Factors Influencing Portal Pressure in Banti's Syndrome*

By

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Factors responsible for elevation of the portal pressure in Banti's syndrome were analyzed in 82 cases of the authors' department. Although the elevation of the portal pressure was more common and usually more remarkable in extent in cases with chronic inflammation or fibrosis than in those with liver cirrhosis, no definite correlation was revealed between the extent of the hepatic fibrosis and the portal pressure. However, the grade of intrahepatic obliteration of portal branches appeared to be a significant factor influencing the portal pressure. A correlation was indicated between the grade of splenomegaly and the portal pressure, although there were a considerable number of exceptional cases. Moreover, splenectomy was generally followed by a decrease in portal pressure, especially in the case of markedly elevated pressure, although the post-operative level was still above normal in most instances. From these observations both the splenic and the hepatic factors seem to be concerned with the increased portal pressure.

The hematology¹⁾, esophageal varices²⁾, and functions and histopathology of the liver^{3,4)} associated with Banti's syndrome have been presented in previous papers. Following these observations, the present communication is concerned with factors leading to the increase of portal pressure in this syndrome.

MATERIALS AND METHODS

Subjects of the study were 82 cases of Banti's syndrome treated in the authors' clinic⁵⁾. Control values were obtained from 50 cases with stomach, bile duct and spleen diseases; these were the same patients used for control data in a previous report²⁾. Portal pressure was analyzed both from the hepatic and splenic aspects. The method for measuring portal pressure was described previously²⁾.

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RESULTS

I. Hepatic Factors

1. *Histopathology*

The hepatic histopathology was classified into three main types, as in a previous report³⁾ (Type I, practically normal histology; II, chronic inflammation or fibrosis arising at the Glisson capsules and extending around them; and III, established cirrhosis), and portal pressure was studied for each type, (Fig. 1). Cases with an extrahepatic occlusion of the portal vein were excluded from this study.

Fig. 1. Relation between the type of hepatic histopathology and the portal pressure.

All but one of the four cases of the Type I histology showed a pressure below 210 mm H₂O; the pressure of the exceptional case, with the spleen weighing 1200 g, was as high as 350 mm H₂O. In 52 cases of the Type II histology, the pressure was below 200 mm H₂O (normal) in five cases, between 200 and 300 mm H₂O in 13, between 300 and 400 mm H₂O in 27 and 400 mm H₂O or higher in seven, 65.4 per cent of the total showing a markedly elevated level of more than 300 mmH₂O. The highest pressure observed in this group was 550 mm H₂O. In the group of Type III histology, four of the 10 cases (40.0 per cent) had a pressure of more than 300 mm H₂O but there were no cases of pressure above 400 mm H₂O. This

group also included four cases with a pressure between 300 and 400 mm H₂O and one case of normal portal pressure (130 mm H₂O).

It was thus revealed that markedly increased pressure was more frequent in cases of fibrosis of the Glisson capsules than in those of established cirrhosis of the liver.

2. *Intrahepatic portal obliteration*

The peripheral branches of the intrahepatic portal vein were identified in Goldner stained tissue slices, and the grade of obliteration of each vessel was expressed on a three-point scale as follows: Negative (-), when there was no evidence of disturbed blood flow (Fig. 2); moderate (+), when the lumen of the vessel was considerably narrowed either by a thickening of the wall due to phlebosclerosis or by a compression from outside by proliferated fibrous tissues (Fig. 3); and marked (++), when the lumen was little or not patent (Fig. 4). Central segments of the portal branches near the hepatic hilus were excluded from consideration. A number of Glisson capsules were studied by this method and the frequency of each grade of obliteration was calculated as a percentage.

Fig. 2. Photomicrogram showing a normal (not obliterated) portal vessel.

Fig. 3. Photomicrogram showing a moderately obliterated (+) portal vessel.

Fig. 4. Photomicrogram showing a markedly obliterated (++) portal vessel.

Specimens with stromal fibrosis so extensive as to preclude identification of the Glisson capsules were not subjected to this study.

