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BANTI'S DISEASE AND SPLENIC ANAEMIA

SYMPTOMATOLOGY AND AETIOLOGY*

BY

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Banti's disease and splenic anaemia have been the cause of much discussion. There is no agreement on whether they are one disease or two, or even if either of them exists as an entity. The names are familiar, but in fact the disease is rare. Few practitioners see many cases and fewer still see them both in children and in adults.

The term "Banti's disease" is commonly used by paediatricians, who nowadays see nearly all the cases in children; it is also sometimes used in America for adults. In Britain adult cases are usually known as splenic anaemia. Textbook descriptions which treat them as one disease commonly present the following picture. "A chronic disease with an insidious onset characterized by splenomegaly, a moderate hypochromic anaemia distinguished by a definite leucopenia, a tendency to severe haematemesis, and terminating in a few cases after some years as cirrhosis of the liver. The spleen is greatly enlarged and often reaches below the umbilicus. Progress is slow and the disease may last twenty years or more." Such a description may serve for the type met with after middle age, but bears little resemblance to the disease as seen in children.

The following points on aetiology may be stated here. It is never hereditary, but may be familial. Neither alcohol nor syphilis is a factor.

Historical

Griesinger in 1866 first described "splenic anaemia" as a syndrome of splenomegaly and anaemia in adults. Banti wrote the first account of his disease in 1894 and published many communications between that date and 1910. He apparently began with a study of the disease in children and then extended it to adult life—thus overlapping Griesinger's adult splenic anaemia: he centred his attention on the spleen, which, like most authorities, he believed to be the essential factor. He described a special pathology for the spleen, a special clinical course for the disease, and a special aetiology. All these views encountered difficulties. In general they have been rejected both in Banti's lifetime and subsequently. Yet it is possible that there is more truth in them than has been commonly believed.

For the aetiology, he claimed that the disease was the result of an unknown toxin which acted primarily on the spleen and secondly but independently on the

liver. For the special pathology of the spleen Banti claimed two principal features, briefly as follows: (1) a fine widespread fibrosis, which does not prevent the spleen from enlarging or result in its subsequent contraction; and (2) proliferation of the endothelial cells of the venous sinuses of the pulp. He gave these changes the name "fibro-adénie." There are various minor points of pathology to which Banti attached importance which may be omitted here. It is agreed that there is no evidence of overactivity of the spleen or increased blood destruction. The pathology of the spleen undoubtedly distinguishes it from the changes in haemolytic and haemorrhagic anaemias. But in the stage of cirrhosis the pathology of the liver cannot be differentiated from alcoholic Laennec's cirrhosis. For the clinical course he described three stages: (1) a stage of enlargement of the spleen and a gradually developing anaemia—the stage lasting from 3 to 12 years; (2) a short transition stage of from 12 to 18 months in which the liver becomes enlarged, with the usual accompaniment of jaundice; (3) a terminal stage of atrophy of the liver, ascites, and cachexia, terminating in death as a rule within 12 months. No one has been able to follow a case through such a course.

It seems that Banti himself became confused in his later studies and articles, for he could not logically defend all his views, as he attempted to do. It must be remembered that he did not know of Gaucher's disease or of achlorhydric hypochromic anaemia, syphilis was not easily identified, alcoholism was rampant, and he was unaware that infective hepatitis and other factors could produce cirrhosis of the liver. It is possible that Banti was led astray by the occurrence of cirrhosis of the liver as the termination of infective hepatitis. Such a case may well give a history of an attack of jaundice with enlargement of the liver, which Banti may have accepted as an instance of his disease. He was certainly in error about the existence of his second stage.

The rarity of the disease makes it difficult to collect enough data. My own series is 15 males and 11 females. Of two cases formerly included, a female case must be omitted as probably being an achlorhydric hypochromic anaemia, and one case terminating in cirrhosis can now be recognized as a sequel of infective hepatitis.

We have thus to study a disease generally described as characterized by splenomegaly, hypochromic anaemia with leucopenia, recurrent haematemesis, and in some

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cases terminating in cirrhosis of the liver. Each of these four features will be considered separately and examined concerning their connexion with each other.

