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Histological study of intrahepatic cavernous transformation in a patient with primary myelofibrosis and portal venous thrombosis

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Summary. Cavernous transformation in the liver was examined histologically by serial section observations, in an autopsy case of portal venous thrombosis and primary myelofibrosis. Cavernous transformation was present from the hepatic hilus to medium-sized portal tracts and was composed of dilated and thin-walled vessels. Serial sections disclosed that these vascular channels were anastomotic and occasionally communicated with occluded portal venous radicles. In places they entered directly into the hepatic parenchyma without accompanying biliary or arterial elements, and also drained into the patent portal venous branches beyond the occluded segment. The study demonstrated that cavernous transformation in the liver develops as hepatopetal collaterals secondary to the portal venous obstruction. Periportal and peribiliary capillary plexus may become cavernous in the presence of portal venous occlusion.

Key words: Portal venous thrombosis – Cavernous transformation – Collateral circulation

Introduction

Extrahepatic portal venous thrombosis with resultant portal hypertension is prevalent in developing countries (Nundy and Nayak 1983). This disease is heterogenous in aetiology. The following causes are suspected as the cause of the thrombosis: umbilical sepsis, acute appendicitis, biliary tract surgery, abdominal trauma and thrombophlebitis migrans (Webb and Sherlock 1979) but the aetiology remains obscure in about a half of the patients. Chronic myeloproliferative disorder is also complicated by portal hypertension associated with portal venous thrombosis on occasion (Oishi et al. 1960; Shaldon and Sherlock 1962). It is well known that cavernous transformation around the occluded portal vein or in the hepatic hilus is seen in cases with portal venous obstruction of any aetiology. Angiographic study of such cases suggested that cavernous transformation is via hepatopetal collaterals carrying portal blood (Laws et al. 1959; Rosch and Dotter 1971). There have been, however, few histological observations of cavernous transformation in the liver (Klemperer 1928; Gibson and Richards 1955; Parker and Seal 1955; Williams and Johnston 1965), and the architecture and histogenesis of cavernous transformation remain unresolved.

We have recently experienced an autopsy case with extrahepatic portal venous obstruction and extensive cavernous transformation in the liver. The aim of this study was to determine the architecture of cavernous transformation and its structural relationship to thrombosed portal veins using serial section observations, and also to find a clue to the histogenesis of cavernous transformation.

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Patient and methods

A 72-year-old woman was admitted to the Fukui Prefectural Hospital in October, 1983, complaining of abdominal fullness, weight loss and thirst of three months' duration. She had been treated as diabetes mellitus for 6 years. Physical examination showed ascites and a cardiac systolic murmur. The liver and spleen were palpable two and three fingerbreadths below the right and left costal margin, respectively. Main laboratory findings were as follows: RBC, $575 \times 10^4/mm^3$; WBC, $14600/mm^3$; platelet, $29.3 \times 10^4/mm^3$; haemoglobin, 12.5 g/dl; circulating RBC volume, 51.6 ml/kg; total serum protein, 6.2 mg/dl with albumin fraction of 53.6% and γ-globulin fraction of 30%; total bilirubin, 1.6 mg/dl; ZnTT, 17 units; TTT, 9.6 units; prothrombin time, 58 s; hepaplastin test, 44%; occult blood in feces, positive; serum HBsAg and rheumatoid facter, both positive. Bone marrow aspiration revealed dry tap and bone marrow biopsy showed fibiosis and highly-increased cellularity con-

