exceptionally sensitive human beings; the substances concerned are probably, but not certainly, the sulphur compounds.

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SPLENOPORTAL VENOGRAPHY FOR EVALUATING ABNORMALITIES OF PORTAL CIRCULATION

BY

A. K. BASU, M.S., F.R.C.S., F.A.C.S.

Director, Department of Surgery, S.S.K.M. Hospital,
 Calcutta; formerly Professor of Surgery, Nilratan
 Sircar Medical College, Calcutta

AND

A. DAS, M.B., M.R.C.P.

Professor of Medicine, Nilratan Sircar Medical College,
 Calcutta

Splenoportal venography by percutaneous injection into the splenic pulp was first performed by Boulvin *et al.* in 1951. A large number of splenoportal venograms have been carried out by different observers and much useful information has been gathered from visualization of the portal circulation. The communication by Atkinson *et al.* (1955) is particularly valuable in this respect. We became interested in the procedure after reading the paper by Dreyer and Budtz-Olsen (1952), and since that time a series of 46 successful splenoportal venograms have been performed by the method of percutaneous injection into the splenic pulp.

Most of these cases were subsequently operated upon for splenectomy, or splenorenal shunt, or ligation of hepatic and splenic arteries. Opportunity therefore presented itself for correlating the pre-operative assessment of the splenoportal circulation, as judged by the venographic procedure, with the actual anatomical state of the circulation, the portal venous pressure, and the naked-eye and histological state of the liver.

This communication is based mainly on the findings of the cases subjected to operation, but also includes a few cases which were not operated on but in which the splenoportal venograms were studied and interpreted along with the clinical diagnosis.

Certain suggestive venographic patterns have been formulated as a result of this study.

Clinical Material and Investigation

Of 54 cases in which splenic venography was attempted, successful venograms giving significant information were obtained in 46 (see Table), 5 were unsuccessful owing to spasm of the splenic vein, and in 3 others the findings were inconclusive. Operations were carried out in 32 cases—12 of tropical splenomegaly of uncertain origin, 10 of splenomegalic cirrhosis, 6 of portal cirrhosis, and 4 of

Analysis of 46 Cases with Successful Venograms

Nature of Case	Operated	Non-operated	Total
1. Tropical splenomegaly ..	12	0	12
2. Intrahepatic obstruction ..	4	2 (1 confirmed at necropsy)	6
3. Cirrhosis of liver:			
Splenomegalic ..	10	3	13
Portal ..	6	2	8
Biliary ..	0	1	1
Nodular hyperplasia ..	0	1	1
4. Suprahepatic obstruction ..	0	5	5
Total ..	32	14	46

intrahepatic obstruction of the splenoportal system. In each of these cases, the portal venous pressure was measured at the time of operation, the naked-eye appearance of the liver noted, and a biopsy taken. When splenectomy was performed the weight of the spleen was recorded and its histology subsequently studied.

The series of 14 cases which were not operated on included 3 of splenomegalic cirrhosis, 1 of biliary cirrhosis, 2 of portal cirrhosis, 1 of nodular hyperplasia following subacute hepatic necrosis, and 2 of intrahepatic obstruction of the splenic vein. In one of the cases in this last group obstruction of the splenic vein was confirmed at necropsy. In the remaining 5 cases the clinical features were suggestive of suprahepatic obstruction of the hepatic venous system.

Results

As a result of this study it seems that the venographic appearances fall into four characteristic patterns.

1. *Pattern of Tropical Splenomegaly of Uncertain Origin* (12 cases, all operated on).—In this type the splenic and portal veins were very dilated and tortuous. In the absence of secondary cirrhotic changes in the liver, collaterals were not present in any case. The bifurcation of the portal vein at the porta hepatis was well seen. The intrahepatic radicals were very faint and the peripheral branches were indistinct. However, in a few cases, when they were faintly visualized, the pattern did not show any distortion (Fig. 1).

2. *Pattern of Intrahepatic Obstruction* (6 cases: 4 operated; 1 not operated; 1 proved by necropsy).—In splenic vein obstruction the dye terminated abruptly at some part in its course (Fig. 2), whereas in cavernomatous transformation of the portal vein (Fig. 3) the dye became diffusely distributed over numerous small tortuous channels (Das and Basu, 1956). In both cases many collaterals were present.

3. *Pattern of Intrahepatic Obstruction due to Cirrhosis of Liver* (23 cases; 16 operated; 7 not operated).—This group can be subdivided into two categories.

FIG. 1.—Venogram in a case of tropical splenomegaly, showing marked dilatation and tortuosity of the splenic and portal veins. The intrahepatic radicles are poorly seen.

