

CLINICAL NOTE

Hepatoportal sclerosis clinical different evolutionary stages: presentation of 3 cases and literature review

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ABSTRACT

Hepatoportal sclerosis (HPS) is characterized by presinusoidal intrahepatic portal hypertension associated with splenomegaly and anemia in patients with non-cirrhotic liver. Liver biopsy is essential, especially to rule out other processes. Being a disease of unknown etiology, the majority of cases have been described in eastern countries. However, it may be an underdiagnosed disease in the West. Symptoms are related to portal hypertension and the clinical spectrum is wide, ranging from anemia with normal liver function tests to bleeding due to esophageal varices. Treatment is directed to the complications and the prognosis is better than in patients with cirrhosis.

We report three cases of HPS presenting at different clinical stages and the findings of liver biopsies, the clinical outcomes and a review of scientific literature.

Key words: Esclerosis hepatoportal. Hipertensión portal idiopática. Enfermedad de Banti.

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INTRODUCTION

Guido Banti, in the late nineteenth century, described a pattern of anemia, gastrointestinal bleeding and marked

splenomegaly (1). Presently Banti syndrome is related to all disorders with portal hypertension and hepatic venous injury without cirrhosis. Over the years other names have been used to refer to this syndrome: idiopathic portal hypertension in Japan, non-cirrhotic portal fibrosis in India, non-cirrhotic intrahepatic portal hypertension, presinusoidal idiopathic portal hypertension, etc. (2).

Hepatoportal sclerosis (HPS) is one of the most common forms of Banti syndrome studied. The term was introduced by Mikkelsen in the sixties to refer to a pattern of non-cirrhotic portal hypertension associated with splenomegaly and anemia (3).

We present three cases of HPS at different clinical stages.

CASES REPORT

Case 1

This is a 60 year old man with a past history of antrectomy and Roux en Y gastrojejunostomy for duodenal ulcer bleeding five years earlier. Four years ago, the patient was referred to our hospital due to abdominal distension. Radiological examinations such as abdominal ultrasound showed the presence of ascites, splenomegaly and a large smooth liver without stigmata of chronic liver disease (Fig. 1A and 1B). The patient denied alcohol intake. Thus, metabolic, autoimmune and viral hepatitis were ruled out. Transjugular liver biopsy was performed and the pathological biopsy specimen showed fibrous septa, preserved hepatocyte architecture, dilated and / or herniated portal veins in the lobule, while in some portal tracts there were no noticeable veins. All these changes were consistent with a portal venous sclerosis type vascular pathology (Fig. 2A and 2B). Catheterization was performed by calculating a hepatic venous pressure gradient (HVPG) of 5 mmHg, free hepatic venous pressure (FHVP) of 5 mmHg and wedged hepatic venous pressure (WHVP) of 10 mmHg.

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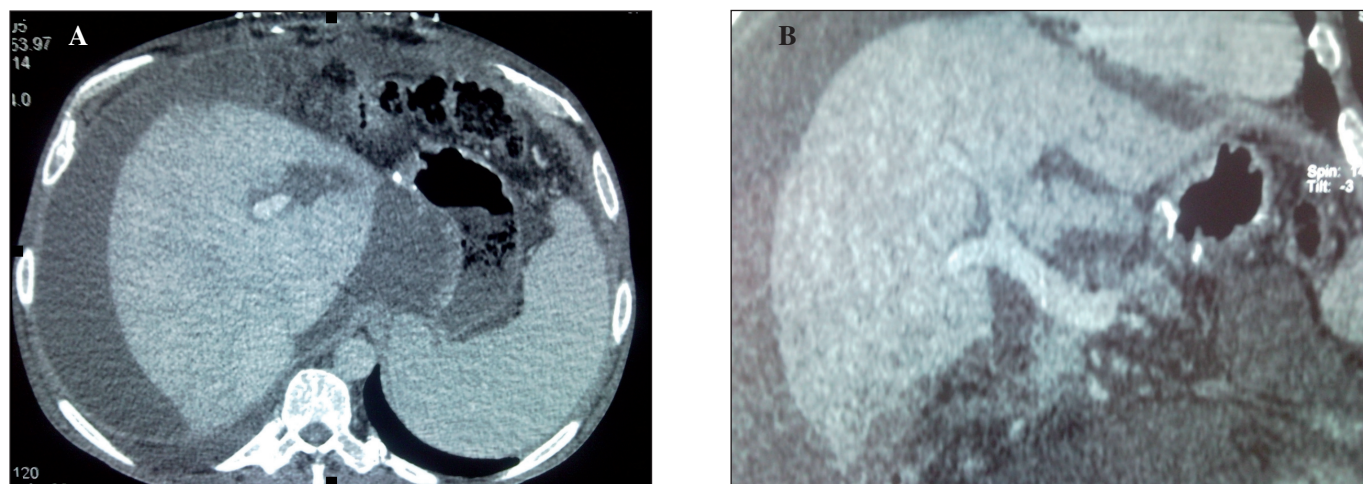