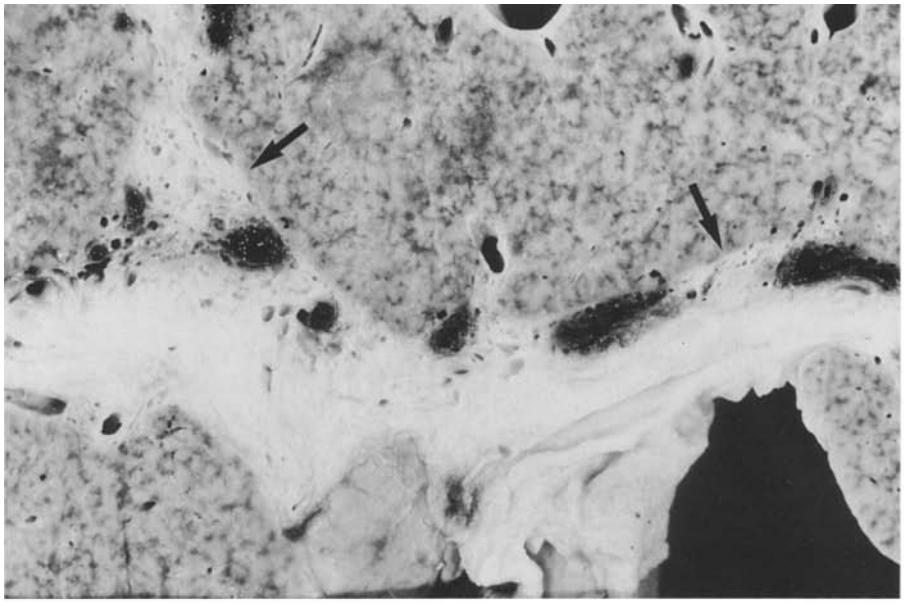

Fig. 1. Cut surface of the liver shows cavernomatous transformation (*arrows*) in the hepatic hilus as well as within portal tracts in the liver

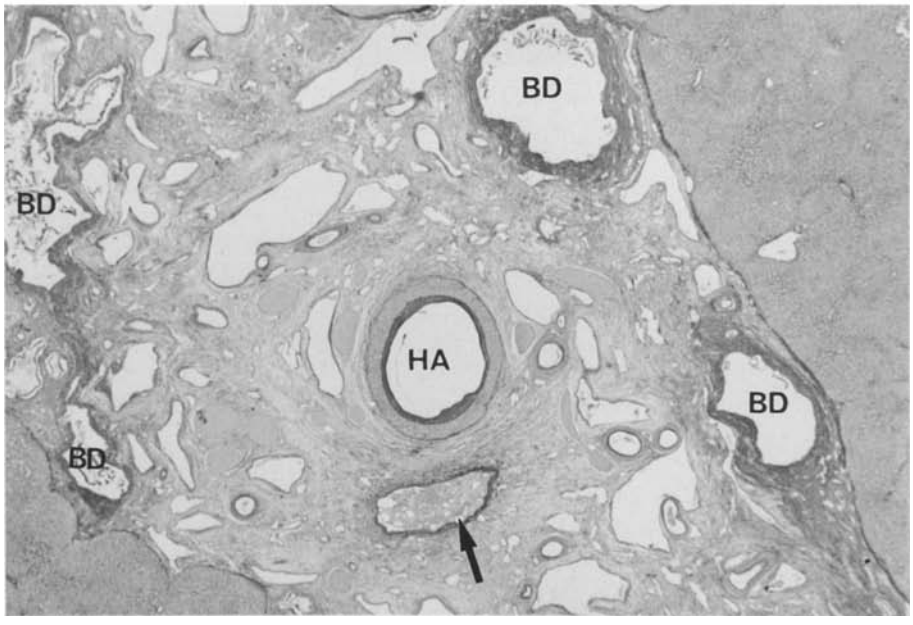

Fig. 2. There are a number of vascular channels within the portal tract, giving a cavernous appearance. A portal venous radicle is seen occluded by old thrombi (*arrow*). The hepatic arterial branch is hypertrophic. Medium-sized portal tract. *HA:* hepatic artery. *BD:* bile duct. EVG, ×5

sistent with a cellular phase of primary myelofibrosis. Ultrasound and scan examination failed to visualize the portal venous trunk. Coeliac and upper mesenteric angiography disclosed complete occlusion of the splenic vein and portal venous trunk, cavernous transformation at the hepatic hilus, and prominent oesophageal and gastric varices. Repeated haematemesis and melaena developed, and the patient died of massive haematemesis in November, 1985. In her clinical course, the platelet count fluctuated from 60×10^4 to $80 \times 10^4/mm^3$, and the WBC count from 20000 to 90000/mm^3.

Autopsy diagnoses were as follows: primary myelofibrosis, intra- and extrahepatic portal vein thrombosis with cavernous transformation in the liver from the hepatic hilus into the liver, ruptured oesophageal varices and massive gastrointestinal bleeding, and splenomagaly (550 g).

Twenty five tissue blocks including cavernous transformation were taken from the liver including the hilar region, and they were fixed in 10% formalin. Paraffin sections were stained with haematoxylin and eosin (H&E) and elastica van Gieson (EVG). More than 1800 histological serial sections were made from the 11 tissue blocks including the cavernous transformation. They were stained alternatively with H&E and EVG stains.