(i) *Pattern of Pure Portal Cirrhosis* (8 cases).—Here the prominent features were (a) distortion, poor visualization, and absence of regular and dichotomous branching of the peripheral intrahepatic radicles; (b) pooling of the dye, often at the site of the proximal intrahepatic radicles; and (c) presence of numerous collaterals, directed upwards as well as downwards. The splenic and portal veins were more or less of normal calibre. The collaterals most commonly seen were those of the left gastric and paraoesophageal series. The inferior mesenteric vein was very commonly visualized. In the main there are two types of appearances. In one the contrast medium is concentrated in a few of the larger branches in the substance of the liver near the hilum. Often there is pooling of the dye at this site. The peripheral branches are not seen at all. The overall appearance is like that of a withered tree (Fig. 4). In another type the peripheral branches are better visualized, but the regular dichotomous branching of the radicles is absent. Both distortion and contraction of the intrahepatic branches are present (Fig. 5).

FIG. 2.—Obstruction of the splenic vein with large upwardly directed collaterals. Portal vein and intrahepatic channels not seen.

peripheral branches are not seen at all. The overall appearance is like that of a withered tree (Fig. 4). In another type the peripheral branches are better visualized, but the regular dichotomous branching of the radicles is absent. Both distortion and contraction of the intrahepatic branches are present (Fig. 5).

(ii) *Pattern of Secondary Portal Cirrhosis Following Long-standing Splenomegaly (splenomegalic cirrhosis)* (13 cases: 10 operated; 3 non-

operated).—Here, although the collaterals were present in many cases and the intrahepatic radicles were similarly distorted, pooled, and partly visualized peripherally, the main splenic and portal veins were dilated and tortuous (Fig. 6). There were two other cases in which the venographic pattern was akin to that described for splenomegalic cirrhosis: one was a case of biliary cirrhosis, and the other a case of nodular hyperplasia of the liver following subacute hepatic necrosis.

4. *Pattern of Suprahepatic Obstruction* (5 cases, not operated).—In this type the intrahepatic radicles of the portal vein were very prominent and were well visualized right up to the periphery. Unlike the pattern in cirrhosis of the liver, there was no distortion of these intrahepatic channels, nor was there any evidence of pooling of the dye (Fig. 7). Collaterals were present in three cases.

Discussion

Amongst the series of tropical splenomegalies without cirrhosis operated on, the weights of the spleens ranged between 1,100 and 3,000 g. Nine had portal venous pressures below 200 mm. of saline and in two others the pressure

was 200 and 300 mm. of saline. In all cases the splenic as well as the portal vein were greatly dilated in spite of there being no significant hypertension in nine. This dilatation was therefore caused by the large splenic effluent and is not an indication of portal hypertension. The absence of collaterals in any of the cases lends support to this view. The tortuosity of the vein is due to the large splenic mass causing distortion of the course of the vein. It was not necessarily due to mechanical displacement of the spleen at the time of injection, as suggested by Fuld and Irwin (1954). This was confirmed at operation in many cases. The faint visualization of the undistorted intrahepatic radicles was presumably due to two factors: dilution and diffusion of the dye on reaching the liver, and its rapid transit through an unobstructed portal bed.

The mechanism of the venographic pattern in the infrahepatic obstruction group is easily understood and has been confirmed in four out of the six cases. In one case—in which the venogram suggested cavernomatous transformation of the portal vein, with numerous upwardly directed tortuous collaterals involving the left gastric, the short gastric, and other unidentifiable veins (Fig. 3)—the anatomical pattern was confirmed at operation. The portal vein was absent and the numerous collaterals could be seen coursing upwards towards the cardia. In three other cases of obstruction of the splenic vein (as judged by venography) the diagnosis as regards the site of obstruction and the nature of collaterals was confirmed in two at operation and in the other at necropsy (Das and Basu, 1956). In another case of portal cirrhosis of the liver the venographic appearance suggested thrombosis of the portal vein (Fig. 8). The contrast medium terminated at the site of origin of the portal vein and was diverted through numerous collaterals. These findings were later confirmed at operation.

FIG. 4.—“Withered tree” appearance of the intrahepatic portal radicles in cirrhosis of liver. There are numerous collaterals, and the splenic and portal veins are not dilated.

FIG. 3.—Cavernomatous transformation of the portal vein. The dye is diffusely distributed at the site of the portal vein and there are numerous upwardly directed collaterals.

FIG. 5.—Absence of regular dichotomous branching of the intrahepatic radicles in a case of cirrhosis of liver. There is pooling of the dye at places. Numerous collaterals are present.