Splenomegaly

The spleen always enlarges but the size varies. In young children it is rarely more than 1 in. (2.5 cm.) below the costal margin, but it may reach the umbilicus. In later ages it may extend into the iliac fossa. Whatever the size, it remains smooth, uniform, and firm.

Relation to Anaemia and Leucopenia.—There is no direct relation between the size of the spleen and the degree of the blood changes and leucopenia. The spleen may be grossly enlarged for years before anaemia develops, and in no instance does it show signs of undue destruction of red cells. Splenectomy has no permanent effect on the anaemia: following the operation there are the usual transient changes of leucocytosis and rise in platelets, formerly mistaken for permanent improvement. The blood changes and the spleen thus are independent.

Relation to Haematemesis.—The incidence and the frequency of haematemesis are not related to the size of the spleen, to any previous enlargement or alteration, or to attacks of pain. Children rarely escape haematemesis, and the first attack often takes place before the spleen becomes palpable, though it is usually felt shortly after. Although haematemesis occurs in a high percentage of cases it may never happen in an adult even with a spleen chronically enlarged below the umbilicus. On the other hand, it may occur for the first time after splenectomy. Although the bleeding in splenic anaemia has often been attributed directly to the splenomegaly by torsion of the splenic vein by the enlarged spleen, these facts exclude such a theory. There is no evidence of a direct relationship between haematemesis and the spleen. It is noticeable that haematemesis is not an outstanding feature in other syndromes of splenomegaly and anaemia.

Relation to Cirrhosis of the Liver.—The development of clinical manifestations of cirrhosis of the liver is distinctly rare. It is commoner in children in whom the splenomegaly has not been more than moderate or of long duration, while it is very rare in adults with large chronic spleens. It may undoubtedly develop subsequent to splenectomy. With regard to the effect of splenectomy on existing cirrhosis with ascites, Howells (1938), in his large series of 94 cases with 51 operations, recorded three cases in which the patients lived for periods up to 18 years after splenectomy. This is exactly paralleled by three of his patients who lived for similar periods without splenectomy. Other conditions in which great enlargement of the spleen develops, such as Gaucher's disease or even in association with anaemia as in malaria, show no tendency to produce cirrhosis of the liver.

There is no evidence that the development of clinical cirrhosis of the liver with ascites results from the condition of the spleen or is influenced by splenectomy. Thus it seems that the enlargement and size of the spleen has no influence on the anaemia and leucopenia, and that it is not the cause of haematemesis or of development of clinical cirrhosis and ascites. It develops independently of and without influence upon the other manifestations of splenic anaemia. The theory has often been advanced that the spleen and the splenic vein are the central manifestations and the cause of the other features of the syndrome. Indeed, recently the term "congestive splenomegaly" has been put forward to cover Banti's disease and splenic anaemia.

Blood Changes

In adults there is a hypochromic anaemia, usually of moderate degree but necessarily increased after haematemesis. There is a definite leucopenia in the older patients, constituting a special feature of the blood changes.

Relation to Splenomegaly.—It has been shown above that there is no relation between the blood changes and the size of the spleen or splenectomy.

Relation to Haematemesis.—In children the blood count is commonly normal at the time of the first haematemesis. A striking feature is the rapidity with which the blood at this age returns to normal even with repeated bleedings. Leucopenia is rare. It is difficult to assess the influence of haematemesis in adults with pre-existing anaemia. Anaemia is mainly related to later life and the duration of the disease rather than to haemorrhage or splenomegaly. It is not influenced by splenectomy.

Cirrhosis of the Liver

Cirrhosis of the liver has to be considered from two separate aspects: (1) the development of the clinical picture of cirrhosis and ascites, and (2) pathological changes in the liver found at necropsy in the absence of clinical manifestations. We are here considering the development of the clinical manifestations.

As stated above, it is a rare termination of the syndrome. Young children most frequently die from a gross haematemesis—one may suppose before cirrhosis has had time to develop.

Care is necessary in evaluating pre-war statistics, especially in adults. The fact that infective hepatitis could progress to cirrhosis of the liver was not recognized until several years after the onset of the war. My own series of 25 cases, including 10 over 30 years of age, are all pre-war. One case of cirrhosis has now been excluded. This leaves two cases of cirrhosis, which are included, but I am doubtful about one of these.

