RESULTS OF SPLENECTOMY

A FOLLOW-UP STUDY OF 140 CONSECUTIVE CASES*

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IN RECENT YEARS, the diverse functions of the spleen in normal physiology have become more clearly defined. A natural accompaniment of this increased understanding has been the development of the concept of "hypersplenism." We are assuming in this study that hypersplenism is a physiopathologic state in which there is overactivity of one or more of the normal functions of the spleen, and its physical evidence is usually, though not always, the presence of splenomegaly. The hypersplenic state is not peculiar to one disease entity, but is the manifestation of a splenic instability, either primary or secondary, which may accompany several clinical syndromes of widely divergent characteristics. Nevertheless, a single therapeutic procedure—splenectomy—is usually indicated in whichever clinical situation hypersplenism exists. Studies of the response to splenectomy in selected groups of cases in which the hypersplenic state has been categorized (for example, congenital hemolytic icterus, thrombocytopenic purpura, or congestive splenomegaly) have yielded valuable information regarding prognosis in these conditions. We considered that a five-year follow-up study of *unselected, consecutive* splenectomies based on the preoperative clinical diagnoses might shed further light on the ultimate outcome of the patient with hypersplenism. A study of this type allows evaluation of the preoperative clinical impression in the light of the patient's eventual postoperative course. Diagnostic criteria and pitfalls and operative indications are brought into bolder relief by retrospective analysis of unselected cases rather than by studying those in which the clinical diagnoses have been definitely established. We also considered that a review of a series of patients whose spleens were removed over a limited period would be more informative than a large series of patients who underwent operation over a long span during which operative indications were less homogeneous. Thus, the records of 140 consecutive patients who had undergone splenectomy at the Mayo Clinic during the three-year period, 1942 to 1944 inclusive, were studied. Cases in which the spleen was removed as a secondary procedure (as in total gastrectomy for carcinoma) or in which splenectomy was performed for traumatic splenic rupture, were not included. By means of personal interviews at the clinic, questionnaires, and letters from relatives and local physicians, we are able to report on the outcome of a majority of these patients during a five-year period since their operations.

CONGENITAL HEMOLYTIC ICTERUS

Of the 140 patients who underwent splenectomy, 38 (27.1 per cent) were diagnosed preoperatively as having congenital hemolytic icterus.

Accessory Spleens. Accessory spleens were noted and removed at operation in five cases (13.2 per cent). All were observed in the region of the hilus of the spleen. Two accessory spleens were noted

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in two cases, and one in each of the other three. All were 2.5 cm. or less in diameter. In all cases, the diagnosis of accessory splenic tissue was confirmed microscopically.

Hospital Mortality Rate. There was one hospital death in this group of splenectomies, a mortality rate of 2.6 per cent. This death occurred in the case of a woman 56 years old who was thought to be in crisis preoperatively. Splenectomy was performed as an emergency measure. Preoperative blood transfusion was considered to be contraindicated. The operation was rendered difficult by much perisplenitis. The patient went into shock postoperatively, and when the abdomen was reopened, she was found to be bleeding from one of the vasa brevia, which was ligated. The patient died despite blood transfusions after the second operation. Necropsy revealed that death was due to intraperitoneal hemorrhage from the splenic bed.

Follow-up Study. Information was obtained concerning the postoperative courses of 29 (78.4 per cent) of the 37 survivors of splenectomy. At the date of this study all of these patients had survived for five years, all were well, and none had had recurrences of their preoperative symptoms.

THROMBOCYTOPENIC PURPURA

In 47 cases (33.6 per cent), the preoperative diagnosis was essential thrombocytopenic purpura.

Accessory Spleens. Accessory spleens were observed and extirpated in seven cases (14.9 per cent). In all instances, the accessory splenic tissue was found in the vicinity of the spleen, either at the hilus, the gastrolienal, or the gastrocolic ligaments. In two cases, three accessory spleens were found; in one case, two were found, and in the others, they were single. All were 1 cm. or less in diameter with the exception of one which was 2 cm. in diameter.

