THROMBOSIS OF THE HEPATIC VEINS

The Budd-Chiari Syndrome

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IT IS THE purpose of this paper to report 2 cases of thrombosis of hepatic veins and review 95 from over 100 in the literature, to emphasize that the syndrome is not always due to one disease process, as is so commonly implied, and to attempt to give a clearer conception of the various other processes which may cause it.

In the majority of reported cases there is gross obstruction of hepatic veins, leading to engorgement and necrosis of the liver and to portal obstruction. In some instances the block occurs as a final episode in an already advanced disease which itself masks the characteristic clinical picture of the Chiari syndrome or leaves no time for its development. There is also a smaller group of cases in which the obstruction is limited to one lobe or to part of a lobe. While there is a pathologic unity which may be expressed by referring to all cases as examples of thrombosis of the hepatic veins, it is felt that descriptive separation is necessary. It is proposed that the name "Chiari" or "Budd-Chiari" syndrome should be retained for cases in which there is gross blockage of the hepatic veins and that cases with more limited lesions, not giving the full picture, should be referred to simply as cases of thrombosis of the hepatic veins. While this paper is primarily concerned with the Chiari syndrome, remarks concerning etiology and pathology cover the minor group also. Two previously accepted cases have been excluded. The patient in Sternberg's second case had thrombosis of the vena cava, but the upper part of the vessel was free, as apparently were the hepatic veins; reference is made only to a fatty liver. In Hoover's second case the diagnosis appears doubtful, and there was no autopsy.

Some reviews deserve special mention. These are the original paper by Chiari, an excellent review of the older literature by Hess, the paper by Thompson and Turnbull, the comprehensive article by Nishikawa containing a report of 10 cases and, more recently, the articles of Satke and Coronini and Oberson.

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PATHOLOGY

Here will be described the pathologic processes leading to obstruction of the hepatic veins and the resulting hepatic changes.

Venous Lesions.—There are three main sites for obstruction. It may occur in the inferior vena cava, in the ostiums of the hepatic veins or in the hepatic veins themselves. It is often difficult to determine whether the thrombosis occurred primarily in the vena cava or in the ostiums of the hepatic veins. In 5 cases the block was due to neoplasm in the cava; in 2 of these the condition was reported as endothelioma (Hallock and others and Unruh) and in 3 as hypernephroma (Armstrong and Carnes; Jacobson and Goodpasture, and Weber). In 20 cases there was thrombosis of the cava—a rare lesion. Block of the upper part is extremely rare. Only 3 to 4 per cent of Pleasants' patients with thrombosis of the inferior vena cava had a thrombus in the upper third of the vessel. In 18 other cases there was mural thrombosis or intimal thickening without block.

In many cases the ostiums of the hepatic veins appear to be the initial site of the block; even when there is extensive thrombosis, scarring is frequently most severe and evidently of longer duration at this site. There remain a number of cases in which the ostiums are free, the most profound changes being in the hepatic veins themselves. Recently, authors have stressed lesions in the walls of the vessels. These are discussed in the section on etiology.

Liver.—The lesions found in the liver depend on the duration of the thrombosis. In the acute stage there is severe venous engorgement, resulting in central lobular necrosis of hepatic cells. Later cirrhotic change develops, and nodular regenerative hyperplasia is common. Old and recent lesions are frequently found side by side in the same liver, confirming the clinical suggestion that numerous acute attacks of thrombosis are common.

In 3 cases (Nishikawa and Hutchison and Simpson) there developed primary carcinoma of the liver. There seems no doubt that this was the true interpretation, and it would appear reasonable to suggest that the carcinoma supervened on regenerative hyperplasia, as occasionally occurs in portal cirrhosis. An enlarged caudate (spigelian) lobe is frequent, as was noted by Nishikawa. It is probable that the thrombotic process misses the usually separate hepatic vein supplying this lobe, enabling compensatory hypertrophy to occur more readily.

Other Lesions—Thrombosis of the portal veins is a rare and usually terminal event. In 2 cases there developed an infarction of the intestines. The only other intestinal lesion noted is a varying degree of congestion. Apart from the vascular lesions mentioned in the next section, the changes described in the spleen are those of severe venous engorgement.

Nishikawa presented extensive charts of the venous anastomoses; these, however, appear too well known for review here.

RELATED EXPERIMENTAL WORK

Simonds and Callaway and Jergesen reported on the changes occurring in the livers of dogs after mechanical constriction of the hepatic veins for ten to fifty minutes. They found swelling and granulation of the hepatic cells, resulting later in complete sinusoidal collapse. Hyaline thrombi were found in many central and sublobular veins, and a large number of mononuclear cells were present, with some proliferation of the sinusoidal endothelium. The picture was reported as resembling the focal necrosis of typhoid. The authors emphasized the presence of lymphatic dilatation, only once mentioned as occurring in a human being (Ohno).

