Case Report
Hemochromatosis resulted from large-dose intravenous iron injection in hemodialysis patients: a report of two cases

Jian-Dong Li, Li Guo, Shan-Shan Guo, Yan-Li Gou, You-Lan Gong, Hang Chen

The Blood Purification Center, The Affiliated Hospital of Hebei University, Baoding City 071000, Hebei Province, China

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Abstract: Iron deficiency is very common in untreated dialysis patients, and hemochromatosis should be rare in theory. However, large doses of intravenous iron injection may cause hemochromatosis. We report two cases of hemochromatosis that resulted from a large dose of intravenous iron injection in hemodialysis patients. Clinical manifestations included liver enlargement, liver fibrosis or even cirrhosis, splenomegaly and other solid organ dysfunctions. Case one manifested as liver cirrhosis and case two manifested as confusion in consciousness. These two cases both manifested as thrombocytopenia, and increased density of the liver and spleen. The two patients’ condition was serious, eventually both patients died a few days later.

Keywords: Secondary hemochromatosis, hemodialysis, intravenous iron injection, cirrhosis

Introduction
Hemochromatosis refers to excess iron deposition in the liver and other solid organs, which can damage the structure and function of these organs. Primary hemochromatosis is an autosomal recessive genetic disorder. Secondary hemochromatosis is caused by other diseases or treatment measures, and causes the excessive deposition of iron in the body mainly during severe chronic anemia and substantial long-term blood transfusions. The clinical manifestations of hemochromatosis are mainly caused by injury to affected organs, such as skin pigmentation, liver enlargement, liver fibrosis or even cirrhosis, splenomegaly, diabetes caused by pancreatic dysfunction, and cardiac involvement. We report two cases of hemochromatosis and details as follow.

Cases report
Case one
A 58 year-old female was admitted with failure to ultrafiltrate and repeated hypotension during dialysis. She had a history of hypertension, diabetes and coronary heart disease. Due to end stage renal disease (ESRD), she had been on hemodialysis for six years. Hypotension occurred during dialysis on July 2014, and she was admitted to our hospital. Signs of ascites were found during physical examination. Shifting dullness was positive. No dilated tortuous vein and projection of the umbilicus was found. Furthermore, there was no significant edema in both lower limbs. When hemodialysis started, blood pressure (BP) was 104/69 mmHg and heart rate was 106 BPM. When 200 ml of water was ultrafiltrated, BP fell to 89/60 mmHg and heart rate rose to 123 BPM. The dry body weigh could not be reached. Tests revealed the following: white blood cell count (WBC) was $4.02\times10^9/l$, hemoglobin (Hb) was 105.3 g/l, and platelet (PLT) was $98.7\times10^9/l$; total cholesterol was 3.24 mmol/l, triglycerides was 1.6 mmol/l, creatinine was 523.45 umol/l, urea was 22.94 mmol/l, serum albumin was 32.33 g/l, globulin was 34.53 g/l, and serum transaminase and bilirubin were normal. Viral hepatitis markers: HBsAg (-), HBsAb (+), HBeAg (-), HBeAb (-), HBCAg (-),
Hemochromatosis in hemodialysis patients

Case one

A patient with hemochromatosis was admitted due to ESRD. The patient had no history of hypertension, diabetes, or cerebral vascular disease. Due to ESRD, the patient received a large dose of intravenous iron sucrose injection (approxi-

mately 300 ampoules, 100 mg of iron/ampoule) in the past four years. Ferritin was 1,500 ng/ml (11.00-306.80 ng/ml). Abdominal CT: massive ascites, left lobe of the liver was slightly enlarged, and splenomegaly (Figures 1 and 2).

We found that the patient received a large dose of intravenous iron sucrose injection (approximately 300 ampoules, 100 mg of iron/ampoule) in the past four years. Hemochromatosis was diagnosed based on ascites, ferritin level, abdominal CT and history of intravenous iron usage. Hypotension during hemodialysis may be associated with reduced effective circulating blood volume. Changes in blood PLT count and albumin level during the past four years are shown in Figure 3. We did some supportive treatment including intravenous albumin, the patient died a few days later.

Case two

A 58 year-old female was admitted with confusion of consciousness. She had no history of hypertension, diabetes, or cerebral vascular disease. Due to ESRD, she went to our hospital on October 4, 2014 and repeatedly complained of discomfort of the whole body without a clear answer. The daughter of the patient said the patient did something out of the ordinary such as forgetting to wear trousers for three days. Signs of ascites were not found, and there was no significant edema in both lower limbs.

