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Letters to the Editor

Aceruloplasminemia: An entity to consider in patients with anemia

Key words: Aceruloplasminemia. Ceruloplasmin. Anemia. Ferritin. Hyperferritinemia. Iron overload. Hemochromatosis. Iron chelator. Desferrioxamine.

Dear Editor,

Aceruloplasminemia is an extraordinary genetic disorder that shares both clinical and analytical features with other gastroenterological diseases such as hemochromatosis, Wilson's disease or Menkes´ disease. Moreover, anemia is usually the first sign of this disorder, a common cause of referral to our specialty.

Case report

A 47-year-old man was referred to our unit with abdominal pain and anemia (Hb 11.4 mg/dl) associated with hyperferritinemia (707 ng/ml). The upper gastrointestinal endoscopy, colonoscopy, abdominal ultrasonography, and upper gastrointestinal series discarded inflammatory activity. Despite presenting low transferrin saturation (3.7 %) we performed genetic testing for hemochromatosis which was negative. As the tests showed no alterations, we requested serum ceruloplasmine concentration and a study of copper metabolism, both of which confirmed the diagnosis of aceruloplasminemia: serum ceruloplasmine concentration under 7 mg/dl (normal range, 22-61 mg/dl), low serum copper concentration 13 µg/dl (normal range, 70-150 µg/dl) and normal urine excretion of copper. We did not perform genetic testing for aceruloplasminemia because it was not available in our center. Abdominal magnetic resonance imaging (MRI) showed abnormally low intensities in the liver in T1 and T2, reflecting iron accumulation in the liver (Fig. 1). No abnormalities were observed in brain MRI or ophthalmological examination.

Discussion

Ceruloplasmin is an enzyme with ferroxidase activity which allows iron incorporation to transferrin and its removal from tissues (1-3). Mutation in CP which encodes ceruloplasmin leads to an iron accumulation in the liver, pancreas and central nervous system (4). Hepatic iron deposition does not cause liver injury (5). Over 40 different mutations have been described, but their determinations are limited due to the large region encoded (6,7). Both affected individuals and their relatives should receive genetic counseling (5).

Clinical features of aceruloplasminemia are retinal degeneration, diabetes mellitus and neurological symptoms but anemia is often found prior to the onset of these manifestations (5,8). It typically manifests itself in the fourth or fifth decade and death occurs around the age of 65 (1,5,8).

It is analytically characterized by total or almost total absence of ceruloplasmin, low serum copper and iron concentration, high serum ferritine levels and undetectable ferroxidase activity (1,9).

It is important to make a differential diagnosis with other entities that present hyperferritinemia, such as metabolic syndrome, inflammatory disorders, alcoholism or hemochromatosis and it should be suspected when anemia is found once the main causes have been discarded (5). Serum levels of ceruloplasmin are also decreased in copper metabolism disorders, so it must be distinguished from Wilson's disease, in which there is an inability to transfer copper into ceruloplasmine precusor protein, and from Menkes' disease, in which intestinal copper absorption is reduced, leading to a deficiency in ceruloplasmin synthesis (5).

Treatment with iron chelating agents can be considered in symptomatic patients whose serum hemoglobin concentration is above 9 g/dl, although they are not very effective in decreasing brain iron stores. Repeated administration of fresh-frozen

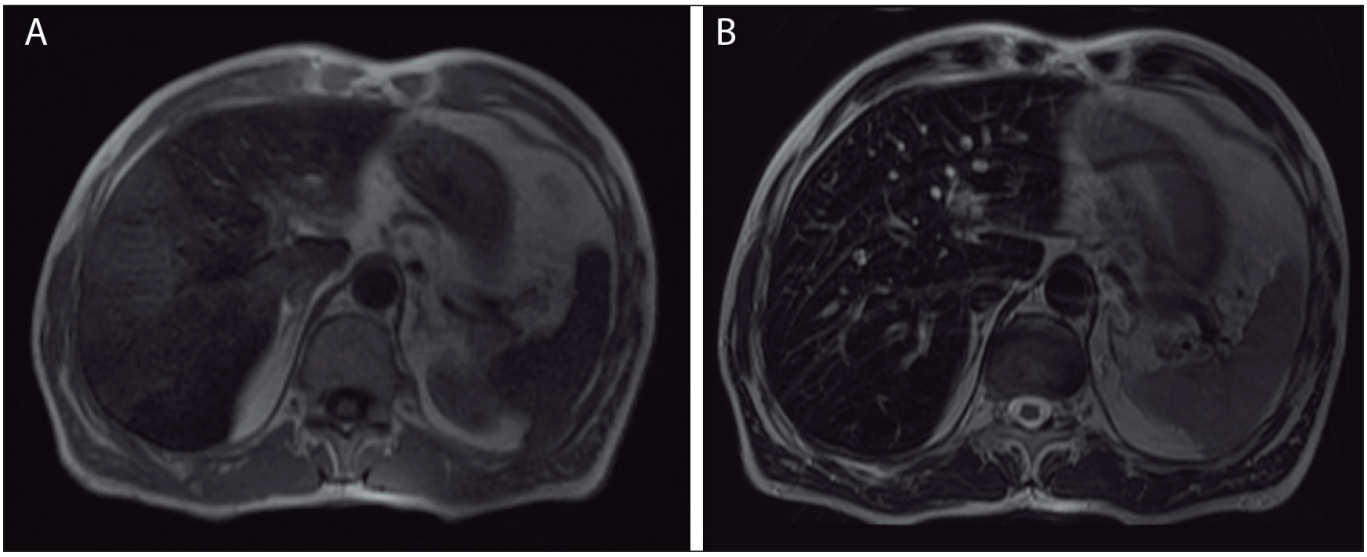

Fig. 1. Abdominal MRI shows low-signal intensities in the liver parenchyma both in T1 (A) and T2 (B), suggesting iron deposition.

human plasma with ceruloplasmin could improve neurological symptoms (5). Phlebotomies are limited because they can worsen anemia and the symptomatology (9).

In summary, aceruloplasminemia is an entity to consider when hyperferritinea or anemia are present since its diagnosis has important prognostic implications.

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