In children the course can sometimes be watched through Banti's first and third stages, though of short duration, to the termination in cirrhosis. It can also occasionally be recognized in the decade of adolescence and the first decade of adult life. Presumably it may occur at any age, but, in spite of a moderate though admittedly by no means exhaustive study of the literature, I have not found conclusive evidence that it develops as a terminal stage in cases in the later decades with very large spleens.

Relation to Splenomegaly.—For reasons given above, splenomegaly cannot be assumed to be the cause of cirrhosis. Can the converse be true that the splenomegaly is the result of cirrhosis? The most commonly accepted explanation of the splenomegaly is that it is produced by rising pressure in the splenic vein. The increasing pressure is ascribed to cirrhosis of the liver, but no cause for cirrhosis is given. This explanation has been criticized. McNee (1932), in his Croonian Lectures, points out that in well-marked cirrhosis the spleen is not always palpable and rarely attains any great size. Clearly the cirrhosis cannot explain the splenomegaly. Nor does the splenomegaly account for the cirrhosis. The two features—cirrhosis and splenomegaly—have no direct relation to each other. The conclusion is that the splenomegaly, the anaemia and leucopenia, and the cirrhosis develop independently of each other. If this is correct there must be an agent which acts independently on the three structures.

Pathology of the Liver and Spleen

The most extensive study of the pathology of the liver and spleen in this group is due to McMichael (1934, 1935), much of his material being supplied by McNee. It is probable that some of the specimens belonged to other syndromes. The morbid histology is fully reported in his articles. His conclusions are briefly as follows.

Spleen.—Splenomegaly is not entirely accounted for by venous congestion. It is due in the main to some factor which produces hyperplasia of the reticulo-endothelial elements of the spleen.

Liver.—The liver is not always enlarged. It may look normal at operation on the spleen and at naked-eye examination after removal at necropsy, but may nevertheless be much diseased on section. Of 42 livers, disease was present in 35.

McMichael states the following conclusions: (1) There is no decisive proof that the liver is undamaged in any stage of "hepato-lienal fibrosis" (Banti's disease and splenic anaemia). (2) In view of the preponderance of positive evidence it is at present impossible to exonerate the liver from a share in the pathological process from the beginning of the disease. (3) The involvement of the two organs, liver and spleen, is probably simultaneous and varies only in degree.

McMichael has clearly in mind from his pathological studies that the liver is always involved throughout the course, whether there is clinical evidence or not, and that the liver and spleen are both affected by the same factor, but independently and not necessarily in the same degree. These conclusions agree closely with the views here expressed, and are derived from a consideration of the clinical features.

Clinical Features at Various Age Groups

These features are here reviewed from the point of view of the picture they present in different age groups. It may be observed that paediatricians commonly use the title Banti's disease, while for adults the title splenic anaemia is more usual. If it is accepted that there is only one syndrome, this usage suggests that there is some appreciable difference in its appearance at various ages.

Age Group Under 10 Years.—Smith and Farber (1935) record a series of 15 cases beginning before the age of 10 years. Of these patients eight were dead before the age of 15 years, six having died before 10 years. Of the seven who were living at the time of the communication, only two were over the age of 15, both being 18 and still having recurrences of haematemesis subsequent to splenectomy. Of the eight deaths, seven were due to sudden gross haemorrhage, the remaining case being post-operative. In the majority of the younger children the first haematemesis occurred when there was no enlargement of the spleen and no anaemia, leaving hepatic cirrhosis as the only reasonable explanation. The splenic enlargement was often not more than moderate, but in three cases it reached to the umbilicus. There was no obvious relation between the size of the spleen and the subsequent prognosis. Nor was there any obvious relation between prognosis and splenectomy, which was performed in 11 cases. Ascites was present in only one case. In three others there was evidence of mesenteric thrombosis.

In two of my four cases under 8 years the liver reached to the umbilicus when first observed and in a third it was easily palpable, but the high incidence is probably chance. Such enlarged livers have been observed elsewhere and tend later to become smaller.

