yielding favorable outcomes [8]. On the other hand, problems associated iron overload through blood transfusion during the perioperative period are rare because blood transfusions are administered to replace blood loss. However, pediatric liver transplantation (LT) with splenomegaly (especially in proportion to the low body weight) could easily lead to iron overload, even with only perioperative blood transfusion. There have been few reports on iron overload through blood transfusion during the perioperative period of LT. This report presents a case performing chelation therapy for iron overload due to repeated transfusions after pediatric LT.

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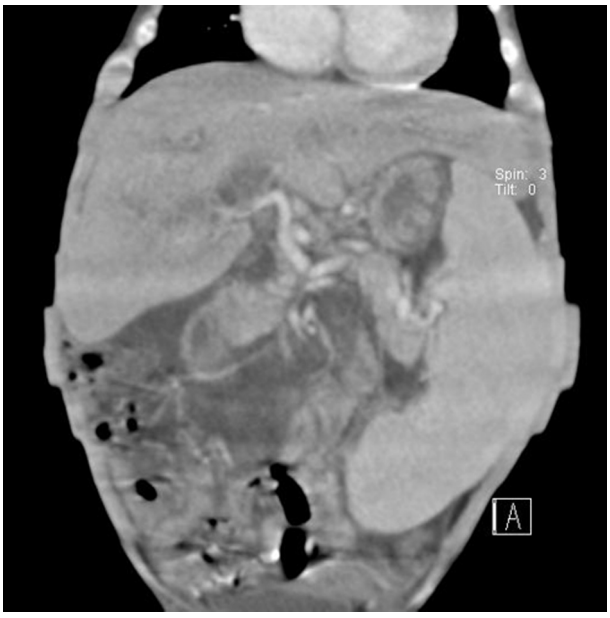

Fig 1. Preoperative abdominal computed tomography (CT). CT scan showed hepatosplenomegaly 1 month after admission; liver volume was 358 mL and spleen volume was 243 mL in CT volumetry.

CASE REPORT

The patient, an 11-month-old female with biliary atresia, had undergone portoenterostomy at 2 months of age. Cirrhosis progressed after surgery, at 9 months of age, and she required mechanical ventilation for pneumonia. She was transferred this hospital for LT at 10 months of age. Her body weight at the time of admission was 5.2 kg (−3.7 SD). An abdominal examination revealed hepatomegaly and splenomegaly. Her Pediatric End-stage Liver Disease score was 23 at that time. Abdominal computed tomography (CT) showed bilateral atelectasis and hepatosplenomegaly. Liver volume was 280 mL and spleen volume was 165 mL in CT volumetry. The patient was weaned from the ventilator 5 days after admission. She was given enteral and parenteral nutrition and medication to improve her general condition and promote weight gain. However, there was no improvement of the liver failure, the liver and spleen enlarged. The liver volume was 358 mL and spleen volume was 243 mL in CT volumetry 1 month after admission (Fig 1). She experienced respiratory failure due to abdominal distention caused by hepatosplenomegaly, and mechanical ventilation was again required 47 days after the patient was transferred. LT was immediately required due to the rapid deterioration of her general condition.

The patient underwent blood type–identical living donor LT at 11 months of age, with her mother serving as the donor. Because of severe adhesions and coagulopathy, the operation time was 15 hours 28 minutes; blood loss was 757 mL. Intraoperative blood transfusion volume was 740 mL. Body weight at LT was 5.2 kg and standard liver volume was 203 mL. The graft was an S2 monosubsegment, weighing 174 g, with the graft volume/standard liver volume ratio being 85.7%. The resected liver weight was 380 g. Primary closure could be performed without reduction in blood supply to the graft, and there were no signs of heart failure. Laparotomy was performed for intra-abdominal bleeding on the second postoperative day. Blood loss during this laparotomy was 280 mL and blood transfusion was 65 mL. Subsequently, the patient showed no vascular complications and biliary complications. She was extubated on postoperative day 20, although she took time to improve her nutritional status and respiratory status, and was discharged from the hospital 109 days after transplantation. The patient is now alive and doing well at 39 months after transplantation.

This patient revealed refractory anemia during the preoperative period. There was no bone marrow suppression or gastrointestinal bleeding. The anemia was thought to be due the negative impact of hepcidin in chronic inflammation and extravascular hemolysis with splenomegaly. Transfusion of RBCs was required frequently, and the total amount of preoperative blood transfusion after the patient was transferred to the hospital was 840 mL (Fig 2). Anemia was prolonged after LT, and frequent blood transfusions (total of 765 mL) were required. Although it initially tended to decrease, the level of serum ferritin gradually began to rise again from approximately postoperative day 10 (Fig 3). There were no findings corresponding to elevation of serum ferritin levels (such as liver damage due to obstruction of blood flow) and rejection (such as acute and chronic infection). In addition to the findings from a physical examination and blood tests, Still's disease, hemophagocytic syndrome, and cancer were negative. Transferrin saturation was also high, and elevation of ferritin was determined to have developed from secondary iron overload due to blood transfusion. Iron chelation therapy using deferoxamine (30 mg/kg/d) was started on postoperative day 58 to prevent progression to organ failure and infection due to iron overload. Both serum ferritin and transferrin

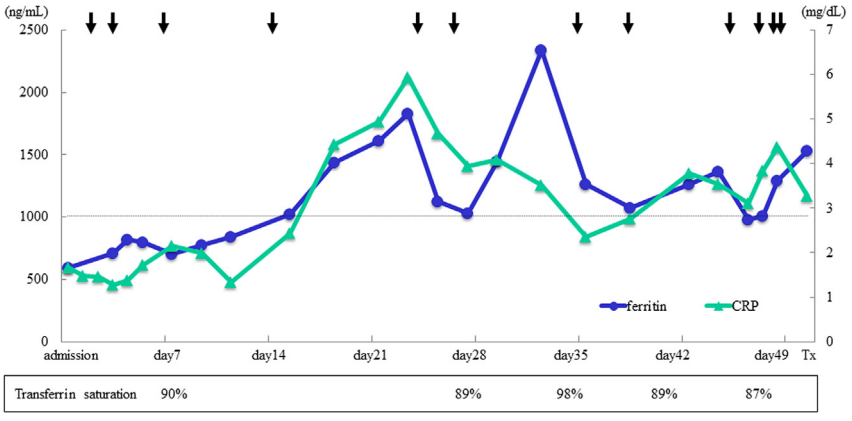

Fig 2. Evolution of serum markers and blood transfusion before transplantation. Time course of serum ferritin (●) and C-reactive protein (▲) before transplantation. The figure also depicts the frequency of blood transfusion (*arrows*).