Hospital Mortality Rate. One hospital death (2.1 per cent) occurred following splenectomy for thrombocytopenia. The patient was a girl of two years who had a one-year history of ecchymosis, six months of frequent severe epistaxis, and a recent episode of hematemesis. On admission, the platelet count was 46,000 per cu. mm. of blood (normal: 125,000 to 300,000). No immature cells were observed in the blood smear. No megakaryocytes were noted in the sternal marrow specimen, which, however, was considered to be a poor specimen. There were no signs of leukemia. No accessory spleens were noted at operation. In spite of multiple transfusions of fresh blood postoperatively, the platelet count remained in the vicinity of 55,000 per cubic millimeter of blood. Postoperatively, the patient continued to exhibit petechiae, and experienced frequent epistaxis. Two and one-half months after splenectomy she died of a cerebral hemorrhage.

Follow-up Study. Follow-up reports of 35 (76.1 per cent) of the 46 survivors were obtained. There were 32 of these patients (91.4 per cent) who were alive and well five years after splenectomy. Four of these 32 patients (12.5 per cent) gave a history of further episodes of either epistaxis or petechiae after operation, but in no instance were these symptoms severe or protracted.

One of the 3 patients who died was a woman of 31 years with a history of purpura, epistaxis, bleeding gums, and menometrorrhagia of 5 months' duration. On admission, neither the spleen nor the liver was palpable. There were mild anemia and a leukocyte count of 6,200 per cubic millimeter of blood. The platelets numbered 57,000 per cubic millimeter of blood. The sternal marrow specimen failed to reveal an adequate number of normal megakaryocytes. The bleeding time was 3 minutes (normal: 3 minutes or less), the coagulation time was 8 minutes (normal: 6 to 10 minutes), and clot retraction was complete at the end of 2 hours (normal: complete in 1 to 2 hours). At operation, a spleen weighing 270 Gm. was removed along with one accessory spleen

1 cm. in diameter situated in the gastrocolic omentum. The results of microscopic examination of the splenic tissue were not remarkable. Postoperatively, there was a good sustained platelet response to splenectomy. The patient returned 2 years after splenectomy complaining of an 8-month history of recurrent episodes of edema of the face and hands which was relieved by blood transfusions. She also complained of pain in the right upper quadrant of the abdomen extending to the right shoulder. There was marked hepatomegaly. Roentgenograms showed increased density of all bones, and the diagnosis of osteopetrosis was made. At this time, the blood hemoglobin was 10.8 Gm. per 100 cc., the leukocyte count 8800 per cubic millimeter of blood and the platelets 22,900 per cubic millimeter of blood. The blood smear exhibited increased regeneration, and occasional myeloid immaturity to the promyelocyte level. Adequate sternal puncture was not possible because of the dense cortical bone. The blood calcium was 7.8 mg. per 100 cc. (normal: 9 to 11 mg.), the phosphorus 3.4 mg. per 100 cc. (normal: 2.5 to 4.0 mg.), and the Bodansky alkaline phosphatase 2.9 units (normal: 5 units or less). The total serum proteins were 4.9 Gm. per 100 cc. (normal: 6.4 to 7.8 Gm.). It was thought that the patient was suffering from Albers-Schönberg disease with myeloid metaplasia. The patient died two and a half years after splenectomy.