The picture presented at this age is one of great severity. The emphasis is on the liver and the fatal occurrence of haematemesis. It is quite unlike the features of splenic anaemia as commonly recorded in adults. With onset under the age of 10 or 12 years the chance of survival to 20 years is slight.

Age Group Between 10 and 20 Years.—In this age group it is difficult to find enough material on which to base definite conclusions, and the following statements are provisional but I think substantially correct. The onset and the course are less acute and prognosis for the duration of life is longer. The body seems to have better powers of recovery from the attacks of haematemesis. Possibly it is because bleeding is less often fatal that clinical cirrhosis and ascites may be as common a cause of death as haematemesis. Of my four cases with onset in this age group, the liver was palpable 1 in. (2.5 cm.) below the costal margin in one case only, which contrasts strongly with the four cases under 10 years. The general picture, compared with the age groups under 10 years, is of a factor acting less powerfully but still mainly affecting the liver and fatal within a limited period of years.

The Later Decades.—Ages around 20 years can be regarded as an intermediate period, but with onset in the later twenties and even more over the age of 30 the picture

appears with the traditional features of splenic anaemia. The disease is chronic and progress is slow. The spleen gradually enlarges and may reach to the iliac fossa, but it remains smooth, firm, and uniform. Anaemia and leucopenia tend to advance. Haematemesis is not so frequent or so serious, and a patient may survive many repetitions over a course of years. The duration may be many years, with only minor disabilities. The incidence of clinical cirrhosis of the liver is low, and needs to be reviewed in the light of the sequelae of infective hepatitis.

Review of the Age Groups.—As one reviews the clinical features in the successive age groups, it appears that the changing picture may be produced by the same factor but of different grades of severity, a factor which can act independently on the liver, spleen, and bone marrow in the decreasing order of rapidity and severity. Its effects are revealed by different structures as the milder forms live on into adult life and the later decades. The severest grades cause death in early life, the brunt falling on the liver and incidentally producing haematemesis in a body not yet possessing reserves of blood and of blood-forming tissues. A less severe but still serious grade appears in adolescence and young adults. Mild grades in subjects who consequently survive into adult life have time to produce their action on the spleen and bone marrow. The hepatic lesions which are insufficient to produce early death are usually also insufficient to produce clinical manifestations of portal cirrhosis, but are recognizable on pathological examination probably in every case.

Aetiology

Banti contended that his disease was due to a toxin which acted both on the liver and on the spleen, but independently. Knowledge was not advanced enough for any suggestion regarding its nature. Parsons, Hawksley, and Gittins (1933) discovered the clinical groups of the condition now known as erythroblastosis foetalis. Hawksley and Lightwood (1934) described toxic changes in the liver, necroses, and in later stages signs of fibrosis. They suggested that some cases of juvenile cirrhosis and even of Banti's disease might originate from icterus gravis neonatorum.

Baird (1937) recorded such a case under the title "atrophic cirrhosis of the liver following icterus gravis neonatorum." The child came under observation at the age of 1 month, having been jaundiced since birth. The liver was enlarged. Four months later the jaundice had gone, the liver reached to the umbilicus, and the spleen was palpable for the first time. The patient was admitted to hospital again at the age of 3½ years on account of enlargement of the abdomen. The liver was now small, hard, and nodular, ascites and distended veins were present, and the spleen was just palpable. There was slight anaemia. Death followed a haematemesis two weeks later, and the liver showed multilobular cirrhosis. It is justifiable to accept this as Banti's disease occurring as a sequel to erythroblastosis foetalis.

These observations were previous to the discovery of the rhesus factor and the elucidation of the aetiology of erythroblastosis foetalis. I have read that after the discovery of the rhesus factor unsuccessful attempts were made to find maternal agglutinins in cases of Banti's disease, but I have not seen any actual references to articles.

Discussion

The clinical features of the syndrome can be traced from the earliest stages of the acute forms in quite young children to the chronic type of splenic anaemia in the later decades. The changing picture is due partly to variations in the original severity of the causal agent, accounting for the widely differing duration of life, and partly to variations in the mode of action on different structures.