ETIOLOGY

Age.—The youngest patient with thrombosis of the hepatic veins mentioned in the literature is Gee's 17 month old patient. Unruh's patient was 1 year old, but in this instance the condition was due to endothelioma of the vena cava. The oldest patient mentioned was 61 years. The average in 86 cases in which age was mentioned was 34 years. Hess gave the average as 28.5 years.

Sex.—Of 88 patients for whom the sex was recorded, there were 50 males and 38 females. This does not agree with previous statements, since Byrom remarked that the condition is twice as common in females and Rolleston that the sexes are equally affected.

Predisposing Diseases.—The syndrome of thrombosis of the hepatic veins may be due to a variety of disease processes; moreover, there can be no doubt that in any one case several factors are usually active. There may be a general disease, such as polycythemia, carrying a pronounced tendency to thrombosis, which in combination with a minor local lesion will cause thrombosis of the hepatic veins. Conversely, there may be a gross local lesion with a minimal general disease. Some of these factors, both general and local, will be considered.

A congenital vascular fault may be the local factor in thrombosis occurring in early life but is not likely to be present in the majority of patients in the older age groups. The theory that there is spread of the obliterative process from the ductus venosus to the hepatic veins, suggested by Moore and Rolleston, has no supporting evidence. The presence of a congenital venous anomaly, such as a valvular fold, is a possibility but would be extremely difficult of proof. The theory of Kretz that repeated trauma, such as occurs because of the coughing in pertussis, might lead to tearing of the venous walls and to subsequent thrombosis has nothing to commend it. The diagnosis of primary peri-

tonitis leading to periphlebitis, as postulated by Mann and Hall and Frerichs, is excluded in all but their cases by the absence of any peritoneal reaction except the mild one so common in long-standing ascites. Venous block by gumma was reported by Fagge, West and Wilks; however, gummas of the liver are now extremely rare, and in all recent cases syphilis can be ruled out by a negative reaction to the Wassermann test. Hart reported an instance of death resulting from treatment with arsphenamine in which miliary granulomas were found around the small hepatic veins and suggested that such lesions might give rise to thrombosis of the hepatic veins. It appears likely that these lesions were really those of a necrotizing arteritis due to hypersensitivity to the arsenical compound. Hart's concept, however, is interesting, and further remarks about general vascular disease as a cause will be made in this article.

Terminal thrombosis related to hepatic suppuration is recorded by Winternitz and Visconti and also occurred in a case in the Massachusetts General Hospital. While this condition is of pathologic interest, it is terminal and is of no clinical interest.

Thompson and Turnbull suggested that eddying of the streams of blood at the junction of the hepatic veins with the vena cava might explain the many cases in which the thrombosis occurred at the ostiums of the hepatic veins; marked obliquity of the entering veins is a possible added factor. It is generally accepted that at the site of alterations in caliber or at the confluence of blood streams deposition of cells and fibrin may occur on the walls of vessels. The authors remarked that such changes are extremely rare at the ostiums of the hepatic veins, but they reported a case in which there was a projecting ledge of thrombus at the venous junction, just where the main block so often occurs in the Chiari syndrome. There seems no doubt that this theory adequately accounts for the great frequency of thrombosis at the hepatic vein ostiums, but other factors must be present to a greater or lesser degree.

Also among general causes for the syndrome must be placed diseases in which there is a well recognized tendency toward thrombosis. There are in the literature 8 cases of polycythemia vera in which the syndrome occurred (Altschule and White, Baehr and Klemperer, Berk, Cole, McAlpin and Smith, Oppenheimer and Ulhorn). Relation of the onset of the illness to pregnancy has been noted four times (Chiari's case 1, Coronini and Oberson's case 8, Lange's case and Nagayo's case 3). I have recently observed a case of leukemia in which thrombosis of the veins of the right lobe of the liver had occurred.

A further probable cause is phlebitis of the hepatic veins, with cellular infiltration of the media, intimal thickening and superimposed thrombosis. Hess, Meyer, Ohno, Pacher and Satke brought forward

strong evidence of this. There seems no doubt that in certain cases it is one of the main local factors leading to thrombosis of the hepatic veins.

Coronini and Oberson expressed the most interesting view, that thrombosis of the hepatic veins can result from a general vascular disease. They found inflammatory changes in the intima of the hepatic veins of a serofibrillary character, often with well defined medionecrosis. The generalized nature of the disease is supported by the finding of similar lesions in the radicles of the portal veins and in the splenic vasculature, resulting in a "fibro-adenie" resembling that described in Banti's syndrome. More rarely the pancreas and the kidney may be affected, and the authors described tissue damage in the heart of the type seen in rheumatism. Stressing the type of the vascular lesions, they suggested a rheumatic basis for thrombosis of the hepatic veins, i. e., an allergic tissue reaction in the sense of Klinge and Rossle.

