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Case report

Non-cirrhotic portal hypertension with hypoxaemia

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SUMMARY Hypoxaemia and digital clubbing are rare but well recognised associations of hepatic cirrhosis with portal hypertension. We report the first European patient with idiopathic non-cirrhotic portal hypertension complicated by these features. Pulmonary physiological studies show the hypoxaemia to be the result of anatomical and physiological intrapulmonary shunting.

Case report

A Caucasian boy of 13 years of age presented with haemoptysis and on examination was found to have splenomegaly. No cause was found for either feature. He remained well until February 1983 when, aged 22 years, a 'flu'-like illness with mild jaundice and dark urine developed. The jaundice cleared after 10 days and clinically was thought to be caused by an acute viral hepatitis but because of persistent lethargy and splenomegaly he was referred to hospital. A history of progressive exertional dyspnoea was obtained and examination revealed central cyanosis, digital clubbing and spider naevi. The lungs were clinically normal. An ejection systolic murmur was heard over the praecordium. There was splenomegaly but no hepatomegaly or ascites. Investigations showed haemoglobin 15·8 g/dl, white cell count $3{\cdot}8\times10^9$/l, platelet count 94×10^9/l, prothrombin time 18 seconds (control 14), serum aspartate and alanine transaminases and alkaline phosphatase were normal, bilirubin 48 μmol/l (24% direct reacting). Direct Coombs test was negative. Screening tests for specific liver diseases including HBsAg, autoantibodies, serum ferritin, caeruloplasmin and α1-antitrypsin were all normal.

Endoscopy showed extensive oesophageal varices. Percutaneous liver biopsy showed changes in keeping with non-cirrhotic portal hypertension. Mesenteric angiography revealed a splenic artery aneurysm with a venous collateral circulation and a patent portal vein; the splenic vein was not visualised. Splenoportography showed a raised splenic pulp pressure (22 mm/Hg) and patent splenic and portal veins. Wedged hepatic vein pressure (WHVP), however, was only minimally raised (7 mm/Hg corrected) confirming that the portal hypertension was of the presinusoidal type. Electrocardiogram and echocardiogram were normal. Chest radiograph showed a slight increase in interstitial shadowing in both lower zones. Pulmonary function tests (Table) confirmed the presence of severe hypoxaemia and suggested

Table *Results of pulmonary function tests*

	Predicted	*Measured*	*% Predicted*
FEV_1 (L)	4·48	4·64	104%
Vital Cap (VC) (L)	5·4	5·14	95%
$\frac{FEV_1}{VC}\times100$		90%	
Residual volume (L)	1·9	2·07	109%
Total lung capacity (L)	7·4	7·41	100%
Transfer factor (ml/min/mmHg)	37.2	15·5	42%
Blood gasses	Air	100% O_2	
pH	7·44	7·43	
PCO_2 (kPa)*	4·13	4·2	
PO_2 (kPa)*	7·6	61·3	
A-a gradient (kPa)*	7·07	28·4	
	Rest	Post exercise	
O_2 Saturation (%) (Breathing room air)	84%	58%	

*Conversion factor: 1 kPa = 7·5 mmHg.

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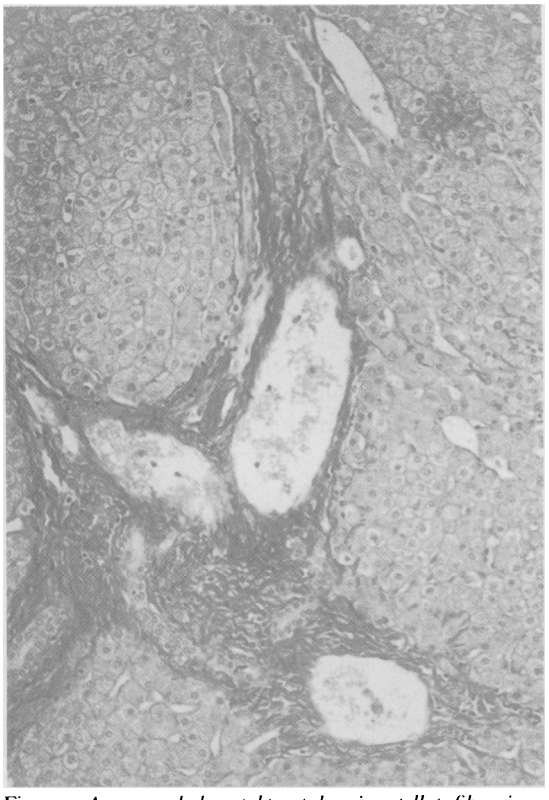

