Studies on Cirrhosis of the Liver

IX Structure of Shunted Blood Vessels in the Autopsied Cirrhotic Liver

By

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The most characteristic changes in the hepatic circulation of cirrhosis of the liver are pathological anastomoses of blood vessels. They appear not only in the extrahepatic portal veins but also within the liver. The formation of the intrahepatic and extrahepatic shunts markedly decreases the blood flow directly concerned with the intrahepatic metabolism, contributing to production of hepatic coma, disturbance of liver cell function, and continuance of liver cell damage.

The results of the investigations of Krez,¹⁾ Popper and co-workers,²⁾ and Hales and co-workers³⁾ showed the presence of porto-hepatic venous anastomoses in the cirrhotic livers. According to Nakamura and co-workers⁴⁾ the quantitative measurement of the intrahepatic shunted blood flow showed considerable intrahepatic shunted blood flow in cirrhosis of the liver. The authors studied the morphological changes and pathological anastomoses of intrahepatic blood vessels in cirrhosis of the liver, as reported in the following study.

MATERIALS AND METHODS

Four human cirrhotic livers were used and acrylic resin was injected through the portal and hepatic veins, and in two of the four through the hepatic artery and vein. The specimens of tissue from six human cirrhotic livers, of which four specimens were from the same livers studied in acrylic resin experiment, were fixed in 10% formalin and embedded in paraffin wax; serial sections of 10 microns in thickness were stained by hematoxylin and eosin, elastic Weigert, Gomori silver impregnation, and the Masson trichrome method for connective tissue.

One human cirrhotic liver was injected through the hepatic veins with 10% aqueous gelatin solution containing blue pigment, and through the portal vein with India ink. The specimen was fixed in 10% formalin, and the vascular distribution of the specimen was studied in the frozen sections, which were 100 microns in thickness and mounted in glycerin.

All of the seven patients had ascites and the two of them had been found to suffer from hepatoma (hepatocellular carcinoma).

In addition to these specimens of the human cirrhotic livers, histological examination of five rat livers with experimental cirrhosis which was produced by oral administration of 0.2 cc/100 g. body weight of carbon tetrachloride three times a week for eight weeks, was carried out. The carbon tetrachloride was used in 13% solution in olive oil.

These rats were killed and their livers were injected by the above technical method of the frozen sections of the specimens of the human cirrhotic liver.

RESULTS

A) Human cirrhotic liver

1) Findings of acrylic resin casts

Gross findings The hepatic veins were flattened by pressure of the proliferating nodules and became tortuous. Their branches were reduced in number. The above-mentioned changes of the hepatic veins were found in all specimens of four cirrhotic livers. The portal veins were also compressed by the regenerated nodules and became slightly tortuous too, but the portal veins were found less affected than the hepatic veins. Some portal branches were arranged in a basket-like fashion around the nodules (Fig. 1). The hepatic arterial branches were found increased in one of two specimens.

Fig. 1. Human cirrhotic liver. Acrylic resin cast. Black - Hepatic veins, White - Portal veins, Arrow - Branch of portal vein.

Anastomoses between the portal and hepatic veins were demonstrated in three of four specimens and some of these anastomoses were often of appreciable size, measuring from 0.5 mm. to 1 mm. in diameter (Fig. 2).

Microscopic findings Acrylic resin did not go into the vessels narrower than those of 25 microns. Vessels injected through both the portal and hepatic veins

Fig. 2. Human cirrhotic liver. Acrylic resin cast. H - Hepatic vein, P - Portal vein, A - Anastomosis between the portal and hepatic vein.

Fig. 3. Human cirrhotic liver. Acrylic resin cast. H - Hepatic vein, P - Portal vein, A - Anastomosis between the portal and hepatic vein. ×60.

Fig. 4. Human cirrhotic liver. Hepatic vein compressed by regenerated nodule. Weigert's elastic fiber. ×35.

Fig. 5. Human cirrhotic liver. The septum contained many blood vessels with broad lumen. Haematoxylin and eosin. $\times 35$.