The second patient was a boy of 12 years who had complained of frequent epistaxis for 4 years before admission. On physical examination the spleen was enlarged 2 fingerbreadths below the left costal border. There was a macrocytic anemia, and leukocytes numbered 12,500 per cubic millimeter of blood. The platelets were 28,000 per cubic millimeter of blood. The reticulocyte count was 6.9 per cent (normal: 0.5 to 2.5 per cent). Blood smears revealed some immaturity. The sternal marrow specimen exhibited a myeloid left shift, a marked increase in erythrocyte regeneration, and a reduction in megakaryocytes. The bleeding time was 10 minutes, and clot retraction was complete at the end of 2 hours. The possibility of a chronic myelogenous leukemia was entertained before operation, but the 4-year history seemed more consistent with the diagnosis of an essential thrombocytopenia. At operation, a spleen weighing 204 Gm. was removed. Two months postoperatively, the patient continued to have purpura, and the blood smear at that time was consistent with the diagnosis of chronic myelogenous leukemia. The patient succumbed to this disease two and a half months after splenectomy.

The third patient of those traced who died within the 5-year period after splenectomy was a woman of 44 years who had complained of recurrent purpura and bleeding gums occurring each spring for 16 years. The platelet count was 54,000 per cubic millimeter of blood and the results of all other tests were compatible with the diagnosis of essential thrombocytopenic purpura. The sternal marrow revealed a normal number of megakaryocytes. The platelet count responded well to splenectomy. When the patient returned to the clinic for her 6-months' postoperative check-up she was feeling well, the platelets were 130,000 per cubic millimeter of blood, the bleeding time 3 minutes, and clot retraction was complete at the end of 2 hours. We were informed by letter that the patient had died a year and a half after splenectomy. The cause of death was not specified.

CONGESTIVE SPLENOMEGALY

The preoperative diagnosis was "Banti's disease" or "congestive splenomegaly" in 45 (32.1 per cent) of the 140 cases in this series.

Accessory Spleens. Accessory spleens were removed and identified microscopically in 13 (28.9 per cent) of the cases. The accessory splenic tissue was usually located in the gastrocolic or gastrosplenic ligament. The accessory spleens ranged in size from 0.5 to 3.0 cm. in diameter. In one case, seven accessory spleens were found at the hilus of the spleen.

Hospital Mortality Rate. In this group, there were four hospital deaths (8.9 per cent). In two cases death was due to intraperitoneal hemorrhage, occurring in one instance on the twelfth postoperative day, and in the second case on the nineteenth postoperative day. The third patient, a man of 60 years, continued to have hematemesis postoperatively. In spite of multiple blood transfusions the patient became comatose and died on the twenty-fifth day after operation. Postmortem examination revealed cirrhosis of the liver, thrombosis of the splenic, superior mesenteric, and portal veins, infarction of the upper part of the ileum, fat necrosis of the pancreas, esophageal varices with rupture and gastro-in-

testinal hemorrhage, thrombosis of the left gastric veins, bronchopneumonia, and mural thrombosis of the left pulmonary artery. The fourth patient who died in the immediate postoperative period was a man of 21 years who experienced a stormy febrile postoperative course with a left diaphragmatic pleurisy and effusion. One month after splenectomy he began to have severe hematemesis, and, despite many blood transfusions, the patient died five weeks after operation. The findings at necropsy were cirrhosis of the liver, ruptured esophageal varices with hemorrhage, and organized thrombosis of the superior mesenteric artery and the splenic, superior mesenteric, and portal veins.

Follow-up Study. Thirty-three (80.5 per cent) of the 41 survivors of splenectomy for congestive splenomegaly have been traced during a five-year period. Seventeen (51.5 per cent) of these patients have survived for five or more years. Seven of the latter have experienced further episodes of hematemesis. Thus, only ten (30.3 per cent) of those traced have been completely well for five years.

Whenever it was possible to ascertain the immediate cause of death, it was found to be due to massive gastro-intestinal hemorrhage. More than half (56.3 per cent) of those who died failed to survive three years after splenectomy.

ACQUIRED HEMOLYTIC ANEMIA

Five patients (3.6 per cent) had preoperative diagnoses of "acquired hemolytic anemia."

Accessory Spleens. In no instance was accessory splenic tissue apparent at laparotomy.

Hospital Mortality Rate. There were no deaths in the immediate postoperative period.

