ANNALS OF GASTROENTEROLOGY 2008, 21(2):130-134

Case report

Idiopathic portal hypertension in a twin treated with TIPS and consequent splenectomy

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SUMMARY

Background: Idiopathic portal hypertension is a disorder of unknown aetiology characterized by portal hypertension secondary to splenomegaly, without cirrhosis. There are no reports on idiopathic portal hypertension occurring in twins. Variceal haemorrhage, a life threatening manifestation of portal hypertension may be treated with transjugular intrahepatic portosystemic shunt in the acute setting. Case presentation: A 36-year-old woman with severe variceal haemorrhage and ascites due to idiopathic portal hypertension was admitted to the Gastroenterology Department. Her twin sister underwent a splenectomy at the age of 12 due to splenomegaly and haemolytic episodes without further complications. The patient, like her twin sister, had also a history of splenomegaly since her childhood, with haemolytic episodes and need for multiple transfusions. Splenectomy was not preferred for her. In the following years, blood group incompatibilities developed after multiple transfusions that precluded any further blood transfusions. A β-thalassemia trait was also present. At admission, because of active variceal haemorrhage we performed a transjugular intrahepatic portosystemic shunt (TIPS) in an emergency setting. A decline of the portosystemic pressure gradient from 26 to 12 mmHg resulted with no further bleeding and with a subsequent reduction of the spleen size from 35 cm to 20 cm in diameter. A transjugular liver biopsy, a few months after TIPS, revealed a mild chronic hepatitis that was attributed to hepatitis C virus infection acquired from transfusions before 1990. A splenectomy was performed and the haematological parameters improved significantly. Despite TIPS obstruction that occurred later, no further oesophageal varices developed, and there was no need for further transfusions. Conclusions: In this patient, idiopathic portal hypertension may have had splenomegaly possibly related to haemolytic episodes as an initial cause, whereas later increased portal vascular resistance developed. In her twin sister, who also had splenomegaly at childhood, there was no development to portal hypertension due to an early splenectomy. Emergency treatment of the portal hypertension with TIPS, followed by a later surgical splenectomy was an effective management option for a follow up period of six years.

Key words: idiopathic portal hypertension, transjugular intrahepatic portosystemic shunt, splenomegaly, splenectomy, thalassemia, twins

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BACKGROUND

Idiopathic portal hypertension (IPH) is a clinical disorder of unknown cause, typically associated with splenomegaly and anemia, without cirrhosis. This entity was initially named Banti's syndrome[1] and later when a more precise definition was available, idiopathic portal hyper-

Abbreviations:

IPH=Idiopathic portal hypertension
TIPS=Transjugular intrahepatic portosystematic shunt
ANA=Antinuclear antibodies
AMA=Anti-mitochondria antibodies
SMA=Smooth muscle antibodies
EBV=Epstein-Barr virus
CMV=cytomegalovirus
HCV=Hepatitis-C virus

tension or hepatoportal sclerosis in the West and noncirrhotic portal fibrosis in Asia.[2] Its clinical course is clearly milder than that of cirrhosis related portal hypertension.[3] Multiple aetiologies may cause IPH, and nearly half of the cases are idiopathic.[4] Hypercoagulability has been proposed as an important cofactor.[5] Increased portal venous flow, partly as a result of increased splenic venous flow secondary to splenomegaly of an undetermined process has been considered as the main contributor to portal hypertension. In some patients, possibly later in the course of the disease, an increased portal vascular resistance plays an important role.[6] In patients with IPH variceal pressure is a strong predictor of variceal haemorrhage, although the risk of bleeding is less than in cirrhotics with the same level of variceal pressure.[7] Transjugular intrahepatic portosystemic shunt (TIPS) is mostly performed for the treatment of variceal bleeding and refractory ascites.[8] TIPS for active bleeding in patients with IPH is indicated with or without partial splenic embolisation.[9]

We present a case of a young woman with IPH treated successfully with TIPS and subsequent splenectomy.

CASE PRESENTATION

A 32-year-old female Greek patient was admitted to the Department of Gastroenterology in 1998 with severe bleeding from oesophageal varices.

At the age of 11, she had splenomegaly with repeated haemolytic episodes and was treated with steroids. At that time, a heterozygous thalassemia was diagnosed. Her twin sister, with a thalassemia trait too, presented with the same clinical picture and a splenectomy was performed at the age of 12. She has been well ever after.

At the age of 20, four units of blood during a caesarean operation were transfused to the patient, after which she developed an acute Coombs positive haemolytic episode, successfully treated with steroids. G-6-PD tested after a few months was normal. At the age of 23, during her second pregnancy, she received five units of blood and again an acute Coombs positive haemolytic crisis developed. The pregnancy was terminated. During the haematological work up that followed, ultrasonography showed splenomegaly, hepatomegaly and a dilated portal vein. Haemoglobin electrophoresis disclosed HbA2 5.7%, Ham test negative, reticulocytes 4%. Antinuclear antibodies (ANA), anti-DNA antibodies and anti-mitochondria antibodies (AMA) were negative while smooth muscle antibodies (SMA) were positive at low titer. The diagnosis was intermediate β-thalassemia and isoimmunisation.