The hepatic cirrhosis, the splenomegaly, and the blood changes develop independently of each other. The seeds of disease for all the organs are present from birth.

The liver suffers most severely and the damage is present throughout life. With the early lesions of necrosis life is short, and in its acutest form the syndrome constitutes erythroblastosis foetalis. The subsequent development of fibrosis may terminate in a few cases in the clinical features of cirrhosis of the liver.

The spleen suffers less and changes are slower to develop. Milder cases live to middle or later decades and the spleen enlarges comparatively harmlessly.

The aetiological factor is rhesus incompatibility in the parents and the action of rhesus agglutinins on the foetus. The disease is the continuing stage of erythroblastosis foetalis in survivors.

The spleen has no influence on the incidence of haematemesis or on the condition of the liver and progress of the lesions, and only a slight secondary influence, if any, on the blood. There is no evidence that splenectomy is beneficial. The operative mortality is high owing to the extensive adhesions.

Summary

Banti's disease and splenic anaemia form the syndrome of erythroblastosis foetalis as it appears in survivors at various ages affected in different degrees of severity.

Splenectomy has no beneficial result.

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THE SURGICAL TREATMENT OF BANTI'S SYNDROME*

BY

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In 1894 Guido Banti, professor of pathological anatomy at Florence, described a disease in which splenomegaly is associated with cirrhosis of the liver and, to use his own words, "which progresses slowly, but it inexorably drags the patient to death." It was later shown that this was not a distinct disease, so the term "Banti's syndrome" was coined. It is loosely applied to patients who attend, in the first place, with large overactive spleens and gastro-oesophageal varicosities, from which there has usually been at least one haemorrhage. It is now known that this condition is associated with portal hypertension (Eppinger, 1920; Rousselot, 1940, 1949) due to interference with the free flow of portal blood, through the liver in cirrhosis or to the liver in extrahepatic obstruction. There may be portal-vein thrombosis as well as cirrhosis. The syndrome therefore develops erratically. It may occur in an otherwise comparatively healthy individual with a normal or only mildly cirrhotic liver, or it may be superimposed on a

case presenting essentially with liver disease. On the other hand, many cases of advanced cirrhosis do not have enlarged spleens or oesophageal varices. Thus the groups of cases overlap each other to a considerable extent. An investigation into treatment should therefore embrace the whole group.

The present report is based on a study of every patient with this syndrome or disease referred to me during the past five years, and whose investigation and initial treatment have been completed. It is in no way a selective group, and the majority with cirrhosis were referred to me on account of haemorrhage, or ascites after failure of medical treatment. They number 68. In 12 the portal obstruction was extrahepatic; in 11 there was mild cirrhosis; in 30 the cirrhosis was advanced; and 15 were in the terminal stages of chronic liver disease.

Group 1: Extrahepatic Portal Obstruction (Table I)

These 12 cases may be divided into two subgroups: (1) those in which portal vein obliteration is the primary condition (8 cases), and (2) those in which the obstruction is secondary or incidental to some other disease (4 cases). In the former the obstruction is probably an extension of the obliterative process affecting the umbilical vein and the ductus venosus at birth (Thompson, 1940). The normal portal vein often disappears and is replaced by a bunch of tortuous varicosities, the so-called cavernoma (Fig. 1). Occasionally the vein is present but constricted. The patients are children or young adults.

It is now generally agreed that the correct treatment is to remove the hyperactive spleen and to anastomose the splenic vein to the left renal vein — end-to-side if possible (Fig. 2), but end-to-end if the renal vessels are not conveniently arranged. There is usually no other serviceable portal venous channel, as shown in Fig. 1. A successful suture anastomosis is curative in that it enables the portal venous pressure to drop to a safe level (Fig. 3).

FIG. 1.—Venogram of portal cavernoma at operation. The portal vein is replaced by many tortuous channels. The dilated left gastric vein establishes connexion with the oesophageal varicosities (Case 49, Table I).

FIG. 2.—Diagram of end-to-side spleno-renal anastomosis, clamps in place.

*Report based on a Hunterian Lecture given at the Royal College of Surgeons on February 7, 1952.