Follow-up Study. Four of the five patients were alive at the date of this study more than five years after splenectomy. In two of these cases the patients were well with no recurrence of former symptoms (jaundice or weakness). One patient had lymphosarcoma for which he had received much roentgen therapy with no evident sustained improvement. The fourth patient continued to have recurrences of extreme icterus and was in a poor state of health.

The patient who died was a man of 58 years who complained of left sciatica and frequent dull nocturnal epigastric distress of a year and a half's duration. There was no family history suggestive of blood dyscrasia. His work-up revealed splenomegaly, a herniated intervertebral disk at the fourth lumbar vertebra, microcytic anemia, leukocytes numbering 16,800 per cubic millimeter of blood with a normal differential count, and a reticulocytosis of 8.9 per cent. The erythrocytes showed increased fragility in hypotonic saline solution, and the serum bilirubin was 5.9 mg. per 100 cc. with an indirect reaction. Sternal marrow examination was not performed. The extirplated spleen weighed 380 Gm. When the patient returned for a check-up one year after operation, a generalized lymphadenopathy was noted. There was anemia, and the leukocyte count was 126,000 per cubic millimeter of blood. Blood smears and sternal puncture confirmed the diagnosis of chronic myelogenous leukemia. The patient died four years after splenectomy.

In summary, in only 40 per cent of these cases of acquired hemolytic anemia have the results of splenectomy been gratifying.

INDETERMINATE SPLENOMEGALY

Splenectomy was performed for "indeterminate splenomegaly" in five cases (3.6 per cent). Microscopic examination of the extirpated spleens suggested the diagnoses in four cases as follows: "Hodgkin's sarcoma," "reticulo-endothelial hyperplasia," "regressing hemangioma of the spleen," and "Banti's disease." In the fifth case the

spleen demonstrated a myeloid metaplasia and the pathologist suggested that "the patient should be followed for the development of myelogenous leukemia" (see paragraph on "Follow-up Study").

Accessory Spleens. There were no accessory spleens in this group.

Hospital Mortality Rate. No hospital deaths occurred.

Follow-up Study. All of the patients have been traced. The patient with the reticulo-endothelial hyperplasia died "soon after" dismissal from the hospital. The patient with Hodgkin's sarcoma died one month after leaving the hospital. The patient who had a hemangioma of the spleen was alive and well at the date of this study. The fourth case deserves special comment. The patient, a woman of 29 years, presented a history of chronic ulcerative jejunitis for which a resection of the upper part of the jejunum had been performed at the clinic in March, 1943. She continued to suffer from recurrent generalized abdominal pain with nausea, vomiting and fever for a year and a half. On physical examination there was marked splenomegaly but no hepatomegaly. Aside from a normocytic anemia, laboratory findings were not remarkable. At operation in November, 1944, a spleen weighing 600 Gm. was removed. There was much perisplenitis and increased vascularity of the splenic pedicle. It was the surgeon's impression that this was a true congestive splenomegaly, probably on the basis of thrombophlebitis of the portal or splenic vein. At the date of this study the patient reported that she was well and active five years after splenectomy. In the fifth case the patient died almost six years postoperatively of chronic myelogenous leukemia.