1) Control cases

Fig. 5 shows the distribution of obliterated portal branches in 34 cases of gastric disorders (22 cases of carcinoma, eight of peptic ulcer, and one each of

Fig. 5. Frequency of obliteration of intrahepatic portal branches in control cases with stomach diseases.

polyp, diverticulum, chronic gastritis and another condition). The incidence of markedly obliterated (+) vessels was below 10 per cent in 10 cases, 10 to 20 per cent in 23, and above 20 per cent in one. All but one of the cases in this group (97.1 per cent) thus showed a frequency of markedly obliterated (+) vessels of 20 per cent or less.

For evaluating the relation between the portal pressure and the obliteration of portal branches, only a marked obliteration (+) was taken into consideration. The incidence of markedly obliterated vessels, in per cent, will be referred to as the obliteration ratio. The result of analysis is shown in Fig. 6, taking the portal pressure on the ordinate and the obliteration ratio on the abscissa. No significant correlation was found between portal pressure and the obliteration ratio.

Fig. 6. Relation between the intrahepatic obliteration of portal branches and the portal pressure in control cases with stomach diseases.

The group of bile duct disorders included six patients of cholecystolithiasis, three of choledocholithiasis and two of carcinoma of the common duct (Table I). The obliteration ratio was less than 25% in all the cases of lithiasis but was above 25% in both cases of carcinoma in which the liver tissues showed a considerable fibrosis around the Glisson capsules. On the other hand, all the cases of lithiasis showed a normal portal pressure of less than 200 mm H₂O and the pressure was 220 mm H₂O in one of the carcinoma cases and 180 mm H₂O in the other. In this group no significant correlation was found between the obliteration ratio and the portal pressure.

The six cases of the group of spleen disorders were patients with hemolytic jaundice (Table II). The pressure was within the normal range and the obliteration ratio below 25% in all cases; there was no significant correlation between them.

In summary, all the control cases, except two choledochus carcinoma cases

TABLE I. Portal Pressure and Frequency of Obliteration of Intrahepatic Portal Branches in Bile Duct Diseases

Case	Age and sex	Diagnosis	Portal pressure (mmH ₂ O)	Frequency of obliteration (%)		
				++	+	-
1	51 F	cholecysto-lithiasis	130	15.3	5.1	79.6
2	63 F	"	135	15.4	10.6	74.0
3	68 F	"	140	9.7	11.3	79.0
4	62 F	"	146	12.9	12.9	74.2
5	52 M	"	170	17.3	25.9	56.8
6	43 F	"	180	9.1	11.7	79.2
7	58 M	choledocholithiasis	125	20.6	19.6	59.8
8	66 F	"	130	23.8	8.6	67.6
9	56 F	"	150	16.1	19.4	64.5
10	58 M	choledochus carcinoma	180	36.4	16.3	47.3
11	44 M	"	220	29.7	35.1	35.2

TABLE II. Portal Pressure and Frequency of Obliteration of Intrahepatic Portal Branches in Hemolytic Jaundice

Case	Age and sex	Diagnosis	Portal pressure (mmH ₂ O)	Frequency of obliteration (%)		
				++	+	-
1	28 F	hemolytic jaundice	110	19.8	13.5	66.7
2	38 F	"	160	14.5	17.0	68.5
3	13 F	"	160	12.7	18.2	69.1
4	30 F	"	170	13.0	13.9	73.1
5	54 F	"	190	22.0	10.0	68.0

with considerable fibrosis of the hepatic stroma, showed an obliteration ratio of less than 25% and a portal pressure of less than 200 mm H₂O, without showing a significant correlation between the two variables.

2) Banti's syndrome

Twenty nine cases were subjected to the analysis. As shown in Fig. 7, the incidence of markedly obliterated (++) portal branches was less than 25% in only six cases, 25 to 50% in 20 and more than 50% in three; in contrast to the control, obliteration ratios of more than 25% were found in the majority (79.3 per cent) of cases.

The relation between the obliteration ratio and the portal pressure is shown in Fig. 8. Twenty-two of the 29 cases (75.9 per cent) had both an obliteration ratio of more than 25% and a portal pressure of more than 200 mm H₂O, indicating that the portal pressure was generally high in cases of high obliteration ratio.

