OBSERVATIONS

Diabetic Hepatosclerosis Presenting With Severe Cholestasis

Diabetic hepatosclerosis (DH) is a novel entity that has recently been characterized by reviewing archived liver biopsies (1–3). Little is known about its clinical presentation.

A 37-year-old man was admitted to our hospital for nephrotic syndrome and a trophic ulcer in the left leg. He had been diagnosed with diabetes 12 years before and treated with insulin ever since. He had nephropathy, neuropathy, retinopathy, and arterial hypertension. There was no history of alcohol abuse. His parents were first-degree cousins, and early-onset diabetes with predominant microangiopathy was present in other family members. A brother had died of renal failure after lower-limb amputation.

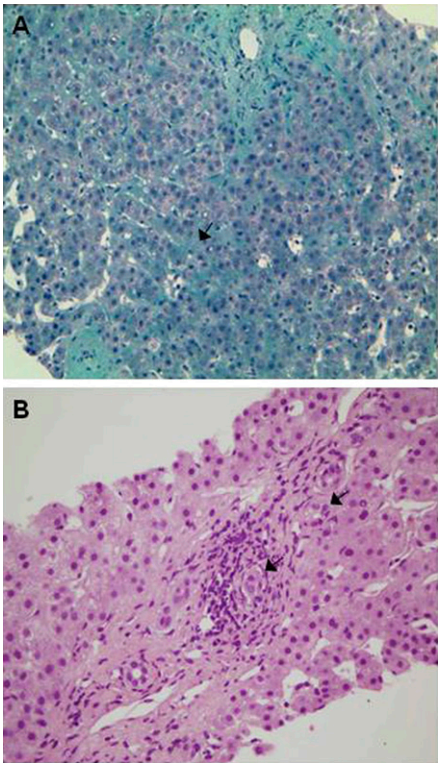

Figure 1—A: *Dense perisinusoidal fibrosis (green areas, as indicated by the arrow) revealed by Masson trichrome staining.* B: *Representative hematoxylin-eosin–stained section showing dysplastic-like modification of the biliary epithelium (arrows), indicative of ductal injury that was postulated to be secondary to acute ischemia. Neither ductular reaction nor ductopenia was observed. Pictures are at ×20 magnification.*

On admission, concentrations of alkaline phosphatase (ALP) and γ-glutamil transpeptidase were increased. Aminotransferases and bone ALP were normal.

Early during hospitalization, sepsis secondary to infection of the leg ulcer and renal failure cooccurred, reciprocally exacerbating one another. The situation rapidly deteriorated despite antibiotic and supportive therapy, requiring hemodialysis first and then amputation of the infected limb. In parallel, cholestasis also worsened: The patient became jaundiced and bilirubin rose up to 441.2 μmol/L, direct bilirubin being 377.9 μmol/L. This trend was not modified by hemodialysis. Therefore, once clinical stability was achieved we studied the hepatobiliary system. Serology for major hepatitis viruses, liver disease–associated autoantibodies, and tumor markers was negative. Blood tests were not suggestive of inherited liver disorders. Ultrasonography and computed tomography did not show any lesion or anatomical anomaly.

A liver biopsy was then performed. Histological examination revealed dense perisinusoidal fibrosis (Fig. 1*A*) and concentric hyaline thickening of the hepatic arterioles. Signs of ductal injury were also noted (Fig. 1*B*). There was no steatosis, necroinflammatory activity, granulomatous infiltration, or copper-associated protein deposition.

Hepatic sinusoids normally lack a true basement membrane (4). In 2006, Harrison et al. (1) described a noncirrhotic form of perisinusoidal fibrosis with basement membrane formation in a series of liver biopsies from diabetic patients and termed it DH. Their observations were subsequently expanded by two autopsy studies (2,3). DH most often occurs in subjects with long-lasting type 1 or 2 diabetes and microvascular disease in other organs, especially the kidney, and has been proposed to represent the hepatic manifestation of diabetic microangiopathy (1–4). It is often associated with hyaline arteriolosclerosis, while, by definition, typical features of nonalcoholic steatohepatitis or alcoholic hepatopathy are absent.

As the entire body of knowledge about DH is based on histological data, the clinical relevance is unclear. Consistent with the elevation of ALP frequently found in the medical records of cases initially identified in liver biopsies (1–3), we report that DH may present with full-blown cholestasis. This latter may be secondary to mechanical compression or ischemia of the biliary ducts caused by perisinusoidal fibrosis.

The family history of our patient raises the question of whether genetic factors may contribute to the pathogenesis of DH. Unfortunately, we could not obtain information about the presence of liver disease among relatives or perform genetic testing because consent was refused.

Although rare, DH should be taken into account in the differential diagnosis of cholestasis in diabetes.

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E.N. cared for the patient. F.G. and T.C. reviewed the histological sections and made the diagnosis of DH. A.P., D.F., and G.M. provided clinical input and reviewed and edited the manuscript. P.A. provided clinical input and wrote the manuscript. P.A. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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