Gaucher's Disease with Ascites: *

Response to Portacaval Shunt

ANTHONY M. IMPARATO, M.D.**

From the Department of Surgery, New York University Post-Graduate Medical School, New York, New York

GAUCHER'S DISEASE occurs infrequently, approximately 280 cases having been recorded [16] by 1955. Gaucher's disease with ascites is more unusual; only three references to it have been found [14, 16, 23] with autopsy in one.[16] This is a report of a fourth case and the effect of portacaval shunt on the ascites.

Case History

Case 1. R. S. A boy, age 10 years, was admitted to the hospital on May 26, 1957 because of abrupt onset of severe ascites.

In 1950, at the age of 2, on the basis of findings of anemia, hepatosplenomegaly, lumbar kyphosis, and abnormal cells in the bone marrow, a diagnosis of Niemann-Pick's disease was made. He responded poorly to treatment, required frequent transfusions, and had recurrent bouts of fever.

During December 1956, he developed abdominal swelling which progressed slowly at first, and then more rapidly until January 1957, when he required abdominal paracentesis. Following removal of ascitic fluid, the family physician noted a 10-pound weight loss. A second paracentesis was required in April 1957, when the abdominal swelling became so tense that the child had marked respiratory embarrassment. When admitted to the hospital, on May 26, 1957 he was chronically ill, in respiratory distress with edematous feet, thin legs, and he had a markedly protuberant, tense, abdomen, with flaring of the costal margins, a mass in the left testicle and bilateral indirect inguinal hernias. Following a third paracentesis, while in the hospital, a suprapubic mass was found which was hard, nodular, nontender and measured 12 to 15 cm., in diameter. The liver and spleen were markedly enlarged. The lumbar spine was prominent. Laboratory tests revealed: Hemoglobin— 10 Gm.; hematocrit—33%; WBC—3,400, with normal differential; serum bilirubin (direct)—0, indirect—0.8 mg.%; total protein—7.5 Gm.%, with albumen—5.5 Gm.%; globulin—2.0 Gm.%; prothrombin time—32% of normal; blood calcium—7.7 mg.%; phosphorus—4 mg.%; cephalin flocculation at 24 hours 1+, at 48 hours 1+; total cholesterol—125 mg.%, 90% of the total cholesterol as esters; fasting blood sugar—80 mg%; nonprotein nitrogen—30; carbon dioxide—52 volume %; bromsulfalein retention—6%, at the end of 30 minutes. Urinalysis revealed specific gravity of 1.030; pH—6.0; volume—110 cc.; white blood cells—530; red blood cells—650; casts —60.

The child was treated with vitamin K_1 and vitamin K parenterally, blood transfusions, paracentesis, and high-caloric, high-protein, high-carbohydrate, low-salt diet. By June 8, 1957, his prothrombin time had not improved, ascitic fluid continued to collect, the peripheral blood picture had improved as the result of frequent small transfusions. Review of bone-marrow slides resulted in the opinion that the cells could represent one of the reticulo-endothelial lipoidoses, either lipochondrodystrophy or possibly Gaucher's Disease. Bone-marrow aspiration was repeated and showed markedly atrophic marrow.

An operative approach was designed to establish a diagnosis, deal with the ascites, if possible, and if the diagnosis proved to be Gaucher's disease, perform a splenectomy as well.

Under general anesthesia on June 8, 1957 the left testicle was removed and submitted for frozen section study. Definite diagnosis could not be made. The abdomen was entered through a long transverse upper-abdominal incision, and approximately four liter of straw-colored fluid were removed. A friable intra-abdominal mass infiltrated the small bowel mesentery in the right lower quadrant. This mass, the markedly-enlarged liver and the very large spleen (aspiration) were biopsied. The pathologist was not certain that the diagnosis was Gaucher's disease. Because of the atrophic bone marrow and no clear-cut evidence of hypersplen-

* Submitted for publication June 15, 1959

** Assistant Professor of Clinical Surgery.

FIG. 1. Gaucher cells within the testicle.

ism, extramedullary hematopoiesis was suspected and splenectomy deferred. The portal pressure was 215 mm. of saline with the manometer held at the level of the portal vein. Systemic pressure at this time was 70 mm. of mercury. With the pathologist's description of infiltrating cells in the liver it was believed that intrahepatic portal obstruction contributed to the ascites and an end-to-side portacaval shunt was performed. The abdomen was then closed. The child's postoperative course was uncomplicated.

A diagnosis of Gaucher's Disease was made on study of the permanent sections (Fig. 1–3), and splenectomy was performed one month later.

At the second operation approximately two ounces of fluid were found in the peritoneal cavity and the portal pressure measured 150 mm. of saline.

During the past 23 months the child has been eating an unrestricted diet; no more ascitic fluid has collected; the flaring of the costal margins has disappeared; the suprapubic mass is almost gone, and the liver seems smaller. Blood examination in February 1959, showed hemoglobin—11:5 Gm.; WBC—14,500; bleeding and clotting time—normal; prothrombin time—84%; cephalin flocculation—1 +, at 24 hours, 2 +, at 48 hours; thymol turbidity—3; and proteins—7.2, 4.8/2.4. In December 1959, the child was still enema free.