Fig. 7. Frequency of obliteration of intrahepatic portal branches in cases of Banti's syndrome.

In three of six cases with an obliteration ratio below 25%, the portal pressure was 140 mm H₂O, 185 mm H₂O and 210 mm H₂O, but the pressure was as high as 260 mm H₂O, 350 mm H₂O and 500 mm H₂O in the remaining three cases. In all of the latter three cases splenomegaly was remarkable (the weight of the spleen being 1350 g, 1200 g and 1100 g, respectively) but an extrahepatic occlusion of the portal vein was not observed. Two of three cases of an obliteration ratio more than 50% (54.8% and 68.0%) showed only a moderately elevated portal pressure (290 mm H₂O and 240 mm H₂O, respectively).

Thus, although it was a general finding that higher obliteration ratios were associated with the higher portal pressures, there were a few exceptional cases. Therefore, the data were then subjected to a statistical analysis. The linear regression of the portal pressure (Y , in mm H₂O) over the obliteration ratio (X , in %) was first estimated to be as follows:

$$Y = 1.18X - 244.7$$

In this situation the rejection limits of Y at a level of significance of 5 per cent are obtainable for a given value of X (X_0) by the following formula:

Fig. 8. Relation between the intrahepatic obliteration of portal branches and the portal pressure in cases of Banti's syndrome.

$$Y_0 \pm t_{0.05} \sqrt{\frac{S_E}{N-2} \left\{ \frac{N+1}{N} + \frac{(X_0 - \bar{X})^2}{S_X} \right\}},$$

at which Y_0 stands for the theoretical value of Y for the given X_0 , N for the number of cases, $\bar{X}$ for the mean value of X , S_X for the square sum of deviation of X from $\bar{X}$, S_E for the square sum of deviation of Y from the regression line, and $t_{0.05}$ for the value of t function at 5 per cent probability. Actually performing calculations, all cases except one were found to be within the rejection limits. The exceptional one, shown in the graph by a cross, was the case showing an obliteration ratio of 17.4% and a portal pressure 500 mmH₂O. When this case was excluded, the linear regression became

$$Y = 2.09X + 205.6$$

and was as shown in Fig. 8. The correlation was significant at a level of significance of 5 per cent, with a correlation coefficient $r = +0.389$.

II. Splenic Factors

In this chapter the relation between the grade of splenomegaly and the portal pressure as well as the post-splenectomy change of portal pressure is

presented. The relation of the portal pressure to the histopathology of the spleen will be reported elsewhere.

1. *Grade of splenomegaly*

Since the weight of the spleen changes with age, the observed weight was divided by the standard weight for age⁶⁾ and the quotient represented the grade of splenomegaly. Table III shows frequency distribution of such grade of splenomegaly in 82 cases of Banti's syndrome. The frequency was the highest for a grade ranging from 7 to 10. The largest value observed in this series was 29.

Fig. 9 shows a scatter diagram of the grade of splenomegaly and the portal pressure in 66 patients for whom both the variables were available. Of 14 cases with a grade of splenomegaly less than 5, the portal pressure was normal in six

TABLE III. Splenomegaly in Banti's Syndrome

Grade of splenomegaly*	No. of cases
2.0—3.0	5
3.0—5.0	16
5.0—7.0	14
7.0—10.0	21
10.0—15.0	18
15.0≤	8
Total	82

* Quotient of the measured to the expected weight⁶⁾ of the spleen.