CLINICAL FEATURES

Abdominal Pain.—Usually pain is the initial symptom. It precedes hepatic enlargement and ascites and is one of the most constant features. It differs in severity, varying from mild discomfort and "indigestion" or a sense of pressure to a severe cramping pain. It is usually epigastric, with predominance under or over the right costal margin, and sometimes radiates to the back and the loins. Some reports mention the occurrence of attacks of pain for years before the final illness, but it appears likely that these represent minor episodes of thrombosis. Sudden stretching of its capsule by the engorged liver substance would appear to be the explanation of the pain.

Ascites.—Large quantities of transudate, occasionally hemorrhagic and rapidly recurring after paracentesis, are usually found. In 5 cases ascites was absent clinically, but in 3 of these it was found at autopsy or on laparotomy. In 1 case death occurred at five days, and there may not have been time for an ascitic collection to develop. It is to be assumed that the development of an adequate collateral circulation is the explanation, and it is of interest that in several cases in which there had been earlier gross ascites there was little fluid at autopsy.

Hepatic Enlargement.—Hepatic enlargement is usually striking, but difficulty in palpation is frequent owing to massive ascites. However, the organ is generally readily palpable after paracentesis. A rapid, tender enlargement is usual, extending as a rule to two or three finger-breadths below the costal margin. In cases in which the disease is of longer duration, the edge recedes, tenderness passes off and the organ becomes harder as cirrhotic changes develop. It is usually smooth and firm, but in a few cases irregular masses due to primary or secondary carcinoma of the liver have been palpable.

Splenic Enlargement.—Enlargement of the spleen is not nearly so frequently noted clinically as is hepatic enlargement. It is not usually gross, extending as a rule about a fingerbreadth below the costal margin. In only 1 atypical case was it of considerable degree.

Venous Collaterals.—The presence of venous collaterals is one of the most important signs. Usually the enlargement is over the upper part of the abdomen and the lower part of the thorax, especially near the xiphoid cartilage, where anastomosis between the superior epigastric, medial xiphoid and internal mammary veins takes place; only a few reports mention a caput medusae. The presence and size of these anastomotic veins are related to the duration of the thrombosis. The few reports mentioning this point suggest that a few weeks are necessary for the development of obvious dilatation. In the second case reported on here the dilatation appeared almost immediately after the thrombosis. In the early stages there may be only dusky engorgement of fine vessels, giving a cyanotic hue. Pleasants pointed out that if there was thrombosis in the vena cava the lower the thrombosis extended, the lower were the collaterals on the abdominal wall.

Edema of the Legs.—Edema of the legs was present to a greater or lesser degree in 43 cases. In many it was transient or limited to the feet. Considerable edema, especially if it extends to the thighs, should strongly suggest that the thrombosis has involved the vena cava. This statement, of course, implies exclusion of other general causes of edema.

Jaundice.—The absence of gross jaundice and the presence of the slight, latent or clinical form are the most important features. Reports vary in their statements on this point, some denying the presence of jaundice, others referring to subicterus. In the few cases in which detailed examination was made, mild icterus was demonstrated. The van den Bergh test has shown an increased indirect value. Six reports mention the occurrence of increased urobilin in the urine, or occasionally of bile. There is too little available information to enable definite figures to be given.

Other Evidence of Hepatic Damage.—Unfortunately, only 5 case reports refer to tests of hepatic function. Sohval mentioned low plasma cholesterol levels, with only a trace of ester fraction. Kahn and Spring noted a cholesterol level of 173.9 mg., and Goldstein a level of 166.3 mg. Satke reported negative reactions to galactose tests in 2 instances, with a positive reaction to the tetrachlor-phenolphthalein test in 1; in the latter instance scanty amounts of leucine and tyrosine were found in the urine.

Vomiting.—Vomiting is mentioned in about one quarter of the cases, usually being most severe at the time of an acute episode.

hematemesis is rare; in most cases it is clearly due to varicose esophageal veins. Melena or rectal bleeding is even rarer.

Diarrhea.—Only five references to diarrhea were found. In 2 cases it was diffuse and watery and may have been related to edema of the bowel wall.

Dyspnea.—Dyspnea is a frequent symptom in cases of massive ascites, being due to upward displacement of the diaphragm.

Pleural Effusion.—This is rare and usually terminal.

Neurologic Signs.—Several authors have mentioned the occurrence of a drowsy state drifting into the picture of cholemia in the terminal stages. Goldstein reported a case in which there were striatal signs. There was a masklike face, poverty of eye movements, monotonous speech, salivation, tremor of the extremities, an oculomotor palsy and left trigeminal hyperalgesia. Striatal lesions resembling those seen in postencephalitic parkinsonism were found at autopsy. This case is a further example of the interesting relation between striatal disease and hepatic damage.

