From the Editor's Desk

Spectrum of Idiopathic Noncirrhotic Portal Hypertension

Liver cirrhosis is the most frequent cause of portal hypertension both in the Western and Eastern world.[1–3] However, portal hypertension may develop in the absence of liver cirrhosis. This condition is known as noncirrhotic portal hypertension (NCPH), which is further classified as prehepatic, hepatic, and posthepatic portal hypertension based on the site of resistance to blood flow.[2,3] Schouten et al[2] suggested that the diagnosis of idiopathic noncirrhotic portal hypertension (INCPH) can be made if liver cirrhosis and common causes of NCPH can be reliably ruled out. They have suggested that in future studies, the term INCPH should be used, as it covers both the clinical and etiological aspects of the disorder. Agreement on uniform nomenclature is an essential requirement for collaborative studies and should be considered a welcome step in the right direction.

In the Indian subcontinent, this condition is known as noncirrhotic portal fibrosis (NCPF).[1,3] This has been reported from different parts of the world under a variety of names, like idiopathic portal hypertension (IPH), hepatoportal sclerosis, and noncirrhotic intrahepatic portal hypertension, etc.

In India, NCPF (INCPH) formed an important group of patients with portal hypertension, and accounted for 23.3% of all such patients in 80s.[1] However, its incidence has considerably decreased over time and accounted for only 5.6% of all cases of portal hypertension.[1] Hence, it is now believed to be a vanishing disease in the subcontinent.[1] Improvement in sanitary conditions and decrease in bacterial infections has lead to a decline in the incidence of the disease. Similar drop in the incidence of new cases has been reported from Japan and other countries.[1,4]

The majority of INCPH patients initially present with signs or complications of portal hypertension, such as, well-tolerated variceal bleeding. A long-term follow-up study of 59 patients with INCPH in one hospital over 30-year period showed a 5-year survival of 90% and a 30-year survival of 55%.[5] Two recent studies suggest that spectrum of clinical presentation could be more heterogeneous, i.e., clinically significant portal hypertension may be lacking or a small proportion of patients may present with the complications of portal hypertension which are sufficiently severe to warrant liver transplantation (Figure 1).[6,7]

The histological hallmark of NCPF (INCPH) is termed obliterative portal venopathy (OPV) by Nayak and Ramalingaswami and includes sclerosis and obliteration of small branches of portal veins.[8] Later, Kameda described the similar findings in Japanese patients.[9] OPV predominates in medium-sized and preterminal veins (0.2–3 mm in diameter) which are easily accessible on liver biopsies.[6] Cazals-Hatem et al[6] assessed the clinical and histological features at presentation, the associated disorders, and the outcome of patients in whom a diagnosis of OPV was obtained via biopsy. Fifty-nine consecutive patients with OPV were retrospectively selected on strict histological criteria. Mean age of these patients at diagnosis was 38.5 years. Initial presentation was portal hypertension (64% of patients) and/or extrahepatic portal vein thrombosis (EHPVT) (22%) or isolated abnormal laboratory tests (20%). A clinically significant portal hypertension was present in 38 patients (64%) and absent in 21 patients (36%). EHPVT was present in 13 patients (22%) at diagnosis. During follow-up (median 8.6 years, range 1–23 years), features of portal hypertension worsened in nearly half of the patients; EHPVT and portal hypertension were finally found in 44% and 88% of patients indicating progression of the liver disease. Severe complications, such as, liver transplantation and/or death occurred in 11 (19%) patients. This is the first study that demonstrated that portal hypertension may be absent in 25% of the patients having OPV on liver histology; these patients also did not have EHPVT. This study has further conclusively demonstrated that deterioration or occurrence of portal hypertension occurs in nearly half of the patients during follow-up; the clinical course of the disease was severe in 19% of patients leading to transplantation or death. The fact that 25% of patients in this study initially presented without evidence for portal hypertension was also unusual compared to previous data on NCPH.[9–11] Many patients underwent a liver biopsy for slight-to-moderate liver test alterations and the diagnosis of OPV occurred by chance.

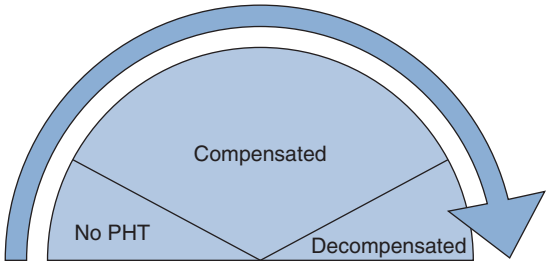

Figure 1 Spectrum of idiopathic noncirrhotic portal hypertension. PHT: portal hypertension.