Figure *An expanded portal tract showing stellate fibrosis extending for a short distance into the parenchyma. Note the dilated and thickened portal vein radicles and the regenerating parenchyma adjacent to the portal tract.* (Haematoxylin picrosirius red)

that in addition to a marked disturbance of ventilation/perfusion of the lungs there was an anatomical shunt of approximately 11% of the cardiac output as shown by the A-a gradient which persisted whilst breathing 100% oxygen.

Because of persistent left upper quadrant abdominal pain he underwent splenectomy in December 1983. At operation the splenic artery was found to be aneurysmal and the splenic vein distended. The spleen was enlarged but the liver appeared macroscopically normal. A wedge liver biopsy showed changes typical of non-cirrhotic portal fibrosis with expansion of the portal tracts by fibrosis and grossly dilated and thickened portal vein radicles; the liver parenchyma was intact apart from a few nodules, some of which showed evidence of cellular regeneration, but there was no evidence of septal fibrosis or cirrhosis (Figure).

His subsequent clinical course has been punctuated by episodes of variceal haemorrhage, and he remains centrally cyanosed.

Discussion

Central cyanosis and digital clubbing are rare but well recognised features of cirrhosis.[1] Lesser degrees of hypoxaemia are more common but probably of little clinical significance.[1] The mechanisms leading to hypoxaemia are uncertain although changes in the pulmonary vasulature have been well documented in both acute[2] and chronic liver disease and post mortem studies have shown the presence of dilated precapillary pulmonary blood vessels and lung 'spider-naevi'.[3] Antemortem perfusion radionucleotide studies have also shown small intrapulmonary arteriovenous communications in both cirrhosis and hereditary haemorrhagic telangiectasia with central cyanosis.[4] The respiratory studies in our case show normal lung volumes, hypoxaemia with a fall in oxygen saturation on exercise, impaired carbon monoxide transfer and a large alveolar to arterial oxygen tension gradient whilst breathing air or 100% oxygen. These findings are compatible with an anatomical shunt at the precapillary level and are in keeping with similar studies reported in cirrhotic patients.[3,4]

The evidence against cirrhosis in this patient is strong. There is portal hypertension of the presinusoidal type with a virtually normal WHVP but a markedly raised splenic pulp pressure (in cirrhosis the WHVP and splenic pulp pressures are raised to a similar degree[5]); no underlying cause for cirrhosis was found; and most importantly, the liver was macroscopically normal at laparotomy. In addition, the histological changes in the liver are typical of non-cirrhotic portal fibrosis.[6,7] The aetiology of this condition is unknown but there are reported associations with arsenic ingestion[8] and exposure to vinyl chloride,[9] however, there is no history of such exposure in the present case. The disease encompasses a spectrum of histological abnormalities in the liver ranging from near normal histology or minor vascular abnormalities (hepatoportal sclerosis[10]) to portal fibrosis with distortion of lobular architecture.[6,7] The disease is rare in western countries but may account for up to 25% of cases of portal hypertension in the Indian subcontinent.[7]

It has been postulated that portal hypertension itself may be an important factor in the development of intrapulmonary shunts.[8] The majority of cases, however, have been cirrhotic patients; only four cases of proven non-cirrhotic portal hypertension with profound hypoxaemia have been previously reported. In the first case the patient was from the Indian subcontinent and although reported to be cyanosed no data on blood gases or pulmonary physiology were given.[7] In the second and third, the portal hypertension was caused by schistosomiasis, a

clearly different aetiology[11] and in the fourth case, by extra hepatic portal vein block; clinical features were not given.[12] Our case therefore represents the first comprehensive report of idiopathic non-cirrhotic portal hypertension with digital clubbing and hypoxaemia and clearly shows that the profound hypoxaemia results from intrapulmonary shunting.

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