Fig. 1. A. Abdominal CT scan: right pleural effusion, ascites, hepatosplenomegaly. B. Abdominal CT: permeable portal vein.

The patient remained stable during the following years and an episode of bleeding from large esophageal varices was resolved by endoscopic treatment and vasoactive drugs. A month later the patient was readmitted for hepatic encephalopathy and was put on the waiting list for liver transplantation. However, the patient died few weeks later, after presenting another episode of acute gastrointestinal bleeding and developing hepatorenal syndrome type 1.

Case 2

A 42 year old male, with no relevant past history, was studied due to 9 year hypertransaminasemia (AST 207 mU/mL, AST 220 mU/mL) (Table I). Viral serology, study of autoimmune and metabolic liver diseases were negative. Several radiological examinations over the years were performed (abdominal ultrasonography and MRI cholangiography) showing only a progressive enlargement of the spleen with incipient signs of portal hypertension. There were no remarkable signs of portal hypertension in endoscopy. Finally, liver biopsy reported a normal liver parenchyma and presence of venous dilatation in the portal space with sclerosis, elastosis and absence of bile duct in large spaces. These changes were compatible with hepatoportal sclerosis (Fig. 2C). The patient was treated with ursodeoxycholic acid and transaminase levels normalized.

Case 3

This is a 49 year old man with no relevant past history where hypertransaminasemia was incidentally detected (GOT 79 mU/mL, AST 160 mU/mL). After negative viral serology, autoimmune and metabolic liver diseases, coinciding with a cholecystectomy, liver biopsy was performed which showed nodular cirrhotic liver and portal vein scler-

osis (Fig. 2D). The patient has remained asymptomatic with normal abdominal ultrasound, gastroscopy and MRI cholangiography.

DISCUSSION

The etiology of the HPS is unknown. Several theories have been proposed trying to explain how the disease progresses, although none has proven to be the cause (4). It has been suggested that chronic or recurrent infections of the digestive tract may trigger portal inflammation. It has also been proposed that exposure to certain toxics such as arsenic, vinyl chloride and drugs such as azathioprine, methotrexate and 6-mercaptopurine could be involved (4). Other studies suggest an autoimmune etiology of this condition since a higher incidence has been noticed in patients with connective tissue diseases. Recently, it has been described the association with celiac disease and a decrease of portal hypertension after introducing a gluten free diet (5). Another hypothesis is that undetectable microthrombosis in the intrahepatic portal vein branches may cause periportal fibrosis, suggesting an association to a genetic

Table I. Analytical features

	Case 1	Case 2	Case 3
GOT (U/L)	60	207	79
GPT (U/L)	24	220	160
GGT (U/L)	31	76	117
Alkaline phosphatase (U/L)	167	295	138
Total bilirubin (mg/dL)	3.2	0.7	0.5
INR	1.6	1.0	1.1
Platelets (10 ³ /μL)	178,000	203,000	217,000