Results

On macroscopic examination, the portal venous system was continuously occluded by old thrombi from the splenic vein at the splenic hilus through

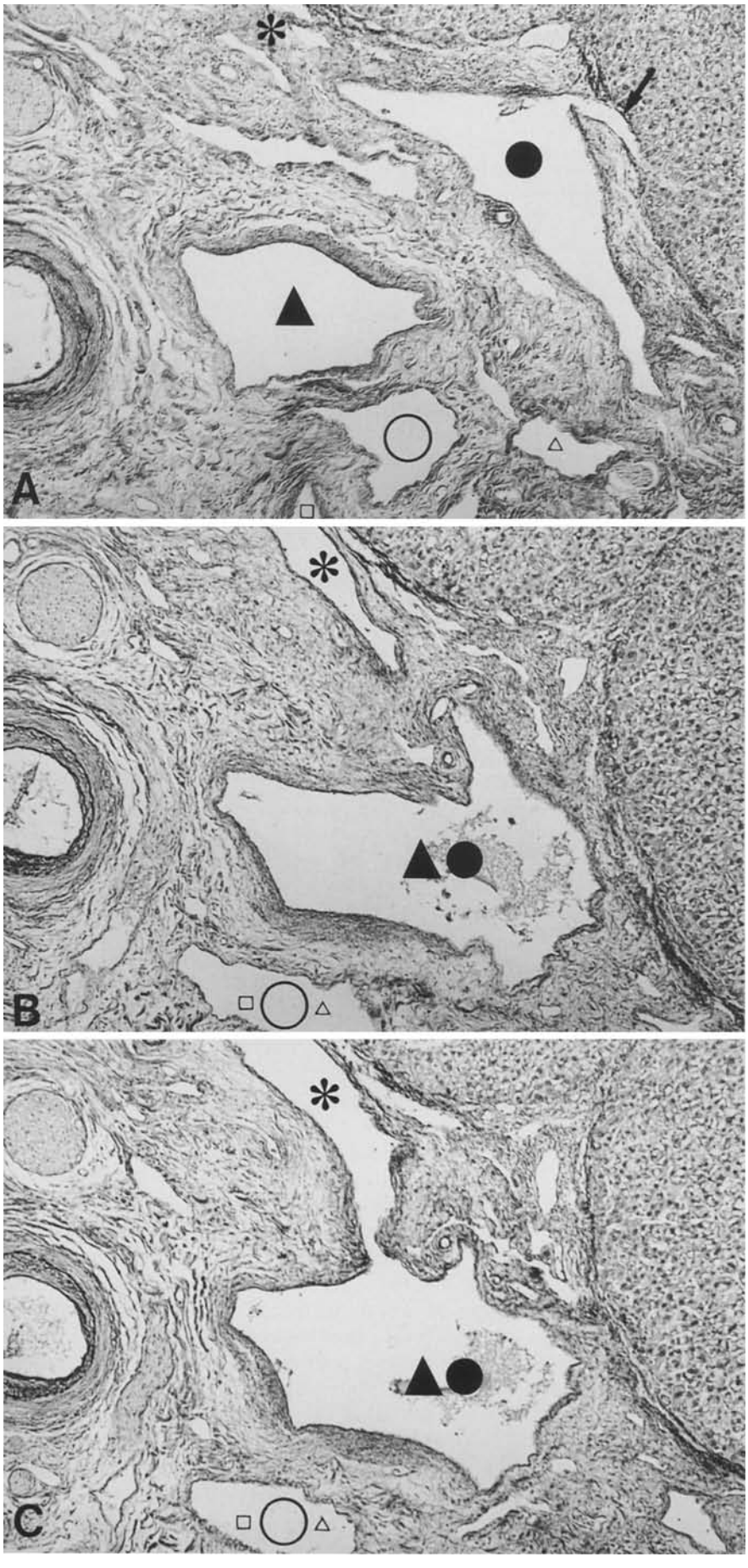

Fig. 3. Serial section observations of the vascular channels of cavernous transformation. (**A**) There are dilated vessels, five of which are marked by symbols, respectively. The arrow indicates an inlet venule-like branch pouring directory into the sinusoid. (**B**) The two vascular channels marked by a closed circle and triangle are seen to anastomose. Three channels marked by an open circle, triangle and square are also anastomosed. (**C**) Further, the vascular channel marked by an asterisk is found to communicate with that vessel marked by a closed circle and triangle. Distance between (**A**) and (**B**), and (**B**) and (**C**) is about 150 μm and 120 μm, respectively. EVG, ×40