Fig. 9. Relation between the grade of splenomegaly and the portal pressure in cases of Banti's syndrome.

cases, ranged between 200 and 300 mm H₂O in three, and 300 mm H₂O or higher in five; the last cases included two patients who showed portal pressure as high as 400 mm H₂O and 480 mm H₂O. In 29 cases of a grade of splenomegaly 5 or more but less than 10, the majority (15 cases) showed a pressure between 200 and 400 mm H₂O; none of the cases was in the normal range and the pressure was as high as 550 mm H₂O in one case in this group. Of 15 cases of a grade of splenomegaly between 10 and 15 most (12 cases) showed a pressure above 300 mm H₂O, including three cases of 400 mm H₂O or higher, but this group also included two cases with only moderately increased portal pressure (200 to 300 mm H₂O) and one with normal pressure (130 mm H₂O). Of eight cases with a grade of splenomegaly 15 or more, six showed a portal pressure of 300 mm H₂O or higher and two in a range between 200 and 300 mm H₂O. In a case with a grade of splenomegaly 29 (3360g in actual weight), the pressure was 430 mm H₂O.

Thus there was a tendency for higher grades of splenomegaly to be associated with higher portal pressures, but there was a considerable number of exceptional cases in which remarkable splenomegaly was not always associated with a remarkable increase in portal pressure.

2. *Effect of splenectomy on portal pressure*

The change in portal pressure after splenectomy was analyzed in 38 cases from two different viewpoints: The pressure before splenectomy and the grade of splenomegaly. The post-splenectomy pressure refers below to that measured at operation after removal of the spleen, before closure of laparotomy.

1) Relation to the pre-splenectomy pressure. For convenience, the cases were divided into four groups according to the portal pressure before splenectomy. The post-splenectomy change in portal pressure for each of these groups is shown in Fig. 10.

Of four cases with a pre-splenectomy pressure less than 200 mm H₂O, splenectomy was followed by a moderate decrease in pressure in three cases; the maximum and average decrements in this group were 45 mm H₂O and 16 mm H₂O, respectively. In the group of 200–300 mm H₂O, all but two of 16 cases showed a marked decrease of pressure, the maximum decrement being 130 mm H₂O and the average 54 mm H₂O. All 15 cases of the group of 300–400 mm H₂O showed a decrease and the maximum and average of the decrement were 140 mm H₂O and 88 mm H₂O, respectively. In two among three cases of the group of 400 mm H₂O or higher, the pressure decreased from 500 mm H₂O to 360 mm H₂O and from 480 mm H₂O to 250 mm H₂O, but the pressure remained little changed in the third case. The average decrement in this group was 127 mm H₂O.

It was thus revealed that the portal pressure generally decreased after splenectomy and the higher the pre-splenectomy pressure the more remarkable the subsequent decrease. Table IV summarizes the distribution of portal pressure before and after splenectomy. By splenectomy, the incidence of a markedly

Fig. 10. Decrease of portal pressure after splenectomy by the pre-operative pressure. Figures in parentheses indicate average decrements.

TABLE IV. Portal Pressure before and after Splenectomy

Portal pressure (mmH ₂ O)	≤200	200-300	300-400	400≤	Total
Before splenectomy	4	16	15	3	38
After splenectomy	11	24	2	1	38

elevated pressure higher than 300 mmH₂O was reduced from 18 cases to on three of 38 cases. However, 24 cases still showed a moderately elevated level (200-300 mm H₂O) after operation.

2) Relation to the grade of splenomegaly. The relation between the grade of splenomegaly and the post-splenectomy change in portal pressure is shown in Fig. 11. The grade of splenomegaly was divided into three classes: Less than 5-10 and 10 or more.

In one of eight cases with a grade of splenomegaly less than 5. The post-splenectomy decrease of portal pressure was remarkable (from 480 mm H₂O pre-operatively to 250 mm H₂O), but the decrease was moderate in the others, the average decrement in this group being 56 mm H₂O. In 21 cases of the second

Fig. 11. Decrease of portal pressure after splenectomy by the grade of splenomegaly. Figures in parentheses indicate average decrements.

group (the grade of splenomegaly 5-10), two showed little change (within 20 mm H₂O) but all other cases revealed a large decrement up to 140 mm H₂O; the average decrement was 74 mm H₂O in this group. Of nine cases with a grade of splenomegaly 10 or more, the extent of post-operative decrease of pressure varied, the average decrement being 59 mm H₂O.