Renal Damage.—Evidence of this is exceptional. Altschule and White reported a case of terminal uremia; however, even in cases of caval thrombosis there is no renal abnormality, as the thrombus is almost invariably in the upper part of the vessel.

Clinical Features of Minor Thrombosis.—The features just described apply to the classic Chiari syndrome with well defined venous block. In other cases the thrombosis is much more limited but may be repeated over years until the full clinical picture emerges. It would be well to bear in mind the diagnosis of thrombosis of the hepatic veins in the presence of obscure pain in the upper abdominal area, especially if there are even minor signs of hepatic damage and if there are points in the history which make a diagnosis of infective hepatitis unlikely. If such an incident should occur in the course of some disease in which thrombosis is common, then the diagnosis would be even more worthy of consideration.

DIFFERENTIAL DIAGNOSIS

The first correct diagnosis was made by Willcocks in 1896. Since then the syndrome has been diagnosed during life in 10 cases, including the 2 cases presented here. The great majority of cases present such a typical picture that there are not many other diseases closely resembling it. There are a few atypical cases in which diagnosis is difficult, such as the 5 in which there was no ascites and Satke's case 4 which appeared to be an instance of isolated splenomegaly. In cases in which the thrombosis occurs as a terminal event diagnosis is impossible.

Thrombosis of the portal veins presents similar features, including sudden onset with pain, ascites and the later development of anastomotic veins. The essential point of difference is the absence of hepatic enlargement and even the minor manifestations of jaundice in uncomplicated cases of portal vein thrombosis. In portal cirrhosis the clinical picture lacks the drama of thrombosis of the hepatic veins. Jaundice if present either will be or will become more pronounced than it is in the Chiari syndrome. The history of a case of cirrhosis is frequently suggestive of the diagnosis, and the age incidence is rather different. Confusion with carcinomatous or tuberculous peritonitis and with adhesive pericarditis is not likely.

PROGNOSIS

The duration is variable, but, as Thompson and Turnbull stated, there are two main groups. In the majority of cases the disease is of short duration, in some lasting only a few days. In the smaller group the disease may last from ten to twenty-eight years. Even in this type, however, there is often a story of a recent sudden episode. Chiari's second case is a good example of this, and examples will also be found in Rolleston's discussion in the paper by Hoover and in the paper by Hutchison and Simpson.

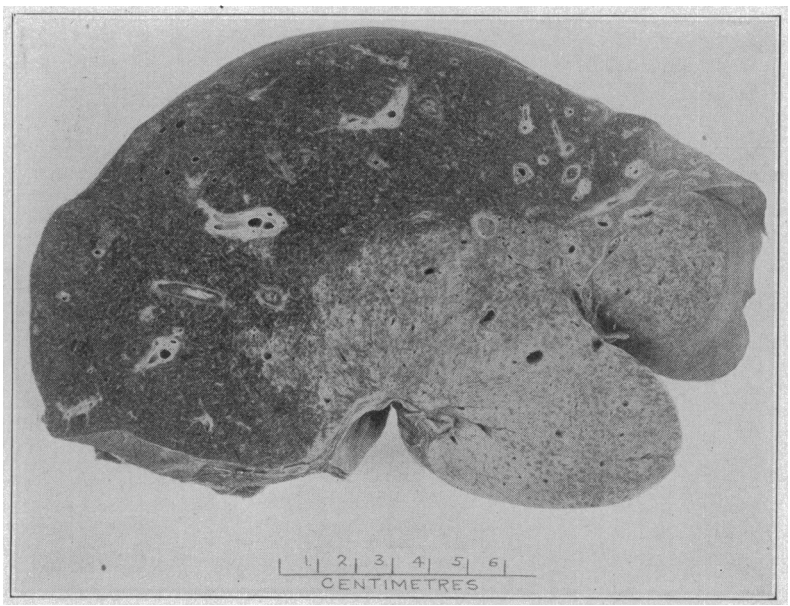
TREATMENT

The treatment of this disease unfortunately does not offer much scope for discussion. It must be on the same lines as the treatment for portal cirrhosis. Byrom's suggestion that paracentesis accelerated death does not appear correct. One gathers that the few patients who did die after tapping were extremely ill before the operation. One point of great importance is that, although this is an extremely fatal disease, patients may live for many years before succumbing, perhaps to a fresh thrombosis. There is no doubt that the fatal termination can be greatly accelerated by operative intervention. Of 9 patients who were operated on, 8 died, the majority within two to three days and 2 within twelve hours.

REPORT OF CASES

CASE 1.—*Clinical History.*—The patient was a miner 31 years of age. He had been in good health all his life, apart from occasional bouts of abdominal pain and diarrhea, until three weeks before his admission to the hospital. He went to work one morning feeling well, but during the day he began to have such severe pain in the abdomen that he was obliged to return home, and by the evening he felt so ill that he had to retire to bed. On attempting to dress the following morning, he found his abdomen so swollen that he was unable to put on his trousers. During the period prior to his admission, the swelling progressed more slowly. After the first few days, pain was not so prominent. There was no vomiting or diarrhea, and his appetite was good.