On admittance she had haematemesis and melaena. Ascites was present. Laboratory tests were as follows: Hb 5.9 g/dl, Ht 17%, White cell count 2500/mm^3 (neutrophils 71%, lymphocytes 22%), platelet count 82000/mm^3, The following tests were normal: urea nitrogen, creatinine, glucose, bilirubin, aspartate and alanine aminotransferases, alkaline phosphatase, lactate dehydrogenase, albumin and total protein, C_3, C_4. Ferritin was 71 ng/ml, serum iron was 13 μg/dl, C-reacting protein 7 mg/dl (normal up to 0.8 ng/dl), anti-HCV positive, HbsAg negative, anti HBs positive, anti EBV and anti CMV negative. On endoscopy oesophageal varices grade III with cherry red spots were found. An upper abdominal ultrasound examination revealed splenomegaly (spleen length 35 cm) with calcifications of the spleen and dilated splenic and portal veins. The portal vein diameter was 20 mm. No transfusions were possible due to multiple incompatibilities.

A transjugular intrahepatic portosystemic shunt (TIPS) was performed for an immediate decompression of the portal system. After catheterisation, a portal vein dilatation was found (Fig. 1) with a portal pressure of 30 mm Hg and a right atrium pressure of 4 mmHg. A 4 cm-long Strecker stent of 10 mm diameter was placed, but was placed too proximal, so that a second one of 6 cm length was needed (Meditech, Boston Scientific, Watertown, MA, USA)(Fig. 2). The portal pressure immediately decreased to 17 mm Hg while the right atrium pressure was 5 mmHg. The patient recovered well. One month after TIPS the size of the oesophageal varices was reduced from grade III to grade

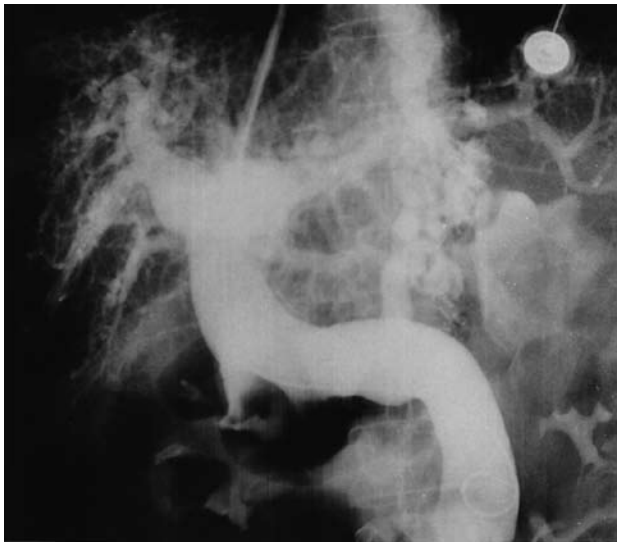

Figure1. Direct portography after intrahepatic puncture reveals dilated and distorted portal and splenic veins. Large oesophageal varices through the coronary vein are also seen.

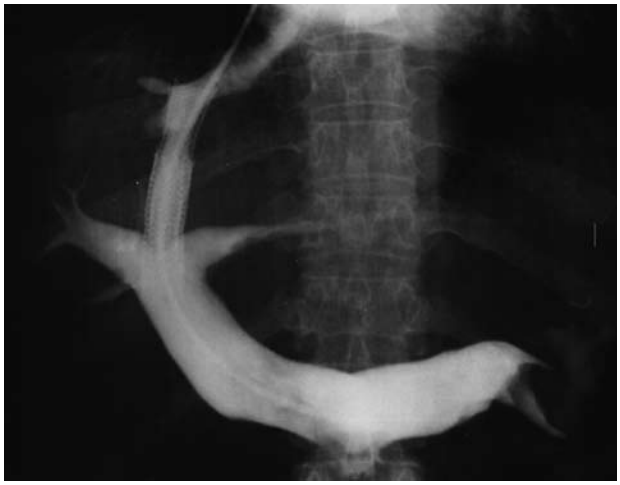

Figure 2. After placement of two metallic stents, the portosystemic shunt is obtained. In this control portography, one week after TIPS, no varices are opacified. Notice the horizontalization of the splenic vein due to decreased size of the spleen.

