中文題目：次發性血鐵沉著症: 因服用過量含鐵補給品導致

英文題目：Secondary hemochromatosis : A rare cause of ingesting overload iron supplementation

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Background:

Hemochromatosis was mostly known as a hereditary disease with a mutation in the *HFE* gene in Caucasians. Secondary hemochromatosis was relatively rare but still important. Without proper therapeutic intervention, the disease can lead to life-threatening complications such as cirrhosis, hepatocellular carcinoma, diabetes, and heart failure. Here we presented a secondary hemochromatosis case that was not due to transfusion, with the habit of using Chinese herbal supplements, from the clinical presentation to the diagnosis.

Case presentation:

A 35-year-old Chinese man with underlying of asymptomatic thalassemia presented with epigastric pain and poor appetite for 3 days. He had progressive yellow skin for 1 week. The laboratory tests revealed total bilirubin/ direct bilirubin : 51.8/ 49.7 mg/dL (0.2-1.5), prothrombin time 19.5 sec (8.0-12.0), AST 105 IU/L (<37), ALT 116 IU/L (<41), alk.phosphatase 192 IU/L (40-129), r-GT 353 IU/L (8-61) and hemoglobin 10.6 g/dL (13.0-17.0), LDH 389 IU/L (135-225), triglyceride 198 mg/dL (<200), creatinine 3.06 mg/dL (0.7-1.20). Laboratory of Iron/TIBC: 99.8% (20-45%), transferrin: 107 ug/dl (200-360) and high level of serum ferritin: 7050 ng/ml (27-300) were noted. The other autoimmune, viral markers, atypical infection were unremarkable. For suspected hemochromatosis related acute liver decompensation, we arranged liver biopsy and the pathology documented diffuse deposition of yellow-brown granules in hepatocytes and Kupffer cells (Fig.1). The yellow-brown granules are positive for iron

stain (4+) and negative for Fontana-Masson and PAS-D stain. The picture is compatible with hemochromatosis, which is favor to be secondary. The Magnetic Resonance Cholangiopancreatography (MRCP) demonstrated marked dark T1 and T2 signal at the liver parenchyma, spleen, pancreas and bone marrow, suggestive of heavy metal deposition and compatible with hemochromatosis (Fig.2). Genetic test was sent for *HEF* gene to rule out hereditary hemochromatosis, which showed no mutation. There was no family history of unexplained liver disease. Tracing his history, he had oral intake of 20 black herbal pills (0.2213gram/pill) per day for 1 year. We sent the black herbal pills for toxicological analysis, and the herbal pill contained high level of ferrum 22864 ppm (μg/g). One the other hand, he had parenteral overload ferrum up to 101mg every day for 1 year.

Discussion:

According to the Food and Nutrition Board, Institute of Medicine in U.S. Recommended Dietary Allowances (RDAs) for daily Iron is 8 mg in male and 18 mg in female at the age of 19–50 years [1]. However, in our case, this young male had oral ingestion up to 101mg of ferrum every day which exceed the body's ability to clear it. These herbal pills contained so high level of ferrum that turned to the result of hemochromatosis. Excess iron deposition in parenchymal tissue causes injury and ultimately organ dysfunction, such as diabetes mellitus and decompensated cirrhosis.

According to the American Association for the Study of Liver Diseases, we can divide the cause of iron overload into three groups: (1) inherited causes of iron overload, (2) various causes of secondary iron overload, and (3) miscellaneous group [2]. Individuals who receive blood transfusions and who have transfusional or parenteral iron overload are the common causes of secondary iron overload.

Early diagnosis of hemochromatosis was not so easy because the symptoms were

mostly nonspecific, such as lethargy, hyperpigmentation of the skin, loss of libido, testicular atrophy, diabetes, abdominal pain, and arthralgias [3]. In hereditary hemochromatosis, patients are often diagnosed by incidentally noted hyperferritinemia without obvious organ damage [4]. To diagnosed iron overload of tissue, liver biopsy was traditionally the gold standard, but it is an invasive procedure. Recently, T2-weighted MRI has been largely replaced it [5].

Early treatment of patients with hemochromatosis with clinical iron overload can improve their morbidity and mortality. The mainstay of treatment has been through phlebotomy [3]. For the patient who cannot tolerate phlebotomy, could be considered for iron chelation therapy, such as deferoxamine or deferasirox.

Conclusion:

Secondary hemochromatosis may be rare and not to be noticed, but early diagnosis with therapeutic intervention may improve the outcome and reverse the damage to multiple organs.

Reference:

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