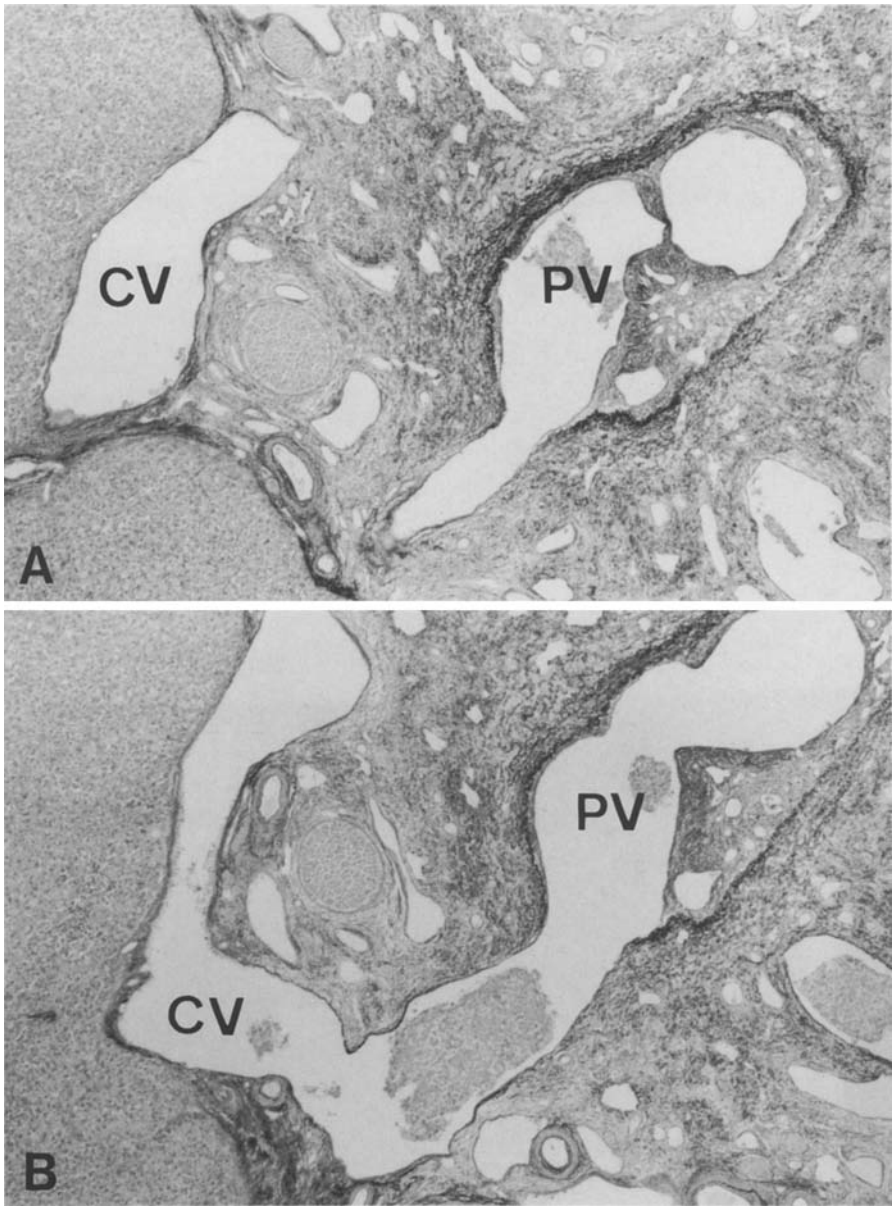

Fig. 4. Serial section observations of the thrombosed portal radicle and vascular channels. Recanalized vessels in the thrombosed portal venous radicle (PV) are seen to communicate with the dilated vessel (*CV*) of the cavernous transformation. Distance between (**A**) and (**B**) is 440 μm. EVG, × 20

the portal venous trunk to intrahepatic medium-sized portal venous branches. Mesenteric veins were, however, free of thrombosis. Cavernous transformation was recognized from the hepatic hilus to the medium-sized portal tracts in the liver (Fig. 1), wherein the portal venous radicles were almost undiscernible grossly (Fig. 1). Hepatic arterial radicles were moderately hypertrophic and bile ducts appeared normal. Cavernous transformation was seen neither around the splenic vein nor around the portal venous trunk in the hepatoduodenal ligament. The liver (1080 g) was slightly atrophic but failed to show cirrhotic change or confluent necrosis.