In summary, there was some correlation between the grade of splenomegaly and the decrement of portal pressure following splenectomy. However, 15 of 21 cases of the group of grade 5-10 still showed a portal pressure of more than 200 mm H₂O and the average decrement of portal pressure was less in the group of grade 10 or more cases than in the grade 5-10 group. Both of these facts suggest a limited significance of splenomegaly as a factor elevating the portal pressure.

DISCUSSION

It has long been discussed whether the increase of portal pressure is caused by hepatic or splenic factors, as yet there is no conclusive solution. The present authors have also studied this problem, using 82 cases of Banti's syndrome treated in their clinic.

First, when the cases were studied from the viewpoint of hepatic his-

topathology, a markedly elevated portal pressure was found much more frequently in cases showing fibrosis of the Glisson capsules (Type II of the authors' nomenclature) than in those with established cirrhosis (Type III). This fact suggests that there is little relation between the portal pressure and the grade of fibrosis in the liver.

The above observation agrees with most of the previous reports. That the elevation of portal pressure was little related to the grade of cirrhosis of the liver was shown by Kimoto *et al.*⁷⁾ Whipple⁸⁾ pointed out that there are large individual variations of portal pressure in cases of cirrhosis of the liver, even between comparable grades of cirrhosis, and also that there is an unnegligible time fluctuation. Cohn⁹⁾ presented cases of unquestionable cirrhosis of the liver showing a normal portal pressure. Furthermore, from an analysis of the relation between the decrease of portal pressure following shunt operations and the condition of anastomoses at a remote time, Raynolds *et al.*¹⁰⁾ suggested the possibility of spontaneous regression of portal hypertension.

There are a number of different opinions as to the hepatic genesis of portal hypertension. Kimoto and Sugiura¹¹⁾ believed an excessive inflow of the arterial blood or a hemodynamic unbalance between the artery and the draining vein (hepatic vein) of the liver to be a significant factor. Herrick¹²⁾ and, later, Saegesser¹³⁾ assumed the development of abnormal shunts between the arterial and portal systems of the liver to be a cause of hypertension. On the other hand, McIndoe¹⁴⁾, Kely *et al.*¹⁵⁾ and Popper *et al.*¹⁶⁾ presented hypotheses to the effect that fibrosis, or regenerated nodules of the parenchyma, exerts compression to the portal or hepatic venous branches increasing resistance against blood flow and leading to an increase of portal pressure. Elias and Petty¹⁷⁾ and Kalk¹⁸⁾, thought both a narrowing of the vessels and an influence of the arterial pressure to be significant in the development of portal hypertension.

That the pathophysiologic feature of Banti's syndrome cannot always be explained by extrahepatic occlusion of the portal vein was evidenced by many investigators especially by those in Japan¹⁹⁻²²⁾. Rousselot²³⁾, one of those who developed the occlusion theory of portal hypertension, observed an elevated portal pressure which was associated neither with extrahepatic portal occlusion nor with cirrhosis of the liver in 15 of 31 cases of Banti's syndrome, and admitted that the result was against the theory. Similar observations were also made by Ravenna^{24,25)}. To interpret such phenomena, a variety of hypotheses have been presented, including the opinion that intrahepatic and extrahepatic sclerosis of the portal system plays a significant role,²⁶⁻²⁹⁾ an allergic theory^{30,31)}. On the other hand, Sakamoto³²⁾ observed a decrease in number of the intrahepatic portal branches in most instances of Banti's syndrome and believed this to represent obliteration of the vessels due to characteristic fibrosis at the Glisson capsules.

In the present series, the behavior of the intrahepatic portal branches was

investigated in 29 cases, excluding those in which fibrosis was so extensive that identification of the Glisson capsules was very difficult. To avoid subjective errors in judgement, the grade of obliteration of the vessel was expressed on a pre-established three-point scale and the frequency of each grade over the total number of observed vessels was calculated in per cent. Moreover, the frequency of completely or markedly obliterated (++) vessels was taken as the final measure of the portal obliteration (obliteration ratio).

