Non-cirrhotic portal hypertension — a new entity in South Africa?

A report of 6 cases

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Summary

Six patients with portal hypertension and well-preserved liver function as well as classic features of non-cirrhotic portal hypertension on histological examination of biopsy specimens are described. Three of these patients also had extrahepatic portal vein occlusion. All patients had varying degrees of portal hypertension and hypersplenism. Three patients underwent splenectomy and the remainder had sclerotherapy to control variceal bleeding. The overall prognosis is excellent if variceal bleeding can be controlled by appropriate measures. Hence recognition of this infrequently diagnosed entity is important for an accurate prognosis and appropriate therapeutic interventions.

S Afr Med J 1991; **79**: 268-270.

Non-cirrhotic portal hypertension (NCPH) is a relatively uncommon and probably underdiagnosed disease in Western countries.[1] It appears to be more common in India and in Japan, where it accounts for 25 - 30% of all cases of portal hypertension.[2] NCPH has been known under various names: non-cirrhotic portal fibrosis;[3] hepatoportal sclerosis,[4] idiopathic portal hypertension;[5] obliterative portal vein obstruction, and obliterative portal venopathy.[6] This distinct syndrome is characterised by portal hypertension without evidence of liver cirrhosis, and the features of the disease resemble those of chronic schistosomiasis.[7]

The diagnosis of NCPH should be considered in the presence of long-standing splenomegaly and also repeated gastrointestinal haemorrhages with preserved or minimally deranged hepatocellular function. The diagnosis is also dependent on the exclusion of more usual causes of portal hypertension by appropriate investigations.

In NCPH the surface of the liver is occasionally nodular and described at the time of laparotomy as resembling 'early cirrhosis'.[4] On histological examination the condition is characterised by the presence of dilated veins, periportal angiomatosis, varying degrees of portal fibrosis and phlebosclerotic obliterative lesions of the terminal portal vein branches.[7] One of the most complete early reports[8] also described irregular capsular thickening, thickening of some portal tracts with radiating fine fibrous septa, and distortion of the lobular architecture with hyperplasia and compression of other areas. Sinusoidal collagenisation, sinusoidal dilatation with or without cellular infiltrates, and cellular inflammatory infiltrates in portal tracts have also been reported.[8,9]

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Accepted 12 July 1990.

The aetiology of NCPH is largely obscure. There are associations with arsenical, vinyl chloride or copper poisoning.[2] Recent reports include protein C deficiency or chronic overdose of vitamin A as additional possible causative factors.[10]

Patients and methods

During 1989 6 patients with NCPH, 2 men and 4 women, were seen at the Liver Clinic, Groote Schuur Hospital, for evaluation of clinical features suggestive of portal hypertension and splenomegaly. Their ages varied from 23 years to 50 years (mean age 35,3 years) and all had signs of portal hypertension with oesophageal varices and splenomegaly or a history of splenectomy (Table I).

Two patients had undergone splenectomy, and variceal bleeds had been recorded in 4 patients. Chronic haemolytic anaemia with hepatomegaly was noted in 1 patient. Patients 3 and 6 had diabetes mellitus and patient 5 had chronic pancreatitis. Hepatic wedge biopsies from 2 patients had been previously diagnosed as unspecified liver fibrosis and micronodular cirrhosis.

All patients had characteristically normal or mildly cholestatically deranged liver function tests (Table II). Patients 5 and 6 had a history of gastric peptic ulcer disease and gallstones. Features of chronic liver disease, such as ascites, palmar erythema, jaundice, fever, gynaecomastia, testicular atrophy and Dupuytren's contracture, were not present in any patient.

Needle biopsy specimens from all patients were available and, in addition, wedge biopsies were taken from 3 patients. The features seen on histological examination and collated in Table III show a regular appearance of fibrosis and/or sclerosis of portal vein branches, fibrous septa radiating from the portal tracts, dilatation of branches of portal and terminal veins (Figs 1 - 4), irregular distribution of blood vessels or periportal hypervascularity (Fig. 3), and areas of hepatocyte hyperplasia with