On his admission to the hospital there was gross ascites, respiration being embarrassed by upward pressure on the diaphragm. On the upper abdominal wall a few enlarged veins could be seen. After paracentesis, an extremely hard, nontender liver could be felt, and no splenic enlargement was noted. There was no edema of the legs. Tapping was carried out three times, a total of 31 liters of pale fluid with a protein content of 1.0 per cent being removed. The liver edge receded during this period, and increasing hardness was noted. There was only slight jaundice immediately before death. No abnormal physical signs were found in the cardiovascular system, lungs or nervous system. Examination of the stools persistently revealed occult blood. The Wassermann reaction was negative. During the last few days of his illness, the patient relapsed into a comatose state, and the mode of death was that so commonly seen in severe necrosis of the liver.



Photograph of a section through the liver in case 1. To the left is the greatly engorged, recently involved right lobe. In the hepatic veins can be seen thrombi of varying ages. To the right is the mass of accessory hepatic tissue, and the large lobules are clearly shown. Above and to the right is a portion of the left lobe grossly scarred from long-standing infarction.

Several diagnoses were considered. Infective hepatitis was excluded by the absence of pronounced jaundice coupled with the presence of recurrent gross ascites. A diagnosis of cirrhosis did not seem tenable for a previously healthy man with a remarkably rapid onset of disease accompanied with pain. The hepatic enlargement made an uncomplicated portal thrombosis most unlikely. The history alone appeared to rule out the diagnosis of a neoplastic process, as did the type of peritoneal fluid. It was felt that the history and clinical findings were so strongly suggestive of thrombosis of the hepatic veins as to warrant a diagnosis of the Budd-Chiari syndrome.

Abstract of Autopsy Report.—The body was that of a well developed but poorly nourished subject. The peritoneal cavity contained about 0.5 liter of clear yellow

fluid. The visceral and parietal peritoneum and the intestines were a dusky red from considerable dilatation of large veins, closely set venules and capillaries. The parietal pleura showed the same engorgement, but the pleural sacs contained no fluid. In the subcutaneous tissues of the lower part of the chest there were many dilated venules. The pectoral muscles showed similar changes, and in addition there were numerous dilated veins. The internal mammary veins were slightly dilated; seven trunks were present. The azygos vein was dilated, having a diameter of 1.5 cm. There was no evident caput medusae, but there were well marked attempts at a collateral circulation in the usual sites. In the pericardium and anterior mediastinum there were many dilated veins and capillaries. The superior vena cava had a circumference of 6.0 cm. just before entering the auricle; the innominate veins were not obviously dilated. The right side of the heart was much dilated; however, beyond a little myocardial scarring there was nothing remarkable. The inferior vena cava showed a vestigial valve 5.0 cm. long and up to 1.5 cm. broad; at 6.0 cm. below the diaphragm the vessel was 8.0 cm. in circumference. There were no thrombi present. The ostiums of the hepatic veins seemed smaller than normal, and one of the superior group had protruding from it a piece of antemortem clot 0.6 cm. long. The liver appeared reduced in size but weighed 1,650 Gm. The right lobe had a finely granular and wrinkled exterior and was dark bluish. On section its lateral half showed occlusion of practically all the hepatic veins by recent, or at least recently organized, thrombi. In the medial portion practically all the hepatic veins were filled by pale, firm, organized thrombi; in some, recanalization was apparent to the naked eye. Recent thrombi were infrequent.

The liver itself was a dark plum color and was firm. Lobular markings were usually not made out; when they were, they indicated small lobules. The appearance was that of so-called red infarction. In the lateral portion were a few scattered yellowish foci of "normal" liver, 0.2 cm. or so in diameter. Springing from the under surface of the right lobe, some 5.0 cm. from its right margin, was an irregular tubular mass of accessory hepatic tissue. It had a rounded termination and constituted one third to one half of the liver mass, measuring 12 by 10 by 6 cm. Its line of demarcation from the rest of the right lobe was irregular but sharply defined. Unlike the other lobes, it was covered by a smooth thin capsule, had a yellowish color and was extremely soft.

The left lobe was reduced in size, being only 2.5 cm. long and 5.0 cm. broad. Its external appearance resembled that of the right lobe, but one third of it was occupied by a pale, depressed, scarred, triangular area. On section most of it resembled the medial portion of the right lobe, but the triangular scarred area contained only a few recognizable vessels and no hepatic cells.