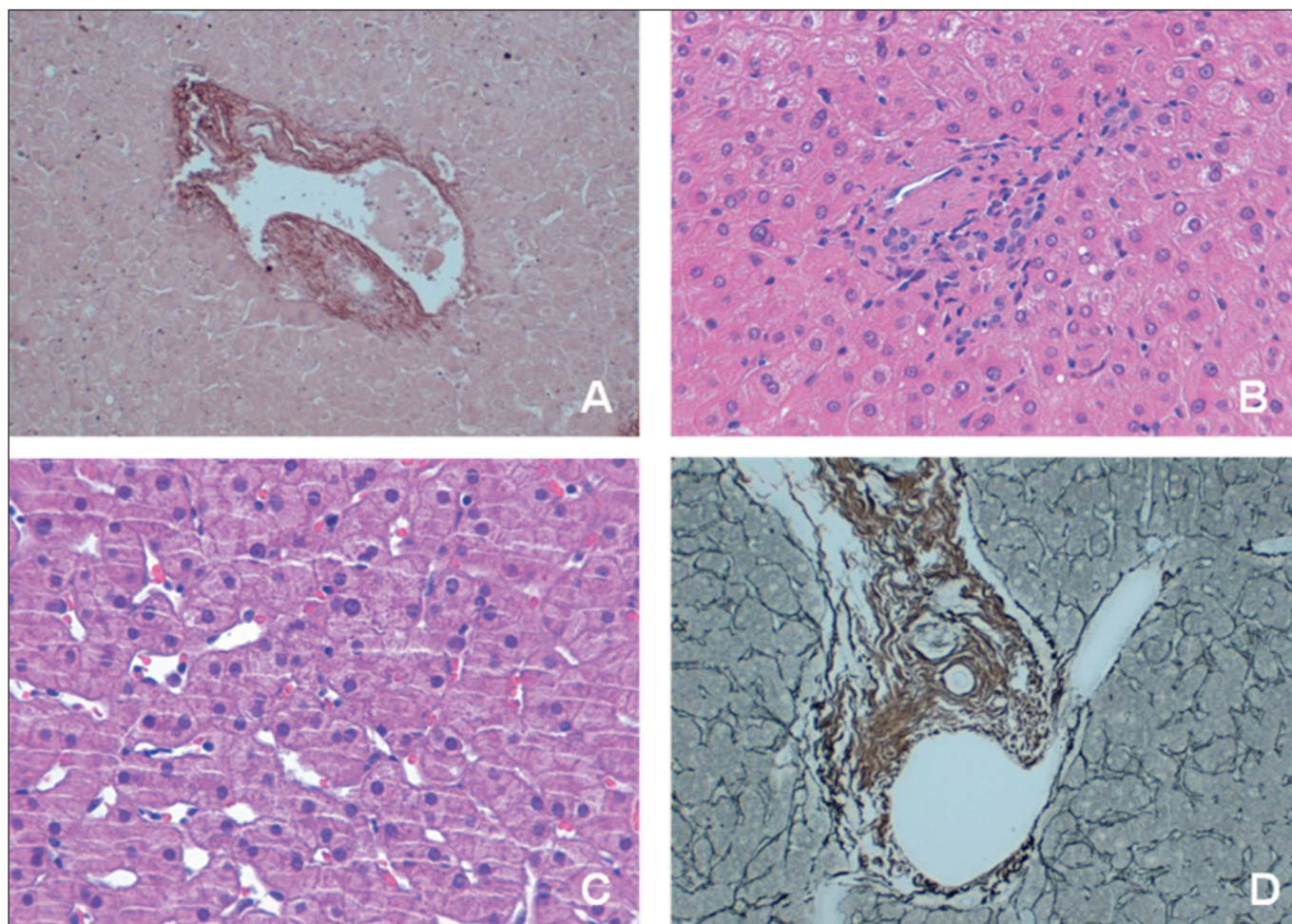


Fig. 2. A. Fibrous protrusion in the lumen of the portal venule (Shikata, 10x). B. Malformation of the vein in a "slot" shape due to portal sclerosis (HE, 20x). C. Detailed image of megasinusoids (HE, 40x). D. Herniation of the portal venule hepatocyte parenchyma (reticuline, 10x).

or acquired thrombophilic disorder (4). Finally, a multifactorial origin has been raised which associates all the theories described.