On microscopic examination, the intra- and extrahepatic portal veins which were completely or partially occluded by old thrombi showed recanalization and duplication of internal elastic lamina with advantitial fibrosis (Fig. 2). Numerous thin-walled dilated vascular channels were found in the region of cavernous transformation (Fig. 2). Some of these thin-walled vascular channels lacked both smooth muscles and elastic laminae, while others were invested with smooth muscle layers partly or circumferentially. These vascular channels were accompanied by neither arteries nor bile ducts. Both thrombosed portal venous radicles and cavernous transformation were rarely found in the smaller

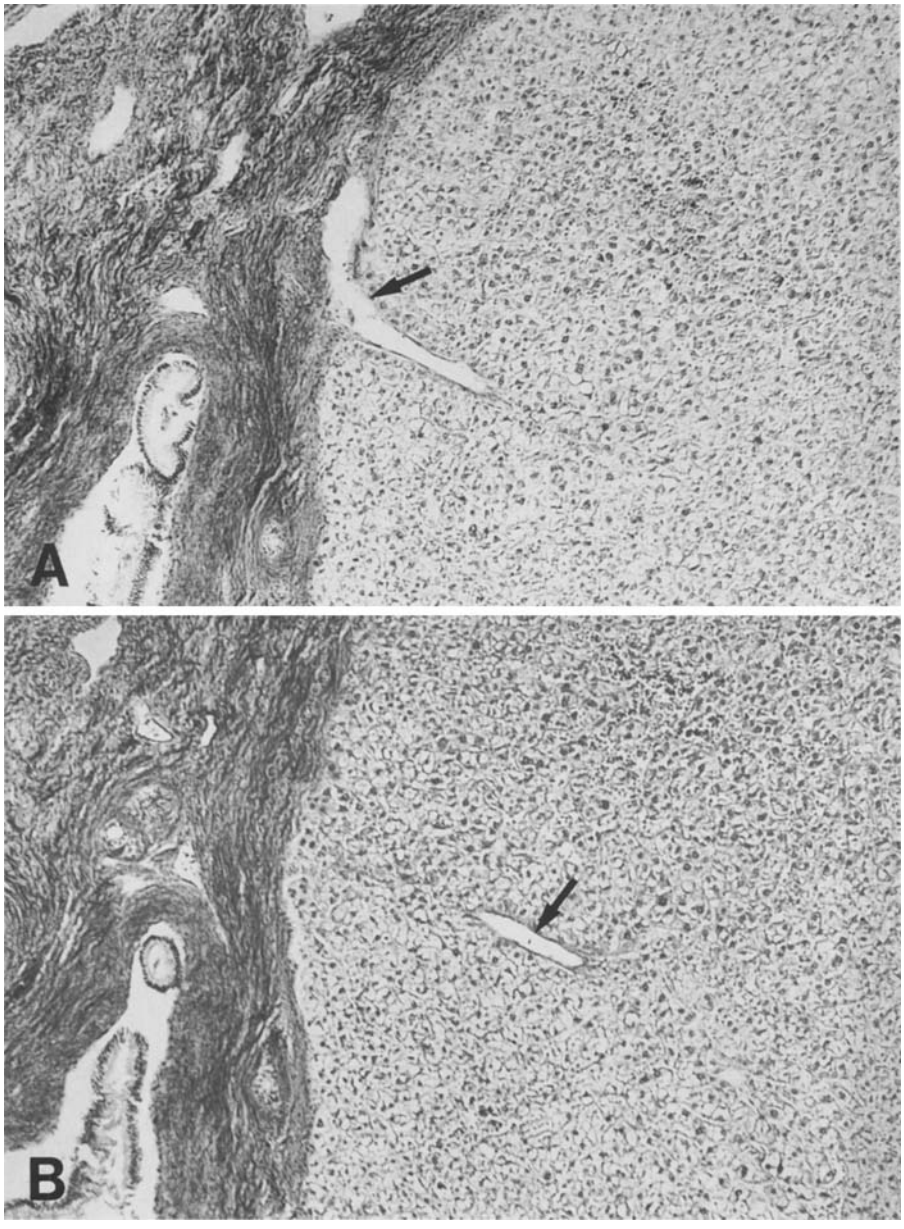

Fig. 5. One vessel of the cavernous transformation is seen to enter into the hepatic parenchyma without accompanying either bile duct or hepatic artery (*arrows*). Distance between **A** and **B** is 20 μm. EVG, ×40