Tests: routine blood test: WBC was 9.1×10⁹/l, Hb was 152 g/l, PLT was 84×10⁹/l; creatinine was 715 umol/l, urea was 22.94 mmol/l, magnesium (Mg) was 1.25 mmol/L, potassium (P) was 1.9 mmol/L, and other electrolytes were in the normal range. Head CT did not reveal any obvious abnormality. The patient continued to complain of discomfort of the whole body during the dialysis. BP remained stable during dialysis. Further tests revealed the following: Viral hepatitis markers: HBsAg (-), HBsAb (+), HBeAg (-), HBeAb (-), HBcAg (-), HBcAb (-), and HCV antibody (-). Ferritin was 1,500 ng/ml (11.00-306.80 ng/ml), parathyroid hormone was 182.50 pg/ml (12-88 pg/ml), ESR was 14 mm/h, CRP was 10.8 mg/L, ANA and anti-dsDNA were negative, LDH was 171.9 U/L, ALP was 123.2 U/L (30-132 U/L), AST was 51 U/L (0-45 U/L), ALT was 33.5 U/L (0-45 U/L), GGT was 94 U/L (7.0-32 U/L), and CHE was 2,206 U/L (4,000-13,000 U/L). Abdominal CT: increased density of liver and spleen, splenomegaly (Figures 4 and 5).

We found that the patient received a large dose of intravenous iron sucrose injection (approximately 400 ampoules, 100 mg of iron/ampoule) in the past four years. Hemochromatosis was diagnosed, although the mechanism of confusion remained unclear. Changes in blood PLT count and albumin level during the past four years are shown in Figure 6. And the patient died 3 days later.
Due to gastrointestinal reactions and low absorption rate, intravenous iron is recommended in dialysis patients; and studies have proven that intravenous iron infusion is superior to oral iron in terms of correcting iron deficiency. The KDIGO Anemia Work Group therefore recommends the use of intravenous iron supplementation [1]. However, the excessive use of intravenous iron infusion can cause the deposition of iron in the body, and subsequently cause hemochromatosis. Intestinal mucosal cells can regulate oral iron absorption. Intravenous iron usage can escape this protective regulation, which results in excess iron deposition in the body. The liver is the first and most serious organ with iron deposition. Excess iron deposition can lead to liver damage and dysfunction. Iron can cause liver fibrosis and eventually cirrhosis. Since there is no obvious necrotizing inflammation, transaminase (ALT, AST) are normal or mildly elevated. When hemochromatosis is suspected, basic laboratory examinations on iron metabolism should be performed, as well as an abdominal CT examination [2, 3]. Liver CT manifestations are characteristics of hemochromatosis. Increased density of the whole liver could be observed in the CT image of non-contrast enhanced scans. CT values fall within 86-132 HU or higher, which is consistent with what we have reported. CT values generally reflect the content of iron concentration. CT manifestations of hemochromatosis also include cirrhosis, hepatocellular carcinoma and portal hypertension [4]. MRI plays an important role in the diagnosis and treatment of hemochromatosis [5]. Compared with CT, ultrasound will not show a very good result when solid organ tissue density is elevated. Liver biopsy is considered the gold standard for hemochromatosis diagnosis.

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**Hemochromatosis in hemodialysis patients**

**Discussion**

Anemia is an important clinical manifestation in patients undergoing hemodialysis, and iron deficiency is very common. Hemodialysis in patients with secondary hemochromatosis is rare in theory. However, the wide use of intravenous iron application has changed this situation.

**Figure 3.** The change of blood platelet count and albumin level during June-2010 and August-2014 in case one.

**Figure 4.** Plain CT scan shows increased density of liver and spleen, splenomegaly in case two. The CT value of liver was 96 HU, the spleen was 89 HU on coronal position.

**Figure 5.** Plain CT scan shows increased density of liver and spleen, splenomegaly in case two. The CT value of liver was 96 HU, the spleen was 89 HU on level.
We found that PLT count and plasma albumin levels had a downward trend in these two patients after applying intravenous iron infusion (Figures 3 and 6). Ayelet Machtei reported a case of neonatal hemochromatosis [6]. The PLT changed from 76 to 142 K/micl (reference values: 150-450 K/micl), albumin changed from 2.2 to 2.9 g/dL (2.8-4.4 g/dL), and ferritin changed from 24,256 to 3,030 ng/mL (10.0-291.0 ng/mL). Furthermore, Masoud M. Malekzadeh reported two siblings with juvenile hemochromatosis, which exhibited more detailed PLT changes along with ferritin changes [7]. The proband’s PLTs (mm³) were 135,000 and ferritin (ng/ml) was >2,000 on first visit. PLTs were 140,000 and ferritin was 2,990 after six months, PLTs were 150,000 and ferritin was 917 after 18 months, PLTs were 183,000 and ferritin was 253 after 24 months, and PLTs were 192,000 and ferritin was 21 after 36 months. Iron deposition in the liver and bone marrow may affect the normal function of liver and bone marrow megakaryocytes, resulting in decreased synthesis of albumin and PLTs. The decline in both PLTs and plasma albumin may be the clinical manifestations of hemochromatosis.

Intravenous iron has its advantages in treating anemia. However, attention should be given on the absence of the iron excretory mechanism of our body and the dose of intravenous iron given. In addition, the use of intravenous iron should be monitored, as recommend by KDIGO.

**Disclosure of conflict of interest**

None.

**References**