COMMENT

Splenectomy can be performed for any of the conditions associated with hypersplenism with a reasonably low mortality rate. An occasional exception to this statement is congestive splenomegaly, in which the operation carries a higher mortality rate than when it is performed for the blood dyscrasias. In our series of 140 consecutive splenectomies there were six hospital deaths, constituting a mortality rate of 4.3 per cent. One death occurred after splenectomy for congenital hemolytic icterus, a second after splenectomy for thrombocytopenic purpura, and four hospital deaths followed splenectomy for congestive splenomegaly. Cole, Walter and Limarzi[4] reported seven hospital deaths in a series of 87 splenectomies, an operative mortality rate of 8.0 per cent. However, five of the seven deaths followed splenectomy for so-called Banti's disease. A contributing factor to the increased risk in these patients is the presence of extensive perisplenitis and the high degree of vascularity in the splenic area due to the many venous collaterals. Four of the five hospital deaths in Cole and associates' series of patients with congestive splenomegaly were due to postoperative hemorrhage, as were two of the four in our series. An interesting postmortem finding in the two additional patients in this category in our series was extensive thrombosis of the portal vessels with gangrene of the small intestine. Quan and Castleman[8] have emphasized the frequency of portal vein thrombosis in patients who had succumbed following transthoracic gastrectomy and incidental splenectomy. Allen, Barker and Hines[1] found that postoperative thrombophlebitis and pulmonary embolism occurred in 5.12 per cent of 391 patients undergoing splenectomy, an incidence higher than that occurring after any other type of operation. In view of the foregoing facts, more liberal prophylactic use of the anticoagulants may be indicated after splenectomy even when the operation has been performed for congestive splenomegaly.

The success of splenectomy for hypersplenic disorders frequently will depend

upon whether accessory spleens have been found and removed. In the event of a recurrence of symptoms, especially in thrombocytopenic purpura, "the uncertainty of finding splenic tissue at [*the second*]* operation makes a surgical procedure prohibitively dangerous."[7] In the series herein reported, accessory spleens were found and extirpated in 25 cases, or 18 per cent. Movitz and Curtis[6] reported the presence of accessory splenic tissue in 56 (31.4 per cent) of 174 consecutive patients undergoing splenectomy and four additional patients on whom laparotomy was performed. The frequency of accessory spleens in these two series plus the fact that they are often multiple emphasizes the necessity for careful search throughout the entire peritoneal cavity.

The two hypersplenic conditions for which splenectomy has been most consistently valuable as a therapeutic measure are congenital hemolytic icterus and primary thrombocytopenic purpura. The results of our study add further support to this contention. At the date of the study, all of the 29 traced patients who had been correctly diagnosed preoperatively as having congenital hemolytic icterus were alive and well at least five years after splenectomy. This finding agrees with those reported in two recent series.[4, 9] Of 32 traced patients with an established diagnosis of primary thrombocytopenic purpura, 87.5 per cent reported a complete and sustained remission. The results are classified as only fair to good in the remaining 12.5 per cent since there have been further mild episodes of epistaxis or purpura. However, all of these patients are alive and carrying out normal activities after splenectomy. Welch and Dameshek[9] reported excellent results in 61 per cent and good results in 19 per cent. In the series of Cole and associates,[4] the results were good to excellent in 23 of 26 cases and fair to good in the remaining three cases.

Hemolytic anemias of the acquired type respond less favorably to splenectomy. In five of the cases in our series the disease was diagnosed as acquired hemolytic anemia. In one case the anemia proved to be secondary to a chronic myelogenous leukemia, of which disease the patient subsequently died. In another instance lymphosarcoma was later discovered to be the basis of the anemia, and splenectomy has been of little or no benefit. The three remaining cases were considered to be of the primary or idiopathic type of acquired hemolytic anemia; results have been excellent in two while the third patient remains severely anemic with recurrent jaundice. Welch and Dameshek reported excellent results in 50 per cent of patients with primary acquired hemolytic anemia, whereas only a third of patients with the secondary type were benefited by operation.

The hypersplenism which is secondary to congestive splenomegaly is rarely a major factor in the patient's ultimate poor prognosis. The majority of patients with so-called Banti's disease succumb to hemorrhage from ruptured esophageal varices. The hypothesis that splenectomy removes enough circulating blood volume from the portal circulation to reduce portal hypertension effectively has declined in favor in recent years. There is also some question as to whether splenectomy diminishes the associated pancytopenia consistently and completely enough to make it justifiable as even a palliative procedure. Of the patients on whom data are here reported who underwent splenectomy for congestive splenomegaly, 80.5 per cent have been traced during a five-year period. Only one half (51.5 per cent) of these patients have survived for five or more years. Recurrent episodes of hematemesis have occurred in 41.2 per cent of the foregoing survivors. Thus, of those traced, only 30.3