Microscopically the hepatic veins, particularly the large trunks, showed thrombi of varying ages. Some were recent, although even these were organized. Others were old and fibrosed, and in these channels of recanalization often showed recent thrombi. Inflammatory changes were not evident. Hepatic tissue in the distribution of the thrombosed veins had disappeared, apart from a thin layer of cells around the portal tracts. The tracts themselves showed an increase of fibrous tissue, and early bile duct proliferation was present near them. In the accessory lobe the lobules were enormous and large vessels and portal tracts were absent, confirming the microscopic appearance of regenerated liver. The spleen was much enlarged, weighing 640 Gm., and the sinusoids were distended by blood. There was an old infarct measuring 5 by 3 cm., with microscopically a number of smaller deep infarcts such as might arise as a result of venous lesions. The kidneys were enlarged (400 Gm.) and showed intense congestion, and there was scanty exudate in some

capsular spaces. The jejunum was edematous and intensely congested, as were the ileum and large intestine.

CASE 2.—*Clinical History.*—A previously healthy girl of 2 years of age took ill suddenly a month before her admission to the hospital, with cyanosis, panting respirations and vomiting. From this she recovered in three days and was well again until six days before her second admission, when abdominal pain developed, lasting a few hours and followed by rapid swelling of the abdomen and, on the next day, of the legs. There was no diarrhea or vomiting. She was found to be extremely pale, with gross edema of the lower extremities and of the abdomen up to the costal margin. There was decided tenderness over the liver area, and she was evidently in great pain, screaming during the examination. A large ascitic collection made visceral palpation difficult, but a tender, smooth liver was palpable three fingerbreadths below the costal margin; the spleen could not be felt. Distended veins coursed upward over the right costal margin. The abdominal circumference at the umbilicus was 22 inches (56 cm.). There were no other abnormal clinical findings. During the first few days following her admission, the patient's condition improved, and the liver diminished in size and tenderness. On the basis of these symptoms, a diagnosis of thrombosis of the inferior vena cava and the hepatic veins was made. Later the abdominal collateral veins became more and more obvious, extending from the lower third of the abdomen to above the costal margin, and lumbar veins also became noticeable. By two paracenteses 12 pints (5.6 liters) of pale yellow transudate were removed. After a fluctuating illness the patient eventually died, fourteen weeks after her admission to the hospital. There had never been any clinical evidence of jaundice, but, unfortunately, no biochemical evidence was sought. The serum protein content ranged from 4.2 Gm. per hundred cubic centimeters (albumin 3.12 Gm., globulin 1.08 Gm.) to 5.23 Gm. (albumin 3.32 Gm., globulin 1.91 Gm.). The lower figure was the initial one, suggesting that hepatic damage was the cause and not loss of protein into the ascitic fluid.

Abstract of Autopsy Report.—The outward appearances were similar to those described during life, namely, massive ascites with large anastomotic veins on the abdomen. The peritoneum was normal, apart from some adhesions between the liver and the diaphragm; 6 liters of ascitic fluid was present. The liver weighed 855 Gm. (normal, 390 Gm.), fixed in solution of formaldehyde. There were many dilated veins between it and the diaphragm. Its surface appeared nodular, and on section it showed necrosis of large portions, with localized areas of regeneration confined largely to the center of the right lobe. Several occluded hepatic veins could be seen, and the picture suggested hepatic necrosis secondary to venous obstruction. Histologically the liver showed marked atrophy of the greater part of the lobules, many showing only a rim of surviving cells. In a few areas there were nodules of regenerating liver. There was little fibrosis of the portal tracts. In association with a few recently thrombosed hepatic veins there was great congestion of the sinuses. The inferior vena cava was examined histologically at levels from the diaphragm to the renal veins. In the intrahepatic portion there was evidence of previous thrombosis, with organization and recanalization. The main hepatic veins entering the vena cava showed complete blockage by organized thrombus, with little recanalization. The greater portion of the vena cava at this level was patent, and the wall showed no abnormality except in relation to the organization, in which areas the muscle was thinned and in places almost completely absent; the elastica in these areas was also scanty. The part of the vena cava below the liver was narrow, with a diameter of 5.0 cm. Just above the level of the renal veins

the lumen of the vena cava was occupied by crisscross bands of fibrous tissue, which was due to organization of the thrombus: in the meshes were several recent thrombi. The renal veins were themselves free, but the right vein showed evidence of an old mural thrombus, and there was an old infarct in the kidney. At one point there was a slight proliferation of the intima of the renal artery. The spleen weighed 83 Gm. (normal, 37 Gm.); there was moderate pulp congestion with prominent germ centers. The esophageal veins were rather more prominent than usual, but they showed no varicosities. A small myocardial artery showed pronounced intimal proliferation, without reduplication of the elastica.