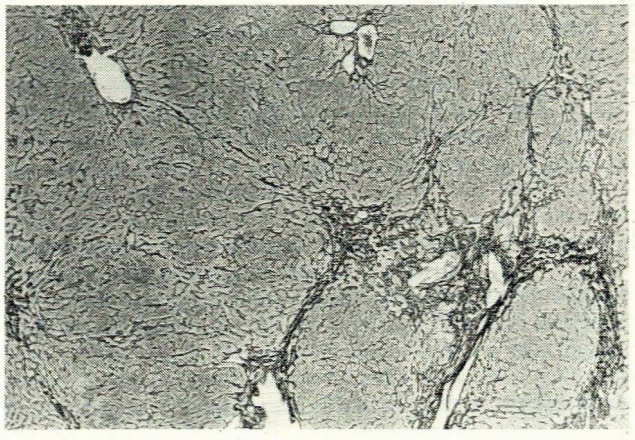

Fig. 1. Low-power view of the liver (patient 4) with non-cirrhotic portal hypertension. Note irregular periportal fibrosis, dilated and irregularly distributed portal vein branches, fine fibrous septa radiating between lobules and nodularity (Reticulin × 35).

TABLE I. BASIC CLINICAL INFORMATION

Patient	Age (yrs), sex	Clinical diagnosis	Duration (yrs)	Portal vein
1	24, F	S, OVB, P	9 mo.	Occluded
2	19, F	S, SCT, OVB	1	Patent
3	50, M	S, O	2	Patent
4	28, M	S, OVB	3,5	Occluded
5	43, F	SCT, OVB, O	28	Occluded
6	48, F	SCT, O	19	Patent

S = splenomegaly and/or hepatosplenomegaly; SCT = splenectomy; OVB = oesophageal variceal bleeding; P = pancytopaenia; O = other (diabetes, chronic pancreatitis).

TABLE II. COAGULATION AND LIVER FUNCTION TESTS

	Prothrombin index	Platelets ($\times 10^9$/l)	ALP	GGT
Normal range	1	180 - 400 000	30 - 115	0 - 50
NCPH (*N* = 3)	1,0 - 1,5	52 - 500 000*	126 - 141	36 - 130
NCPH + occluded portal vein (*N* = 3)	1,2 - 1,9	47 - 218 000	128 - 243	94 - 400

* After splenectomy.
ALP = alkaline phosphatase; GGT = gammaglutamyltransferase.

TABLE III. HISTOLOGICAL EXAMINATION OF BIOPSIES

			Fibrosis		Vein dilatation			
Patient	Type of biopsy	Sub-capsular	Portal	Septal	Portal branches	Terminal	Areas of hyperplasia	Other
1	Needle	?	+ –	+	+	+	+ –	Dilated sinusoids
2	Needle, wedge	+++	+++	++	+	+	+	Irregular distribution of veins with Zenker's infarct
3	Needle, wedge	–	+	+	++	+	–	Portal round-cell infiltration of irregular distribution
4	Needle wedge	++	+	+++	++	+	++	Nil
5	Needle	?	+	++	+	+	+	Sinusoidal dilation with collagenisation
6	Needle	?	+	++	+	+	–	Irregular distribution of veins

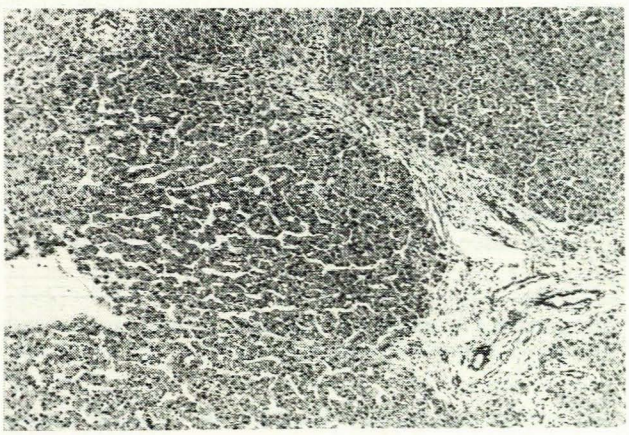

Fig. 2. Tru-Cut biopsy from patient 2 shows an enlarged, sclerotic portal tract. Portal vein is narrowed and replaced by numerous thin-walled channels (lower right corner). On the left is dilated terminal hepatic vein (H and E × 210).