Fig. 6. Human cirrhotic liver. Atrophy of liver cells and sinusoids with the collagenous walls. Gomori silver impregnation. $\times 250$.

Fig. 7. Human cirrhotic liver. Surviving sinusoids in the septum. Gomori silver impregnation. $\times 60$.

in all examined specimens were numerous and tortuous, and the numerous porto-hepatic venous anastomoses were demonstrated in three of four specimens (Fig. 3).

Fig. 8. Photograph of the paraffin model, H - Hepatic vein, P - Porta vein, A - Anastomosis between the portal and hepatic vein.

2) Findings of the histologic serial sections

In all of six specimens, hepatic veins were compressed and strictured by regenerated nodules of various sizes (Fig. 4). Portal veins, protected by their natural sheath of connective tissue, were found less affected than the hepatic veins in this process. The septums contained numerous vessels with broad lumen (Fig. 5). Sinusoids between atrophied liver cells were widened and their walls underwent collagenous changes (Fig. 6). It appears that the disappearance of the liver cells and proliferated connective tissue keep step with the advance of the above-mentioned changes, and in the septums the sinusoids are dilated and their walls undergo the collagenous changes (Fig. 7). Therefore, it is reasonable to presume that the multiple vessels in the septums are the pre-existing central and portal veins, and a large number of them is originated from the persisting sinusoids. Anastomoses between the portal veins and the hepatic veins were demonstrated in two specimens on the serial sections of six specimens. It seems that the porto-hepatic venous anastomoses develop from the pre-existing sinusoids in the septums. The serial sections of the confirmed porto-hepatic venous anastomoses were reconstructed by paraffin model. In the reconstructed paraffin model, three-dimensional figure of the anastomosis was demonstrated (Fig. 8).

3) Findings of one specimen injected with different colored gelatin

The hepatic veins were compressed by regenerated nodules, and portal branches containing India ink were irregularly tortuous. In the septum there were more vessels injected through the portal vein than the vessels injected through the hepatic vein, and the multiple vessels were prominent in the broad septums. Many communications were demonstrated between the portal and hepatic veins as mixture of the different colored injection masses, measuring from 8 to 65 microns in diameter (Fig. 9).

In the studied human cirrhotic livers, anastomoses between the portal and

Fig. 9. Human cirrhotic liver. H - Hepatic vein, P - Portal vein, Arrow - Anastomosis between the portal and hepatic vein. $\times 100$.

Fig. 10. Rat cirrhotic liver, H - Hepatic vein, P - Portal vein, Arrow - Anastomosis between the portal and hepatic vein. $\times 60$.

hepatic veins were demonstrated in five of seven specimens. Grossly visible porto-hepatic venous anastomoses were less frequently observed than microscopic anastomoses measuring from 8 to 100 microns in diameter. Anastomosis between the hepatic artery and hepatic vein was not observed.

B) Findings of the experimental cirrhotic rat livers injected with different colored gelatin

The hepatic veins were compressed by the regenerated nodules and became tortuous in all specimens of five rats. Histological normal architecture of the liver was distorted and the increase in connective tissue was found. These septums contained a network of numerous vessels injected with different colored gelatin through both the portal and hepatic veins. Communications between the portal and the hepatic veins were demonstrated in four of five rats, but the porto-hepatic venous anastomoses in cirrhotic rat livers were found less frequently than the anastomoses in the human cirrhotic livers (Fig. 10).