COMMENT

Case 1 clearly shows the result of repeated thromboses over a long period. The triangular area in the left lobe of the liver was evidently of long duration. The rest of the lobe and the medial portion of the right lobe had been more recently involved, and the lateral portion of the right lobe more recently still. It is interesting in this respect to recall the attacks of abdominal pain. The thrombosis had evidently occurred in the hepatic veins near the ostiums, but unfortunately all the thrombi were so old that no conclusions could be reached as to their pathogenesis. The splenic infarcts strongly suggested that there had been involvement of the veins in the spleen as well as of those in the liver; there was no evidence of vascular lesions in other organs. The possible relation of the vestigial valves to the thrombosis is of interest.

In the second case the thrombosis probably commenced about the ostiums of the hepatic veins and spread to the cava and to the hepatic veins proper. Here again the age of the thrombi obscured their pathogenesis, but support for the theory of a general vascular disease was given by the renal infarct, the nature of which suggested a venous thrombosis as the cause, and by the vascular lesion in the myocardium.

SUMMARY

Two cases of the Chiari syndrome have been reported and 95 reviewed. It is concluded that the syndrome may result from a number of disease processes, and an attempt is made to clarify these and also to define the clinical picture. It is also suggested that minor degrees of thrombosis of the hepatic veins occur and that the diagnosis should be borne in mind in cases of obscure pain in the upper abdominal area, especially when there is any evidence of hepatic damage.

BIBLIOGRAPHY

Altschule, M. D., and White, G.: New England J. Med. **220**:1030, 1939.
Armstrong, C. D., and Carnes, W. H.: Am. J. M. Sc. **208**:470, 1944.
Baehr, G., and Klemperer, P.: M. Clin. North America **14**:391, 1930.
Berk, L.: Beitr. z. path. Anat. u. z. allg. Path. **90**:507, 1932.
Budd, G.: Diseases of the Liver, London, J. Churchill, 1845, p. 147.

Byrom, F. B.: London Hosp. Gaz. **33**:234, 1929.
* Cambier, P., and Dagnelie, J.: Scalpel **87**:255, 1933.
Carcinoma of Pylorus, Infiltrating Duodenum and Mesentery, Cabot Case 29192, New England J. Med. **228**:622, 1943.
Chiari, H.: Beitr. z. path. Anat. u. z. allg. Path. **22**:1, 1899.
Cholangitis with Abscess Formation and Thrombosis of the Hepatic Veins, Cabot Case 27431, New England J. Med. **225**:661, 1941.
Churton, T.: Tr. Path. Soc. London **50**:145, 1899.
* Cohn, cited by Chiari.
Cole, N. B.: M. Clin. North America **16**:1255, 1933.
Coronini, C., and Oberson, G.: Virchows Arch. f. path. Anat. **298**:251, 1937.
Dickinson, A. M.: Surgery **9**:567, 1941.
East, T.: Proc. Roy. Soc. Med. **26**:272, 1933.
Fabris, A.: Arch. per le sc. med. **28**:221, 1904.
Fagge, C. H.: Principles and Practice of Medicine, London, J. & A. Churchill, 1886, p. 295.
* Fedorovich, D. P.: Sovet. khir., 1936, no. 5, p. 894.
Fisher, T.: Bristol M.-Chir. J. **20**:209, 1902.
Frerichs, F. T.: Diseases of the Liver, London, New Sydenham Society, 1861, vol. 2, p. 432.
Gee, S. J.: St. Barth. Hosp. Rep. **7**:144, 1871.
Goldstein, J.: Wien. Arch. f. inn. Med. **21**:243, 1931.
* Goudsmit, J.: Geneesk. gids **7**:697, 1929.
* Hainski, cited by Chiari: Inaug. Dissert., Gottingen, 1884.
Hallock, P.; Watson, C. J., and Berman, L.: Primary Tumor of Inferior Vena Cava, with Clinical Features Suggestive of Chiari's Disease, Arch. Int. Med. **66**:50 (July) 1940.
Hart, C.: Virchows Arch. f. path. Anat. **237**:44, 1922.
Hess, A. F.: Am. J. M. Sc. **130**:986, 1905.
Hoover, C. F.: Obstruction of the Hepatic Veins, J. A. M. A. **74**:1753 (June 26) 1920.
* Huebschmann: Abhandl. d. k. Lep. Carol. deutsche Acad. d. Naturforsch., no. 16, p. 97; Zentralbl. f. allg. Path. u. path. Anat. **24**:218, 1913.
Hutchison, R., and Simpson, L.: Arch. Dis. Childhood **5**:167, 1930.
* Issel, E.: Zentralbl. f. d. ges. Physiol. u. Path. d. Stoffwechsel. **2**:331, 1907.
Jacobson, V. C., and Goodpasture, E. W.: Occlusion of the Entire Inferior Vena Cava by Hypernephroma with Thrombosis of the Hepatic Vein and Its Branches, Arch. Int. Med. **22**:86 (July) 1918.
Kahn, S., and Spring, M.: Ann. Int. Med. **14**:1075, 1940.
Kelynack, T. N.: M. Press **114**:633, 1897.
Koeberle, F., and Pfleger, R.: Wien. Arch. f. inn. Med. **34**:73, 1940.
Kraft, E.: Frankfurt. Ztschr. f. Path. **29**:148, 1923.
Kretz, R.: Ergebn. d. allg. Path. u. path. Anat. **2**:498, 1904.
* Kuhne, L., and Priesel, A.: Med. Klin. **17**:127, 1921.
* Lambron, cited by Budd.
Lazarus-Barlow: Tr. Path. Soc. London **50**:147, 1899.
Lichtenstern, R.: Prag. med. Wchnschr. **25**:325, 1900.
* Lifshits and Chernov: Klin. med. **17**:131, 1939.
* Likhtsier: Klin. med. **17**:137, 1939.
McAlpin, K. R., and Smith, K. E.: New York State J. Med. **38**:101, 1938.
Mann, J. D., and Hall, I. W.: Edinburgh M. J. **16**:56, 1904.
Meyer, O.: Virchows Arch. f. path. Anat. **225**:213, 1918-1919.