The vast majority of cases of HPS have been described in eastern countries, especially India and Japan, but many cases have been detected worldwide. It is believed that in the West this disease is underdiagnosed because of it is extremely rare. Being the main reason for this a low index of suspicion and the need for multiple tests, including liver biopsy, none of which can give an accurate diagnosis (1). It is possible that at early stages of the disease the only clinical sign is a slight elevation of transaminases, as in two of our patients.

According to a couple of series with more cases reported, the HPS is slightly more common in females, predominantly in the third and fourth decade of life (6,7). Our three patients were male, white, natives of Spain and in the middle ages. Clinically, symptoms related to portal hypertension: pancytopenia, bleeding esophageal varices or hypertensive gastroenteropathy and splenomegaly are predominant. Ascites and hepatic encephalopathy are rarely

seen. Anemia is the most common laboratory finding, liver function tests are usually normal or slightly elevated, with scarce modification with the progression of the disease. Its association with hepatic tumors is uncommon (8).

One of our patients met the clinical criteria and, having ruled out most diseases commonly associated with portal hypertension, it was decided to perform a liver biopsy which provided the diagnosis of HPS. However, these patients are usually asymptomatic with an elevation of transaminases as in two of our patients. Therefore, in cases of unknown cause elevation of transaminases only liver biopsy could confirm the diagnosis of HPS.

For the diagnosis of HPS we use the criteria by the Japan Committee for the Study of Idiopathic Portal Hypertension (Table II).

The hemodynamic pattern of the HPS is characterized by presinusoidal intrahepatic portal hypertension with notorious elevations of hepatic portal pressure and normal or slightly elevated wedged hepatic venous portography, with a consequent normal hepatic venous pressure gradient.

Liver biopsy is essential, especially to rule out other processes, despite being invasive and not providing a definite information. Detected lesions can be heterogeneous and it is frequent to get a normal tissue sample, especially at early stages. Different degrees of fibrosis, portal or periportal thickening, with intimal sclerosis and thrombosis of small intrahepatic portal branches can be found. All these determine sinusoidal dilatation and aberrant neovascularisation, sometimes with herniation of portal veins (4). Lack of cirrhosis, necrosis or inflammatory phenomena is characteristic.

In recent years endoscopic treatment (sclerotherapy or band ligation) associated with vasoactive drugs has been used to control acute variceal bleeding with an efficiency close to 95% and has replaced the bypass surgery as the treatment of choice. Procedures such as transjugular intrahepatic portosystemic shunt and splenic embolization have also been used with good results (9). In case of significant hypersplenism, splenectomy would be indicated. No studies have been published to date regarding treatment with ursodeoxycholic acid (UDCA). Empirical treatment with UDCA was started in one of our patients achieving normalization of transaminases, however, no pathophysiological explanation could explain the response to treatment. Liver transplantation is a therapeutic option in those few patients who progress to liver failure (10), with good results. Most liver transplantations performed in the West for this disease have been performed with a preoperative diagnosis of cryptogenic cirrhosis.

The prognosis of these patients is better than those with portal hypertension associated with cirrhosis, depending on the duration of the disease being worse when it diagnosed in youth. After ten years of follow up, survival is 90% and mortality is mostly associated with esophageal variceal bleeding (1).

In conclusion, HPS can occur at different clinical stages from a slight elevation of transaminases with ultrasonographic data with or without portal hypertension to its most advanced complications similar to those of liver cirrhosis. In patients with elevated transaminases of unknown etiology HPS is a diagnostic possibility where only liver biopsy can help to confirm diagnosis.

Table II. Criteria of the Study Japanese Idiopathic Portal Hypertension (modified from reference 9)

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- a) Definite presence of portal hypertension (defined by the presence of esophageal varices)
 - b) Absence of cirrhosis
 - c) Permeable hepatic veins with normal or minimally elevated hepatic venous pressure gradient
 - d) Permeable extrahepatic portal vein
 - e) Normal or almost normal liver function tests
 - f) Reduction of one or more series of blood cells counts
 - g) Portal fibrosis with no diffuse nodule formation
 - h) Demonstrated notorious elevation of portal pressure
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