Congenital hepatic fibrosis associated with von Recklinghausen’s disease

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ABSTRACT

Congenital hepatic fibrosis is characterized by a ductal plate malformation with duct-like structures and fibrosis. It manifests clinically with portal hypertension and may be associated with multiple congenital defects. We present the case of a 16-year-old male with splenomegaly, leukopenia and thrombocytopenia, esophageal varices, and a histopathological diagnosis of congenital hepatic fibrosis. He exhibits “café au lait” spots and “Lisch” nodules, with a diagnosis of von Recklinghausen’s disease. Congenital hepatic fibrosis belongs to the so-called fibropolycystic diseases, in which there is a disordered interaction between cells and the extracellular matrix. von Recklinghausen’s disease affects tissues derived from the neural crest and its diagnosis is based on clinical criteria. It is associated with multiple diseases. We describe its association with congenital hepatic fibrosis for the first time.

Key words: Congenital hepatic fibrosis. Portal hypertension. von Recklinghausen’s disease.

INTRODUCTION

Congenital hepatic fibrosis (CHF) is an autosomal recessive disease that may be familial or sporadic (1). In CHF there is a malformation of the ductal plate, which is a circular embryonic structure appearing in the eighth week of gestation that is formed by primitive hepatocytes, which differentiate into cholangiocytes. The ductal plate surrounds the mesenchyme of portal tracts and, after a process of extensive involution and remodelling, intrahepatic bile ducts develop (2). As a consequence of this malformation, with persistence of abnormal portions and remodelling areas in the ductal plate, there are ductal-like structures of biliary origin and fibrosis that do not alter hepatic architecture. This fibrosis would affect venous resistance in portal branches, thus developing portal hypertension. There would also be abnormalities in intrahepatic portal branches with a reduction in size (3).

CHF clinically manifests during childhood and adolescence with hepatomegaly, splenomegaly, and signs of portal hypertension such as esophageal varices. It may be associated with congenital defects of the kidney (cystic dilatations of the distal tubules and collecting ducts), cerebellum (hemangiomas), lungs (emphysema), heart, vessels (aneurysms), or intestines (lymphangiectasia) (4).

We present its association with von Recklinghausen’s disease for the first time.

CASE REPORT

A 16-year-old boy with no personal or familial history of disease consulted for thrombocytopenia and a diagnosis of hepatic cirrhosis. At physical examination we saw multiple “café au lait” spots all over his trunk (1-7 cm in size) (Fig. 1) and marked splenomegaly. Laboratory findings: leukocytes 3,700/mm³; platelets 52,000/mm³; creatinine 0.76 mg/dl; urea 26 mg/dl; prothrombin time 100% (n.v. 70-110); AST 30 U/l (n.v. up to 40); ALT 48 U/l (n.v. up to 40); AP 174 U/l (n.v. up to 306); total bilirubin 1.20 mg/dl (n.v. up to 1); albumin 4.17 g/dl (n.v. 3.5-5); HBsAg (-); anti-HBc (-); Anti-HCV (-); ANA (-); AMA (-); ASMA (-); ceruloplasmin, alpha1-antitrypsin, percentage transferrin saturation, and total bile acids within normal values.
sonography: liver with multiple echogenic linear images (compatible with fibrosis) that circumscribe pseudonodular areas. Dilated portal vein (15 mm) and umbilical vein rechanneled with hepatofugal blood flow. Intrahepatic veins in the portal venous system were small and with a low flow. The gallbladder and bile ducts were normal. Marked homogeneous splenomegaly (19 cm). Kidneys were normal. No ascites.

Endoscopy: grade-I esophageal varices. Laparoscopy: liver with a nodular aspect and fibrous bands. Hepatic biopsy: areas of periportal fibrosis, with ductal-like structures of cuboidal epithelium, that circumscribe nodular areas without altering lobular architecture. There was no necrosis, cholestasis, or significant inflammation. Histopathological diagnosis: congenital hepatic fibrosis (Figs. 2-4). Ophthalmological examination: hamartomas (light brown pigmented neoformations, well circumscribed, 1-2 mm in diameter) in the anterior surface of the iris (Lisch nodules) characteristic of von Recklinghausen’s disease (Fig. 5). The patient evolves favorably with periodical medical follow-up.
During childhood and adolescence (19). This disease affects tissues derived from the neural crest. It is characterized by the presence of cutaneous pale yellow-brown macules or “café au lait” pigmented spots, usually rounded or ovoid with the major axis parallel to cutaneous nerves. Their color is due to a hyperpigmentation of epidermal basal cells (20). The presence of more than 5 of these spots with a diameter greater than 1.5 cm is pathognomonic for von Recklinghausen’s disease (19,21). Neurofibromas and ophthalmological alterations may also be seen, including optic nerve gliomas and iris hamartomas (Lisch nodules) (21,22).

The diagnosis of von Recklinghausen’s disease is based on clinical criteria (19). In our case it was based on the presence of “café au lait” spots and “Lisch” nodules. It may be associated with intracranial and spinal astrocytomas, gastrointestinal (and rarely hepatic) neurofibromas, neuroendocrine tumors (pheochromocytoma, gastrinoma, insulinoma, somatostatinoma), carcinoid tumors, pancreatic adenocarcinoma, melanoma, vascular dysplasia (stenosis of the renal artery), and ostearticular disorders (scoliosis, cysts, pseudoarthrosis) (19-21,23-26). We have found no description of its association with congenital hepatic fibrosis in the literature.

In von Recklinghausen’s disease there are alterations in the NF-1 gene coding for the neurofibromin protein, which acts as tumor suppressor through the regulation of Ras-MAPK, having a distinctive function during wound healing processes and vascular proliferation, and in the composition of myelin (19,27).

In conclusion, we believe that knowledge on the association between CHF and von Recklinghausen’s disease is relevant for a better diagnosis, treatment, and follow up of patients involved.

REFERENCES