doi: 10.1016/S0973-6883(11)60122-9

On the other end of the spectrum of INCPH, the patients do behave like end-stage liver disease and develop features of decompensation in the form of ascites, jaundice, or hepatic encephalopathy. In these patients the complications of portal hypertension are sufficiently severe to warrant liver transplantation.[12–17] In a recent study, Saigal et al[7] have demonstrated that small fraction of patients with NCPF (INCPH) (~5%) do develop ascites, jaundice, and hepatic encephalopathy making it difficult to differentiate it from cirrhosis of liver. The diagnosis of NCPF (INCPH) was missed prior to the liver transplant and had a pre-transplant diagnosis of cirrhosis of unknown or some known etiology. The indication for transplant was primarily based on complications of portal hypertension because majority of these patients had low MELD score. The explants livers showed OPV and portal to portal fibrosis. The authors suggested that NCPF (INCPH) should be suspected in cases of chronic liver disease with negative etiological work-up, relatively preserved liver functions and a low MELD score. The authors also reported an overlap NCPF group which has features of both NCPF and cirrhosis and was not reported earlier. This was seen in 10 patients in which cause of chronic liver disease was hepatitis C in 5, hepatitis B in 1 and nonalcoholic fatty liver disease in 4 patients. All 10 patients in this group also had characteristic OPV. This may be in continuum with the spectrum of NCPF (INCPH) not defined earlier. The existence of 2 diseases in a single patient may portend a poor prognosis as progression to end-stage liver disease may be faster.

These 2 interesting studies completes the spectrum on INCPH.[6,7] While the one end is represented by changes of OPV on liver biopsy without clinically significant portal hypertension, the other end is represented by end-stage liver disease with complications of portal hypertension necessitating liver transplantation in these patients.

REFERENCES

1. Sarin SK, Kumar A, Chawla YK, et al. Noncirrhotic portal fibrosis/idiopathic portal hypertension: APASL recommendations for diagnosis and treatment. *Hepatol Int* 2007;1:398–413.
2. Schouten JN, Garcia-Pagan JC, Valla DC, Janssen HL. Idiopathic noncirrhotic portal hypertension. *Hepatology* 2011 May 13. doi: 10.1002/hep.24422.
3. Rajekar H, Vasishta RK, Chawla YK, Dhiman RK. Noncirrhotic portal hypertension. *J Clin Exp Hepatol* 2011;1:94–108.
4. Imai F, Kuga K, Komaba M, et al. Interim report on IPH survey. In: *Report of the Research Committee on Aberrant Portal Hemodynamics* 1992, Futagawa S, ed. Tokyo: Ministry of Health and Welfare 1993:107–10.
5. Kingham JG, Levison DA, Stansfeld AG, Dawson AM. Noncirrhotic intrahepatic portal hypertension: a long term follow-up study. *QJ Med* 1981;50:259–68.
6. Cazals-Hatem D, Hillaire S, Rudler M, et al. Obliterative portal venopathy: portal hypertension is not always present at diagnosis. *J Hepatol* 2011;54:455–61.
7. Saigal S, Nayak NC, Jain D, et al. Noncirrhotic portal fibrosis-related end-stage liver disease in adults: evaluation from a study on living donor liver transplant recipients. *Hepatol Int* 2011 Jan 12. [Epub ahead of print]
8. Nayak NC, Ramalingaswami V. Obliterative portal venopathy of the liver. Associated with so-called idiopathic portal hypertension or tropical splenomegaly. *Arch Pathol* 1969;87:359–69.
9. Kameda H. Obliterative portal venopathy: a comparison study of 184 cases of extrahepatic portal obstruction and 469 cases of idiopathic portal hypertension. *J Gastroenterol Hepatol* 1986;1:139–49.
10. Dhiman RK, Chawla Y, Vasishta RK, et al. Noncirrhotic portal fibrosis: experience with 151 patients and a review of the literature. *J Gastroenterol Hepatol* 2002;17:1–11.
11. Hillaire S, Bonte E, Denninger MH, et al. Idiopathic noncirrhotic intrahepatic portal hypertension in the West: a re-evaluation in 28 patients. *Gut* 2002;51:275–80.
12. Bernard PH, Le Bail B, Cransac M, et al. Progression from idiopathic portal hypertension to incomplete septal cirrhosis with liver failure requiring liver transplantation. *J Hepatol* 1995;22:495–9.
13. Elariny HA, Mizrahi SS, Hayes DH, Boudreaux JP, Hussey JL, Farr GH Jr. Nodular regenerative hyperplasia: a controversial indication for orthotopic liver transplantation. *Transpl Int* 1994;7:309–13.
14. Radomski JS, Chojnacki KA, Moritz MJ, et al. Results of liver transplantation for nodular regenerative hyperplasia. *Am Surg* 2000;66:1067–70.
15. Loinaz C, Colina F, Musella M, et al. Orthotopic liver transplantation in 4 patients with portal hypertension and non-cirrhotic nodular liver. *Hepatogastroenterology* 1998;45:1787–94.
16. Dumortier J, Bizollon T, Scoazec JY, et al. Orthotopic liver transplantation for idiopathic portal hypertension: indications and outcome. *Scand J Gastroenterol* 2001;36:417–22.
17. Blanc JF, Bernard PH, Le Bail B, et al. Vascular pathology of the portal vein distal branches: a rare cause of liver transplantation and a protean clinical presentation [in French]. *Gastroenterol Clin Biol* 2000;24:667–70.

Radha K Dhiman MD DM FAMS FACG
Department of Hepatology,
Postgraduate Institute of Medical Education and Research, Chandigarh – 160012, India