I. A transjugular liver biopsy was performed at this time showing signs of a mild chronic hepatitis, with a slight enlargement of portal tracts and scanty periportal hepatitis with a mild increase of the fibrous connective tissue forming thin septa within liver lobules. Bile duct proliferation was evident in several portal tracts. These findings were attributed to the HCV infection. No increase of the peribiliary vascular plexus was noted. On upper abdominal ultrasound the size of the spleen was reduced from 35 cm to 20 cm maximal diameter. Six months after TIPS her haematocrit remained low at 20%. One year after TIPS a surgical splenectomy was performed. The WBC returned to normal and platelet count rose to 1.100.000 immediately after splenectomy. Six months after splenectomy the stent was patent, the haematocrit gradually rose to 36% and the platelet count was 680.000/μl. One year after splenectomy TIPS was thrombosed but oesophageal varices did not recur. Six years after the initial TIPS placement, she remains well, with normal haematocrit and platelet count.

CONCLUSIONS

The clinical course of our patient was characterized by splenomegaly, intermediate β-thalassemia, and a haemolytic syndrome presented at childhood, for which steroids were given. Her twin sister with the same manifestations at childhood was treated by splenectomy at childhood and remained well since then. Through the different therapeutic management of the same condition of the twin sisters, an experimental setting was created that was ideal for the long-term assessment of the two therapeutic approaches. In retrospect, it is clear that the clinical course of our patient and the final manifestation of IPH would have been different had she undergone the splenectomy at an early age like her twin sister did.

The question of whether IPH is in any case connected to the thalassemia trait still remains. However, intermediate β-thalassemia is a very common condition in Greece whereas IPH is an exceptional rarity. Splenomegaly is a common feature both for thalassemia and IPH, but the size of the patient's spleen was quite disproportionate to the rather moderate splenomegaly seen in intermediate thalassemia. Therefore a direct connection of the two diseases is unlikely. However, we think that splenomegaly was the initial condition that in the long term had led to portal hypertension. Indeed, the spleen may play a primary role in the pathogenesis of IPH, at least in some patients: splenomegaly of an undetermined aetiology may secondarily increase splenic venous flow, and portal venous flow leading to an initial elevation of the portal pressure and later to increased portal vascular resistance.[6]

SMA were positive in our patient. A large survey by questionnaire of IPH in Japan disclosed that 12% of 160 cases were associated with one or two autoimmune diseases [10]. In another study from Japan a disturbance of the antigen-presenting ability of non-T cells was observed. [11] A woman with IPH has been reported with associated autoimmune thyroiditis.[12] However we believe that HCV infection present in our patient due to blood transfusions before 1990 is probably responsible for the presence of SMA, a common association according to previous reports.[13,14] Alternatively an immunological disturbance or chronic antigenic stimulation that may be related to the pathogenesis of IPH cannot be excluded.

The liver biopsy findings of this patient consisted of only mild changes of portal tract enlargement due to connective tissue increase with thin septa formation and mild inflammatory infiltrations, as well as bile duct proliferation. These histological findings differ from those described by Levison et al[15] since there was no irregular capsular thickening, or distortion of lobular architecture. However, they do share common features like enlarged portal tracts and radiating fine fibrous septa. Bile duct proliferation observed in our patient is one of the main parameters claimed to distinguish between IPH of the West and noncirrhotic portal fibrosis of the Indian subcontinent, occurring in more than one third of patients in the last condition.[16] The hepatic arterial lumen was not increased, a feature of IPH which differentiates this condition from alcoholic fibrosis and cirrhosis, as described recently [17] Our findings differed from those described in Japanese

patients where incomplete septal cirrhosis as a late manifestation of IPH was the main finding.[18] The timing of the liver biopsy it should however be kept in mind which coincided with the marked recession of the portal hypertension and the concomitant HCV infection.

Since its first clinical application in 1989, TIPS is mainly performed for the treatment of variceal bleeding and refractory ascites in patients with portal hypertension.[8,19,20] In patients with IPH TIPS, partial splenic embolization and percutaneous transhepatic obliteration represent the main interventional radiological alternatives for treatment. In a study of five patients with IPH, good midterm results with oesophageal and gastric varices obliteration were reported using partial splenic embolisation with only one patient reported to have a TIPS procedure.[9] Same good results at a 28-month follow up were reported with partial splenic embolisation in a recent case series of six patients.[21] In our patient TIPS performed after the first severe bleeding episode of oesophageal varices resulted in an immediate decrease of the portosystemic gradient from 26 to 12 mmHg, with an impressive improvement of ascites and varices. This improvement made a surgical intervention for the removal of the spleen possible, resulting in a definite amelioration of the haematological picture.

In conclusion, idiopathic portal hypertension in our patient had probably splenomegaly as an initial cause, whereas later increased portal vascular resistance developed. This development to IPH was restrained in her twin sister as a result of an early splenectomy at childhood. Emergency treatment of the portal hypertension with TIPS, followed by surgical splenectomy later was effective during a follow up period of six years.

ACKNOWLEDGEMENT

Written consent was obtained from the patient and her twin sister for publication of the study.

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