Discussion

The surgical therapy in this child was directed toward establishing a diagnosis and attempting to relieve ascites. Clinically, the diagnoses considered [7] were of one of the lipoidoses (Gaucher's), juvenile cirrhosis and malignancy of the testicle with abdominal metastases and secondary ascites. Bone marrow studies had been misinterpreted once and noninformative two years later. Aspiration biopsy of liver or spleen was avoided because of the prolonged prothrombin time. The testicular mass was hard, nodular and strongly suggested malignant disease.

The intra-abdominal mass also suggested malignant tissue. Frozen section study was inconclusive and because portal pressure seemed higher than it should be for a cachectic child,[15, 19] end-to-side portacaval shunt was performed. Until permanent sections confirmed the diagnosis of Gaucher's Disease without extramedullary hematopoiesis,[16] it was believed that splenectomy

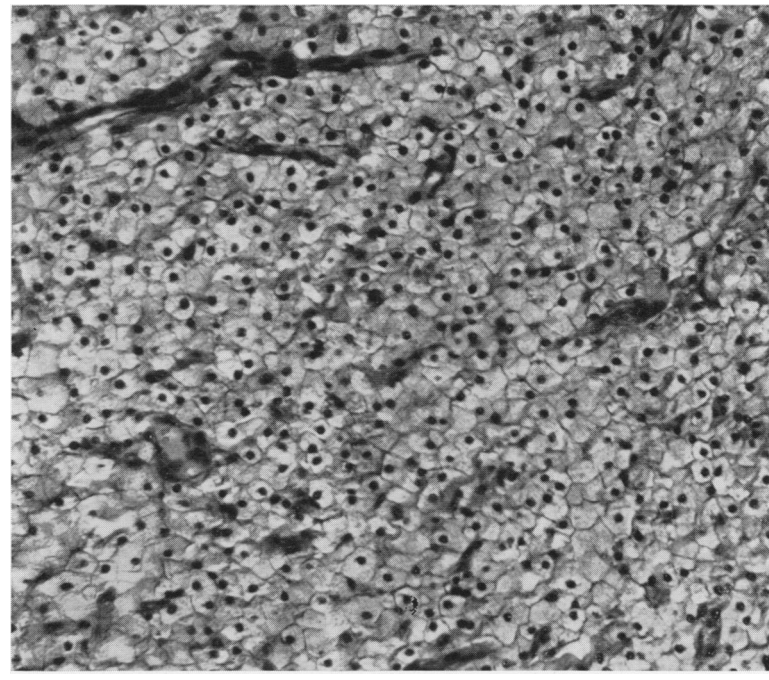

FIG. 2. Liver biopsy with extensive replacement of liver parenchyma by Gaucher cells.

should be postponed. The interval between shunt and splenectomy (one month) was sufficient to indicate the effect of operation on the ascites. There was no demonstrated effect on the hematologic picture by splenectomy except that transfusions have not been required and the white blood cell count is higher.

Gaucher's Disease is generally defined as an uncommon familial disorder of metab-

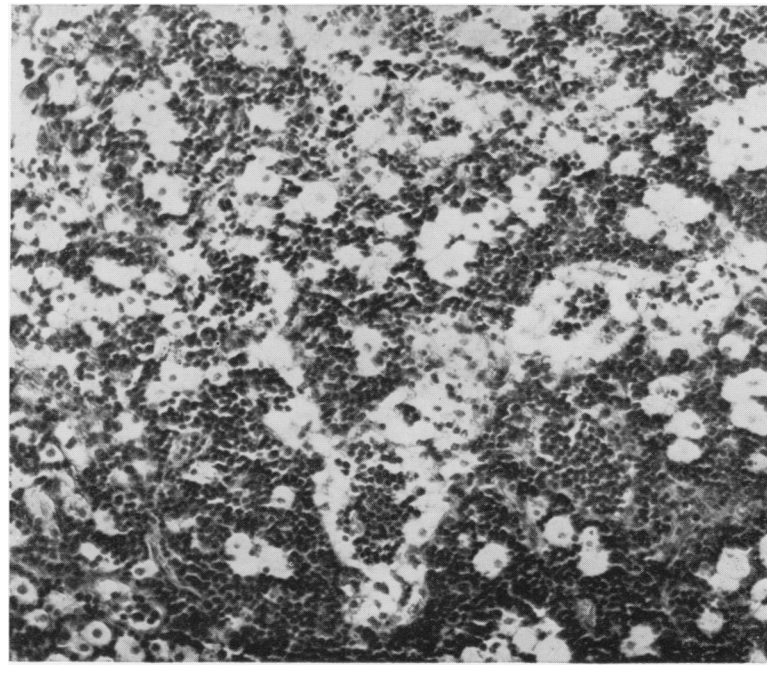

FIG. 3. Mesenteric lymph node showing nests of Gaucher cells.

olism occurring predominantly in patients of Jewish origin in which there is an abnormal storage or retention of cerebrosides within the cells of the reticuloendothelial system. The swollen cells which have been intensively studied by DeMarsh [2] assume a characteristic appearance and are usually easily identified as "Gaucher Cells." Insofar as can be ascertained, symptoms [3, 4, 13, 16, 22] are produced by invasion or persistence of large numbers of these cells in characteristic areas of the body with sites of predilection being spleen, liver, bone marrow, conjunctiva, and deep lymph nodes.