portal tracts. The hepatic parenchyma had a number of foci of extramedullary haematopoiesis, but appeared otherwise normal.

Serial section observations showed that the vascular channels comprising cavernous transformation were anastomosed to one another in places, appearing as a vascular plexus (Fig. 3A, B and C). Direct luminal connections between these vascular channels and recanalized vessels in thrombosed portal veins were shown by serial section observations (Fig. 4A and B). Some of the vascular channels were found to enter directly into liver parenchyma without accompanying bile duct or hepatic artery (Fig. 5A and B) and finally drained into the dilated sinusoid here and there. The vascular plexus forming cavernous transformation was found to communicate with patent smaller portal venous radicles just beyond the thrombosed portal venous radicles (Fig. 6A, B and C).

Discussion

Laws et al. (1956) and Rosch and Dotter (1971) showed angiographically that cavernous transformation is a brush-shaped arrangement of vessels which run along the portal vein proper and is a hepatopetal collateral pathway appearing in the portal phase, and that this transformation seems

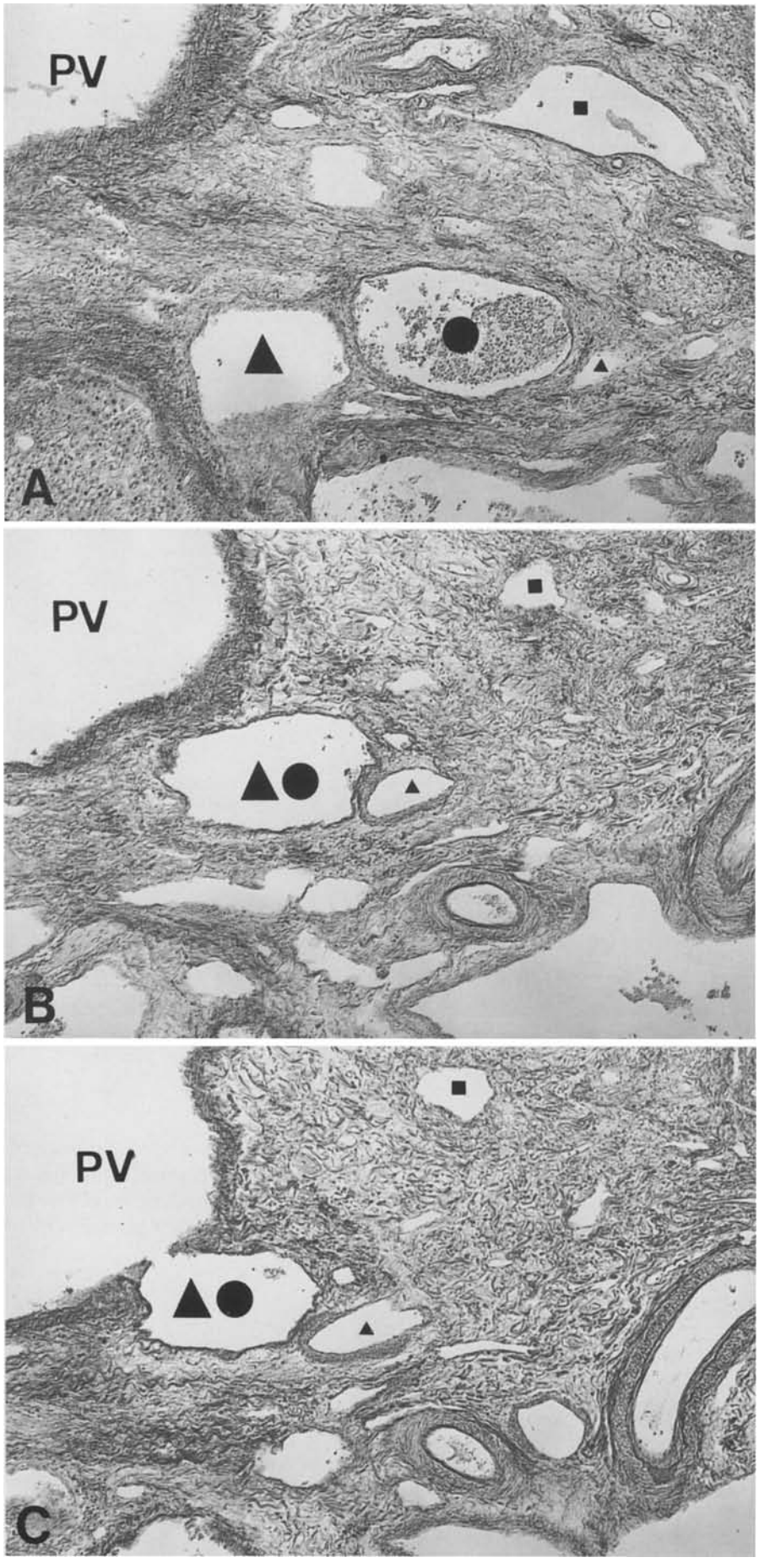

Fig. 6. A There are vascular channels, two of which are marked by a large circle and triangle. The upper left large vessel is patent portal vein. **B** The vascular channels marked by the large circle and triangle are found to anastomose and to approach the patent portal vein on the upper left. **C** The vascular channels marked by the large circle and triangle are found finally to communicate with patent portal venous radicles. The vessels marked by small triangles and squares are the same vessels, respectively. Distance between **A** and **B**, and **B** and **C** is 120 μm and 40 μm, respectively. *PV:* patent portal venous radicle. EVG, ×40

to be a continuous network from the hepatic hilus to the medium-sized portal tracts. It was found in the present study that the vascular plexus of the cavernous transformation either occasionally communicated with thrombosed portal venous radicles showing recanalization on one hand or entered into the hepatic parenchyma directly or poured into the patent portal venous radicles just downstream to the thrombosed ones, on the other. Thus, this study demonstrated histologically that cavernous transformation was formed secondarily in order to by-pass the thrombosed portal venous radicles, as suggested in the angiographic study.