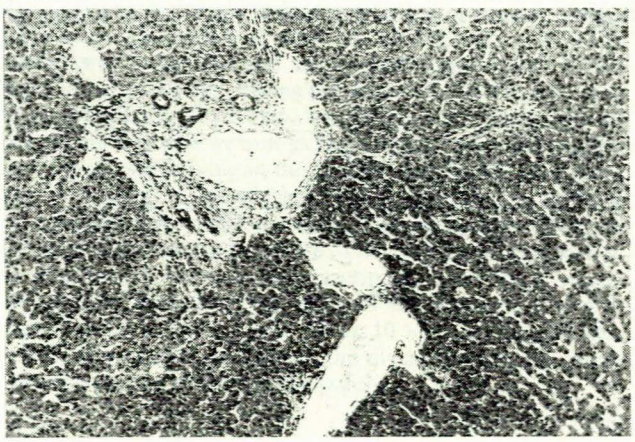

Fig. 3. Broadening and fibrosis of portal tract, periportal angiomatosis in wedge biopsy from patient 2 (H and E × 240).

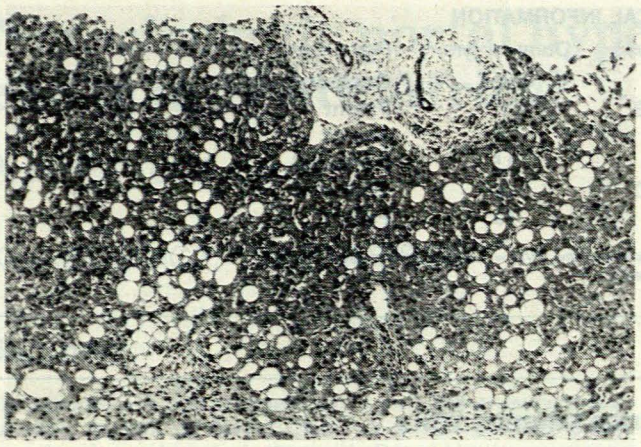

Fig. 4. Tru-Cut liver biopsy (patient 3) shows moderate fatty changes and sclerosis of portal vein branches (upper right corner) (H and E × 240).

compression of adjacent lobular structures (Fig. 2). Less common features were sinusoidal dilatation or collagenisation, portal round-cell infiltrates, and intrahepatic portal vein thrombosis with consecutive hepatocyte atrophy (Zenker's infarct).

Cirrhotic nodular rearrangement of the lobular architecture or features characteristic of schistosomiasis, such as portal calcification, parasitic ova or reactive granulomas, were noted. Pronounced septal fibrosis was a feature of all 3 wedge biopsies and irregular capsular thickening was also evident in 2 biopsies.

Based on these histological and clinical features, the possibility of NCPH was considered. Further ultrasonography and angiography revealed occlusion of portal veins in 3 patients. No evidence of other intra- or extrahepatic causes of portal hypertension was found.

There was no apparent association with arsenical, vinyl chloride, copper, toxins or alcohol poisoning. The course of the disease was relatively benign in all patients, except for patient 1, who bled massively from grade IV varices and died from an oesophageal perforation and haemoperitoneum after sclerotherapy.

Discussion

Six cases of NCPH were diagnosed at Groote Schuur Hospital in 1989. The paucity of description of this disease in previous hospital records indicates that NCPH has not been recognised as such and is thus probably underdiagnosed. Histological examination of hepatic specimens, particularly wedge biopsies, is crucial for the diagnosis and, indeed, Kingham *et al.*[1] have stated that the diagnosis of NCPH is entirely based on histological evidence. In our experience close collaboration between members of the Departments of Medicine, Radiology and Pathology is necessary to establish this diagnosis. The interpretation of a single needle biopsy may lead to the diagnosis of incomplete septal cirrhosis,[11] unspecified fibrosis, macronodular cirrhosis or no abnormality at all. The results of exclusively extrahepatic portal vein obstruction, such as portal vein thrombosis, include parenchymal atrophy, dilated terminal hepatic veins and minor portal fibrosis. Differential diagnoses include schistosomiasis, nodular regenerative hyperplasia, and perisinusoidal fibrosis of a toxic or alcoholic nature.[2] A long-term follow-up study of NCPH[1] has indicated a relatively good prognosis compared with portal hypertension related to other disease processes. Two of our patients (cases 2 and 4) with 19 and 28 years' history of the disease, respectively, confirm the excellent life expectancy if death from haemorrhage can be prevented by appropriate measures.

In conclusion, we emphasise that NCPH is probably underdiagnosed in South Africa and that proper diagnosis is important because of the very different prognosis from that of cirrhosis with portal hypertension.

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