In 50 control cases of various gastric, biliary and splenic disorders, all except two cases of carcinoma of the common bile duct showed an obliteration ratio of less than 25%. The portal pressure was normal (less than 200 mm H₂O) in all but one of these cases and there was no significant correlation between the pressure and the obliteration ratio of the portal branches. However, it should be noted that those cases of normal hepatic histology showed some obliterated intrahepatic portal branches, although the incidence was less than 25% in the majority. On the other hand, the majority (23 cases, 79.3 per cent) of the 29 cases of Banti's syndrome revealed an obliteration ratio of 25% or higher. Moreover, a statistically significant positive correlation was demonstrated between the obliteration ratio and the portal pressure.

It was therefore concluded, as far as the morphology of the liver was concerned, that the grade of portal obliteration, rather than the grade of fibrosis, is to some extent concerned with the portal pressure. This result indicates that a hepatic factor cannot be denied in the pathogenesis of an increase of portal pressure.

The incidence of splenomegaly in Laennec's cirrhosis was reported to be 74 per cent by Rössle³³⁾, 69 per cent by Eppinger³⁴⁾ and 50 per cent by Jäger³⁵⁾; the spleen in these cases weighed two to, at most, three times the normal weight. In 82 cases of the present observation the weight of spleen ranged from two to as much as 29 times the normal weight: From seven to 10 times in 21 cases and from 10 to 15 times in 18. The average weight of the spleen in Banti's syndrome in the Japanese was reported to be 845 g (300–1060 g) for autopsy cases and 995 g (400–2070 g) for surgical cases by Miyake *et al.*³⁶⁾ Therefore it is apparent that the spleen in Banti's syndrome in the Japanese is larger than that in hepatic cirrhosis.

Rousselot²³⁾, on the basis of actual pressure measurements, introduced the concept of portal hypertension and regarded an occlusive mechanism to the portal vein to be the cause. Linton *et al.*³⁷⁾ then classified portal hypertension into intrahepatic and extrahepatic categories, according to the site of occlusion, and thought that the latter condition led to a congestive enlargement of the spleen which was equivalent to Banti's syndrome. However, cases of Banti's syndrome without any evidence of intrahepatic or extrahepatic portal occlusion have been reported^{7, 24, 25, 38)}. Furthermore, a complete ligation or a partial narrowing of the portal vein failed to induced persistent splenomegaly in experimental studies^{39–43)}.

These facts question the proposition that an increase of portal pressure is actually the sole factor in the pathogenesis of splenomegaly. It is possible that the spleen itself plays a significant role in its own enlargement in Banti's syndrome.

Concerning this problem, the relation between the portal pressure and the grade of splenomegaly (the quotient of observed weight of the spleen to the expected standard weight) was studied in 66 cases of the present series and a tendency was found for higher grades of splenomegaly to be associated with higher portal pressures. There were, however, a considerable number of exceptional cases; five of 14 cases with a grade of splenomegaly less than 5 showed a markedly elevated portal pressure (300 mm H₂O or higher) and two of 18 with huge spleens (the grade being 15 or higher) had a portal pressure of less than 300 mm H₂O. Miyake *et al.*³⁶⁾ and Kimoto *et al.*⁷⁾ failed to establish a definite relationship between the weight of the spleen and portal pressure.

It is also known that splenectomy is immediately followed by a considerable decrease of portal pressure^{21,44,45)} and this fact has been understood to be owing to the loss of blood flow from the spleen into the portal system. The above phenomenon was confirmed in 38 cases of the present series and it was also shown that the higher the portal pressure the more remarkable the post-splenectomy decrease of portal pressure. This certainly suggests a significant role of the spleen in the pathogenesis of portal hypertension. However, since 24 of the 38 cases (63.2 per cent) still showed a pressure above normal after removal of the spleen, the splenic factor is supposed not to be an exclusive one.

Summarizing the above results, the portal pressure was revealed to be related significantly with intrahepatic obliteration of the portal branches and to some extent with the grade of splenomegaly. It was also shown that the portal pressure decreases after splenectomy in most instances, more markedly in cases with higher pre-splenectomy pressure. Therefore it may be concluded that both hepatic and splenic factors are concerned in the pathogenesis of Banti's syndrome; neither of these can be claimed to be insignificant.

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