* Meystre: Trav. d. Inst. d. Stilling Lausanne, 1904.
Moore, F. C.: Med. Chron. **36**:240, 1902.
Nagayo: Verhandl. d. deutsch. path. Gesellsch., 1914, p. 4.
Nishikawa, P.: Mitt. a. d. med. Fakult. d. k. Univ. zu Tokyo **20**:151, 1918.
Norman, I. L., and Allen, E. V.: Am. Heart J. **13**:257, 1937.
Ohno, S.: Mitt. a. d. med. Fakult. d. k. Univ. zu Tokyo **27**:215, 1921.
Oppenheimer: Tr. A. Am. Physicians **44**:338, 1929.
Osler, W.: J. Anat. & Physiol. **13**:291, 1879.
Pacher, W.: Beitr. z. path. Anat. u. z. allg. Path. **78**:243, 1927.
* Pallette, E. C.: California & West. Med. **45**:324, 1936.
Penkert: Virchows Arch. f. path. Anat. **169**:337, 1902.
Pitt, G.: Tr. Path. Soc. London **46**:75, 1895.
Pleasants, J. H.: Johns Hopkins Hosp. Rep. **16**:363, 1911.
Rendu and Poulain: Bull. et mém. Soc. méd. d. hôp. de Paris **18**:555, 1901.
Rigdon, R. H.: Bull. Johns Hopkins Hosp. **53**:162, 1933.
Rolleston, H. D., and McNee, J. W.: Diseases of the Liver, Gall Bladder and Bile Ducts, ed. 3, New York, The Macmillan Company, 1929, p. 86.
Rosenblatt: Jahres. ü Leist. d. ges. Med. **1**:267, 1867.
* Saborowski: Klin. med. **9**:1308, 1930.
Satke, O.: Deutsches Arch. f. klin. Med. **165**:330, 1929.
Savin: Tr. Ophth. Soc. U. Kingdom **54**:326, 1934.
Schminke: Zentralbl. f. allg. Path. u. path. Anat. **25**:544, 1914.
Schuppel, in von Ziemssen, H. W.: Cyclopaedia of the Practice of Medicine, New York, W. Wood & Co., 1880, vol. 9, p. 833.
Simonds, J. P., and Callaway, J. W.: Am. J. Path. **8**:159, 1932.
Simonds, J. P., and Jergesen, F. H.: Am. J. Path. **20**:571, 1935.
Sohval, A. R.: Hepatic Complications in Polycythaemia Vera, with Particular Reference to Thrombosis of Hepatic and Portal Veins and Hepatic Cirrhosis, Arch. Int. Med. **62**:925 (Dec.) 1938.
Sternberg, C.: Verhandl. d. deutsch. path. Gesellsch. **10**:131, 1906.
* Taylor, F. R.: J. Bowman Gray School Med. **1**:38, 1943.
Thompson, T., and Turnbull, H. M.: Quart. J. Med. **5**:276, 1912.
* Thran, J. H.: Ueber einen Fall von Lebervenenthrombose, Inaug. Dissert., Kiel, 1899.
Ulhorn, E.: Klin. Wchnschr. **42**:2037, 1932.
Umbreit: Virchows Arch. f. path. Anat. **183**:102, 1906.
Unruh: Deutsche med. Wchnschr. **22**:746, 1896.
Visconti, P.: Riforma med. **53**:490, 1937.
Weber, F. P.: Proc. Roy. Soc. Med. **8**:6, 1915.
West, S.: Tr. Path. Soc. London **42**:155, 1891.
Wilks, S.: Tr. Path. Soc. London **13**:123, 1862.
Willcocks, F.: Tr. Path. Soc. London **47**:67, 1896.
Winternitz, M. C.: Bull. Johns Hopkins Hosp. **22**:396, 1911.

* Original unobtainable. Information obtained from abstracts.