The venographic pattern in cirrhosis of the liver is more obscure and requires careful elucidation. A careful review of our material shows that the intrahepatic radicles are distorted by the fibrotic process. Further, the degree of distortion is roughly proportional to the extent of the fibrosis. The left main branch of the portal vein at the hilum of the liver was often not seen at all. In general, these findings are in conformity with those of Atkinson *et al.* (1955).

Additional features in this pattern are the presence of numerous collaterals, which is explained by the degree of portal hypertension. In our cases this ranged between 340 and 385 mm. of saline. The lumen of the splenoportal trunk was not dilated in the absence of significant splenomegaly. We therefore feel that portal hypertension, *per se*, does not necessarily lead to dilatation of the splenic and portal veins.

As is to be expected, when cirrhosis had supervened in long-standing cases of splenomegaly, the pattern was a mixed one—showing dilatation and tortuosity of the splenoportal system, characteristic distortion of the intrahepatic radicles, and presence of collaterals. The same expected pattern was seen in a case of biliary cirrhosis and one of subacute hepatic necrosis, both associated with splenomegaly. The enlarged spleen in these two cases contributed to the dilatation of the splenic vein.

In five of our cases the venographic pattern was found to be significantly different from other types, particularly with regard to the intrahepatic channels. Four of these cases conform to the clinical picture described for veno-occlusive disease of the liver (Stuart and Bras, 1955). One of these was a case of polycythaemia vera, and the histological appearances of the liver biopsy material was highly suggestive of suprahepatic obstruction. The fifth case was one of congestive cardiac failure with hepatomegaly. The intrahepatic radicles were well seen right up to the periphery of the hepatic parenchyma. They showed normal regular dichotomous branching. There was no distortion or contraction of the branches, and pooling of the dye was not seen. Collaterals were present in three cases, and their visualization presumably depended upon the degree of the portal hypertension. This type of appearance may be attributed to obstruction to the outflow of the blood from the liver that may result from hepatic venous thrombosis or from rise of pressure in the inferior vena cava through congestive cardiac failure or constrictive pericarditis. We have therefore called this type the pattern of suprahepatic obstruction. In later stages of this type actual cirrhotic changes in the liver may supervene and alter the characteristic venographic pattern.

This investigation indicates that portal hypertension can be assessed with a fair degree of accuracy from the venographic patterns. The presence of collaterals is the most significant indication in this respect. For example, of the

FIG. 6.—Appearance in a case of splenomegalic cirrhosis. The splenic and portal veins are dilated and tortuous, and collaterals are present.

FIG. 7.—Appearance suggestive of suprahepatic obstruction. The intrahepatic radicles are well visualized up to the periphery and there is normal dichotomous branching. Collaterals are present.

FIG. 8.—Non-visualization of the portal vein due to thrombosis in a case of cirrhosis of liver. Numerous collaterals are present.

six cases of portal cirrhosis—which were operated upon in our series of cases—collaterals were present in five. In each of these the portal pressure was above 300 mm. of saline. On the other hand, preoperative clinical indications of portal hypertension, such as recurrent haematemesis (2 cases), presence of prominent abdominal venous collaterals (4 cases), ascites (4 cases), and oesophageal varices as seen in skiagraphy (2 cases), were less frequent.

Similarly in cases of tropical splenomegaly, those showing collaterals on venography invariably had raised portal venous pressure and cirrhotic changes in the liver. By contrast, in cases of splenomegaly without collaterals there was no significant portal hypertension. There were, however, rare exceptions to this general observation.

In our opinion, therefore, the presence of collaterals in splenoportal venography is a positive indication of portal hypertension and appears earlier than other clinical evidences.

Portal venography, it seems to us, is also of value in the assessment of liver cirrhosis. The changes in the intrahepatic pattern described previously and the presence of collaterals together give an accurate estimate of the presence as well as of the extent of the fibrotic process of the liver.

Before operation, infrahepatic obstruction can be diagnosed with certainty by portal venography alone. Not only can the site of obstruction be accurately determined but often its nature can also be assessed.

With regard to suprahepatic obstruction, although we have suggested a characteristic venographic pattern on the basis of our clinical experience, further confirmation is necessary by operation, necropsy examination, or catheterization studies of the hepatic veins.

Venographic appearances in all these types of cases could be of great help to the planning of the operation—as regards both its indication and its nature. In tropical splenomegaly the absence of collaterals and the normal appearance of the intrahepatic radicles would signify absence of portal hypertension and liver changes and therefore splenectomy alone would be justified. On the other hand, the presence of such changes would often indicate a shunt procedure in addition. In infrahepatic obstruction the venogram would help the surgeon to anticipate the exact site and often the nature of the obstruction. For splenic vein obstruction, splenectomy would suffice in many cases, whereas in cases of portal vein obstruction a shunt operation would again be indicated.