Gaucher cells in the spleen usually produce enlargement of that organ with secondary hypersplenism, pancytopenia [3, 13, 16] or dissociated deficiencies [3, 13] of one or more of the blood elements. The hematologic disorder seems to be most characteristic of the disease, and usually follows a long course. Splenectomy almost always reverts this hematologic picture.[3, 13, 22]

Bone marrow invasion produces thinning of cortices with typical lesions of the femora (Ehrlenmeyer flask) and occasionally collapse of vertebral bodies. Rarely bone marrow is destroyed sufficiently to produce hematopenia which does not respond to splenectomy. Conjunctival infiltration produces characteristic pingueculae.

Gaucher cells in the liver produce relatively few changes other than enlargement of the organ, occasionally alterations in tests of isolated liver functions,[3, 4, 13, 16, 22] including prothrombin time, thymol turbidity, albumen and globulin production. Rarely is there evidence of severe or widespread liver damage. Ascites is a rare accompaniment of the disease and only three specific references [14, 16, 23] to it have been found. Only two other case reports have been located.[16, 23]

The course and possible mechanism of ascites in this patient is of interest not only because of its rarity but also because of its possible contribution to the understanding of the mechanism of ascites in general.

Ascites may appear in a variety of clinical conditions including congestive heart failure, constrictive pericarditis, Budd-Chiari syndrome, Laennec's cirrhosis, and severe portal hypertension, until recently explained by the application of Starling's hypothesis [21] to the portal circulation. In patients with cirrhosis of the liver with ascites, elevated portal pressure has been thought to be a factor. It is not possible, however, to correlate elevated portal pressure with ascites in cirrhosis.[1, 9, 10, 25, 26] All combinations of elevated or normal portal pressures, hypoproteinemia, esophageal varices and ascites seem to occur. Other mechanisms considered have included retention of sodium,[5] abnormal metabolism of water,[20] related to an antidiuretic substance in the urine, and adrenal cortical hyperactivity.[6] Additional mechanical factors, namely, obstruction to the venous outflow tracts [9] (hepatic veins) and possibly to the hepatic lymphatics [18] have been proposed. The liver surface rather than the extrahepatic portal circulation as a possible source of the ascitic fluid has also been demonstrated.[21]

Clinically, some patients with cirrhosis have been subjected to end-to-side portacaval shunt with a fall in portal pressure and have been relieved of ascites. Some have been reported to have responded to hepatic artery ligation.[8] McDermott [11] recently emphasized the importance of combined hepatic and portal decompression.

There are marked species differences in the experimental production of ascites. It has been produced as a sequel to fibrosis of the liver from deposition of silica,[24] constriction of the thoracic portion of the inferior vena cava [8, 9, 17] and constriction of the main portal vein.[26] Correlation with elevation of the portal pressure has been disputed; Volwiler found none; Laufman found that even with thoracic inferior vena caval obstruction those animals showing elevation of portal pressure developed ascites. Experimental work in animals must

be transposed to the human with great caution.

A mechanism of ascites comparable to that in carcinomatosis peritoneii did not seem applicable to this patient since there was no such dissemination of cells. Figure 1 shows the biopsy of the mass in the small bowel mesentery to consist of involved mesenteric lymph nodes. The almost complete replacement of liver (Fig. 2) by Gaucher cells, without evidence of widespread derangement of liver function, suggests that the ascites was predominantly due to a mechanical factor with possible obstruction to both the portal and hepatic flow analogous to Rousselot's fibrotic liver preparations. In one case of Gaucher's Disease, with ascites, in which autopsy is reported,[16] the ascites was thought to be related to intrahepatic portal obstruction. The fall in portal pressure, coinciding with disappearance of ascites, supports this contention. Failure to provide retrograde decompression of the liver neither confirms nor denies the concept of outflow tract obstruction,[11] since mere rerouting of 70 to 80 per cent [21] of the blood flow to the liver might suffice to decompress the intrahepatic venous flow enough to restore pressure and osmotic relationships.

Not enough is known about Gaucher's Disease with ascites to discuss the importance of other possible mechanisms which might contribute to ascites. It is recognized that in a complex disease of unknown etiology hard and fast conclusions based upon study of one variable cannot be drawn.

Summary

A 10-year-old boy, ill since age three, was proved to have Gaucher's Disease with involvement of skeleton, liver, spleen, testicle and mesenteric lymph nodes. Rapidly progressive ascites appeared suddenly and disappeared following portacaval shunt. Splenectomy was subsequently performed. The child has remained free of ascites for two and one half years. The nature of Gaucher's Disease and the possible mechanism of the ascites are discussed.

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