A lean man with nonalcoholic fatty liver disease

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A 23-year-old man was admitted to Shinshu University Hospital for further examination of liver dysfunction in 1993. He was asymptomatic and weighed 50 kg and his body mass index was as low as 17.3 kg/m^2. Physical examination revealed only mild hepatomegaly. Laboratory tests showed elevated alanine aminotransferase and gamma-glutamyltransferase. Fasting glucose, insulin, glycohemoglobin, lipid profiles, ammonia, immunoglobulin, ferritin, and ceruloplasmin concentrations were all normal. Viral markers and autoantibodies were negative. Abdominal ultrasonography showed increased echo texture of the liver parenchyma. Laparoscopy showed a yellowish liver, and a biopsy revealed macrovesicular and microvesicular steatosis with pericellular fibrosis (Figure), which was consistent with alcoholic steatofibrosis, although he drank no alcohol. He was treated with ursodeoxycholic acid and released.

Ten years later the patient suddenly became confused and was referred to our hospital for liver failure. His plasma ammonia and citrulline levels were markedly elevated. DNA analysis of the citrin gene revealed a homozygote for a Ser225X mutation, leading to a diagnosis of adult-onset type II citrullinemia (CTLN2). We performed an urgent liver transplantation[1]. His consciousness cleared and his ammonia and citrulline levels normalized. Neither liver dysfunction nor hepatic steatosis has recurred since.

Hepatic steatosis, including steatohepatitis, is one of the common phenotypes of CTLN2 [2]. Most of the CTLN2 patients are not obese, and apparently healthy without any neuropsychological symptoms, probably due to metabolic adaptation, so it is difficult to be diagnosed as having CTLN2 in asymptomatic patients only representing with fatty liver. Therefore, in non-obese patients with nonalcoholic fatty liver disease, the possibility of CTLN2 should be considered.

Figure Legend

Figure: Histological findings of this patient.

Laparoscopic liver biopsy was performed in 1994. Histologically, macro- and microvesicular steatosis with pericellular fibrosis was observed (A, hematoxylin and eosin staining, x 400; B, Azan-Mallory staining, x 200).

References

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