In portal hypertension due to cirrhosis of the liver, visualization of a patent portal vein would enable the surgeon to plan a portacaval shunt if necessary, whereas its non-visualization—as in one of our cases—would indicate portal vein thrombosis and would preclude such a procedure. Further, the presence of secondary portal hypertension in cases of suprahepatic obstruction, as judged by the presence of collaterals, would lead to consideration of portacaval anastomosis.

Summary and Conclusion

Splenoportal venography has been performed successfully in 46 cases, 32 of which were operated on. The operative findings are correlated with the venographic appearances.

The clinical material consisted of 12 cases of tropical splenomegaly of uncertain origin, 13 cases of splenomegalic cirrhosis, 8 cases of portal cirrhosis, 1 case of biliary cirrhosis, 1 case of subacute hepatic necrosis with nodular hyperplasia, 6 cases of infrahepatic obstruction, and 5 cases of suprahepatic obstruction.

Four types of characteristic venographic patterns are described and discussed. These are for: (a) tropical splenomegaly of uncertain origin uncomplicated by cirrhosis of the liver; (b) infrahepatic obstruction of the portal venous system; (c) intrahepatic obstruction due to cirrhosis of the liver and splenomegalic cirrhosis; and (d) suprahepatic obstruction of the hepatic venous outflow.

The value of portal venography in assessing the presence of portal hypertension and cirrhosis of the liver is discussed. Visualization of the collaterals is one of the earliest indications of portal hypertension.

In infrahepatic obstruction, portal venography gives an accurate indication of the site and some indications of the type of obstruction.

The venographic findings could be of great help in the planning of a suitable operative procedure in abnormalities of portal circulation.

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NEOSTIGMINE-RESISTANT CURARIZATION

BY

A. R. HUNTER, M.D., F.R.F.P.S., F.F.A.R.C.S.
Anaesthetist, Royal Infirmary, Manchester

One of the greatest attractions of the competitive myoneural blockers is their reversibility by antidote drugs. Indeed, it has become almost an article of faith with those who use agents of this type that it is safe to maintain curarization right up to the time at which the abdomen is closed, in the sanguine expectation that the paralysis will then be undone by neostigmine. It was therefore somewhat disquieting to be called by a registrar some two years ago to see a patient in whom the administration of this drug had failed to produce the expected recovery. Since that date four other cases of this type have been reported to me by registrars. Details of a sixth case were received from another source.

The Syndrome

In every instance the patient was elderly and dilapidated, and yet, though ill, was fit by ordinary standards for general anaesthesia. After premedication with morphine and atropine or papaveretum and scopolamine in safe amounts, anaesthesia was induced with a suitably small dose of thiopentone; the patients were intubated with the aid of suxamethonium, and breathing began again after a perfectly normal interval of a minute or two. Subsequently, anaesthesia was maintained with nitrous oxide and oxygen, together with small doses of pethidine and thiopentone. Relaxation was obtained in four of the cases by giving gallamine triethiodide and in two from D-tubocurarine. In none of the cases was the dose excessive for the duration and magnitude of the operation performed. At the end of the operation neostigmine was given in two lots of 2.5 mg., each with 1/100 gr. (0.65 mg.) of atropine. Spontaneous respiration returned, but in every case its amplitude was insufficient to maintain life. The patients continued with depressed respiration until, in spite of adequate assistance of the breathing, death from circulatory failure ensued some 6 to 8 hours after the end of the operation.

Apart from maintenance of adequate ventilation the following resuscitative measures were employed.

Vasopressor drugs were given in all instances to maintain the blood pressure when it declined. "Tensilon" was given to three of the six patients in repeated doses of 10 mg. with sufficient atropine (usually 1/200 gr.—0.32 mg.) to prevent muscarinic effects. It produced only an evanescent improvement in the breathing, which after some five minutes returned to its previously depressed inadequate level. Additional increments of 1.25 mg. of neostigmine also improved the situation a little in these cases, but there was again a tendency to relapse after some 10 to 20 minutes. In no case was it possible to obtain complete recovery by giving this drug, but its administration never aggravated the situation. All the patients received a large dose of nikethamide, which produced in its turn an even more poorly sustained period of recovery. The intravenous administration of potassium in the form of Nabarro's solution was tried in two of the cases. In one of these there was a definite improvement, although completely normal respiration did not recover before ultimate circulatory failure occurred. In the other instance where this solution was used no response whatever was obtained.

The surgical conditions from which these patients were suffering were all of the nature of an ileus with or without peritonitis. Two of them had acute cholecystitis. In another case the source of the infection was not apparent even at necropsy, and in yet another a 36-hour perforation of a