With regard to the feeding vessels to these vascular plexuses of cavernous transformation, the followings have been suggested: suprapancreatic veins (Williams and Johnston 1965), accessory portal vein (Gibson and Richards 1955) and paraportal veins (Laws et al. 1955). The feeding vessels could not been be identified in the present case, though thrombosed portal veins with recanalization were found to communicate with the cavernous transformation, suggesting that portal vein might have been a partial feeder.

The vasculature from which these vascular plexus have been derived is also obscure. Many authors (Klemperer 1928; Gibson and Richards 1955; Parker and Seal 1955; Ohnishi et al. 1984) considered that cavernous transformation is developed by dilatation of veins running parallel along the portal vein (paraportal vein) (Ohnishi et al. 1984), though such a venous system is poorly described under normal conditions. Some investigaters claimed that the cavernous collaterals are newly developed by proliferation from the obstructed portal veins themselves, as a form of neovascularization (Bechtelsheimer and Conrad 1980). In normal livers, portal tracts are supplied exclusively by hepatic arterial branches which give off a network of capillaries within the portal tract (MacSween and Scothorne 1979). The capillary network is particularly dense in the peribiliary tissue and also around the portal venous branches. The former is termed "peribiliary capillary plexus" (Murakami 1978), and the latter "periportal plexus" (Ohtani 1978). It seems likely that both of these capillary plexuses take part in the formation of cavernous transformation under portal venous occlusion. A case of portal venous obstruction in which cavernous transformation developed mainly in the peribiliary area (Ogawa et al. 1987), supports the participation of the peribiliary capillary plexus in cavernous transformation. It is possible that "internal root" communicating portal vein and peribiliary plexuses (Murakami 1978) in normal livers may participate in the connection between cavernous vascular channels and portal venous branches in the presence of portal venous occlusion. The vasculature entering into the hepatic parenchyma alone in the present case may have been derived from either inlet venule or "radicular portal vein" which links peribiliary plexus and hepatic sinusoid in normal conditions (Murakami 1978). Further investigations on the physiological and pathological states of microcirculation in the portal tract are necessary to clarify the formation of cavernous transformation.

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