DISCUSSION

A) Human cirrhotic liver

McIndoe⁵⁾ said that the venous branches were perceptibly reduced in number. Hales and co-workers²⁾ stated that the venous beds were reduced and venous reduction was often associated with fibrosis. The venous reduction was most pronounced in the hepatic veins, associated with fibrosis, and may be produced as a result of the venous obstructions due to regenerated nodules. Portal veins, protected by their natural sheath of connective tissue, were found less affected than hepatic veins, as proposed by Kely and co-workers⁶⁾. Some of portal branches were arranged, as Popper and co-workers²⁾ well explained, in a basket-like fashion around the nodules. Recently "hepatic origin" theory of the formation of ascites in liver cirrhosis, was advocated. Milnes-Walker⁷⁾ reported that both the intrahepatic and post-sinusoidal obstructions were important factors of pathogenesis of ascites. In our seven patients with liver cirrhosis ascites was found in all cases, and hepatic venous obstruction due to regenerated nodules of various sizes was found in all specimens. Anastomoses between the portal and the hepatic veins were revealed in five of seven specimens. If the resin cast method or color injection method was employed in all specimens, the porto-hepatic venous anastomoses would be revealed numerously in all specimens. These results corresponded with those of intrahepatic blood flow measured in liver cirrhosis by Nakamura and co-workers¹⁾. According to Popper and co-workers²⁾, in cirrhotic livers, anastomoses between the portal and hepatic veins were visible only in the vicinity of the coronary and falciform ligament by vinylite injection cast method, whereas porto-hepatic venous anastomoses in size from 10 to 70 microns in diameter were frequently observed in the cirrhotic livers which were injected with colored gelatin and India ink. Hales and co-workers³⁾ observed that gross anastomoses between the portal and hepatic veins were present in 8% of the cirrhotic livers, some of which measured over 1 mm. in diameter by the vinylite injection cast method. In the present investigation, which was performed by the method of acrylic resin casting, the porto-hepatic venous anastomoses were demonstrated from 0.5 mm. to 1 mm. in diameter in two specimens, but grossly visible porto-hepatic venous anastomoses were less frequently observed than microscopic anastomoses from 40 microns to 100 microns in diameter. Popper and co-workers²⁾ reported that vessels communicated between the portal and hepatic veins develop from the pre-existing sinusoids in the septums; their thought seems rather proper than Moschowitz's⁸⁾ thought of newly formed granulomatous vessels. It appears that porto-hepatic venous anastomoses are presented numerously in cirrhotic livers containing broad septums. In the present investigation we could not confirm yet the evidence of anastomosis between hepatic artery and portal vein or hepatic vein.

B) Rat liver

Popper and co-workers²⁾ said that in their experimental cirrhosis vascular connections between branches of the portal and hepatic veins were only occasionally noted and the septums, at least in the early stage, could be injected only from branches of the hepatic veins, but in the final stage could be injected from both portal and hepatic veins. In the present investigation, the septums contained a network of numerous vessels injected with different colored masses through both portal and hepatic veins, and anastomoses between portal and hepatic veins are revealed too.

SUMMARY

The intrahepatic blood vessels and intrahepatic shunted blood vessels were investigated in seven human autopsied cirrhotic livers by means of vascular acrylic resin casting, the injection of different colored gelatin through the vessels, and the histological examination of serial sections.

In all the cirrhotic livers, the changes were most prominent in the hepatic veins, which were compressed by the regenerated nodules of various sizes, became tortuous, and were reduced in number.

The portal vein was found less affected than the hepatic veins, but some of its branches were arranged in a basket-like fashion around the nodules.

The septums contained many blood vessels with broad lumen, which were considered to derive from surviving sinusoids. It is reasonable to presume that the porto-hepatic venous anastomoses develop from the pre-existing sinusoids included in the septums.

Anastomoses between the portal and hepatic veins were demonstrated in five of seven specimens. Grossly visible porto-hepatic venous anastomoses were less frequently observed than microscopic anastomoses measuring from 8 microns to 100 microns in diameter.

Histological studies of the serial sections revealed porto-hepatic venous anastomoses in two of six specimens. Three-dimensional figure of the porto-hepatic venous anastomosis was demonstrated in a reconstructed paraffin model.

Histological examinations of the livers of five rats with cirrhosis due to carbon tetrachloride, which were injected with different colored gelatin, revealed the flattening and tortuosity of the hepatic veins in all rats, and porto-hepatic venous anastomoses in four of five rats.

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