* Our italics.

per cent have had satisfactory long-term results. This discouraging figure casts serious doubt on the justifiability of splenectomy alone as a curative procedure in congestive splenomegaly; on the other hand, it should stimulate further investigation along other therapeutic lines such as total gastrectomy[2] or the various venous shunts.[3, 5]

Discounting the five cases with "indeterminate splenomegaly" as a preoperative diagnosis, the preoperative impressions about five of the 107 traced patients proved to be erroneous. In two of these cases (one diagnosed as primary acquired hemolytic anemia and the other as essential purpura) the patients died of chronic myelogenous leukemia. In the third instance (diagnosed as essential thrombocytopenic purpura preoperatively), osteopetrosis with myeloid metaplasia was the final diagnosis. In these three cases splenectomy might have been avoided by a higher index of suspicion with greater emphasis on the bone marrow studies. In the first case sternal puncture was not performed preoperatively. In the second instance a preoperative sternal marrow specimen showed a myeloid left shift and a reduction in megakaryocytes; the clot retraction time was normal. In the case of myeloid metaplasia, megakaryocytes were reduced in number and abnormal in appearance.

CONCLUSIONS

1. Splenectomy is indicated in all instances of primary hypersplenism; in carefully individualized cases of secondary hypersplenism splenectomy may provide effective palliation.

2. Splenectomy will be curative in the great majority of cases of congenital hemolytic icterus and primary thrombocytopenic purpura.

3. In about half of the cases of acquired hemolytic anemia of the primary type, splenectomy produces sustained remissions.

4. Splenectomy is justifiable as a diagnostic measure in the presence of splenomegaly when the presence of agnogenic myeloid metaplasia has been excluded by means of bone marrow studies.

5. The discouraging results of splenectomy in the great majority of cases of congestive splenomegaly should stimulate further investigation for a procedure of curative value.

6. The high incidence of accessory splenic tissue demands careful exploration of the entire peritoneal cavity at laparotomy.

7. Greater emphasis on preoperative bone marrow studies will clarify the indications for and contraindications to operative intervention.

BIBLIOGRAPHY

[1] Allen, E. V., N. W. Barker and E. A. Hines: Peripheral Vascular Diseases. Philadelphia, W. B. Saunders Company, 1946, 871 pp.

[2] Baronofsky, I. D.: Portal Hypertension; With Special Reference to the Acid-peptic Factor in the Causation of Hemorrhage and Extensive Gastric Resection in Its Treatment. Surgery, **25**: 135, 1949.

[3] Blakemore, A. H.: Portacaval Anastomosis. Surg., Gynec. & Obst., **87**: 277, 1948.

[4] Cole, W. H., L. Walter and L. R. Limarzi: Indications and Results of Splenectomy. Ann. Surg., **129**: 702, 1949.

[5] Linton, R. R., I. B. Hardy, Jr. and W. Volwiler: Portacaval Shunts in the Treatment of Portal Hypertension. An Analysis of 15 Cases With Special Reference to the Suture Type of End-to-Side Splenorenal Anastomosis With Splenectomy and Preservation of the Kidney. Surg., Gynec. & Obst., **87**: 129, 1948.

[6] Movitz, D. M., and G. M. Curtis: Surgical Significance of the Accessory Spleen. (Abstr.) Surgery, **20**: 308, 1946.

[7] Norcross, J. W.: Indications for Splenectomy. S. Clin. North America, **27**: 616, 1947.

[8] Quan, Stuart and B. Castleman: Splenic-vein Thrombosis Following Transthoracic Gastrectomy and Incidental Splenectomy. New England J. Med., **240**: 835, 1949.

[9] Welch, C. S., and W. Dameshek: Splenectomy in Blood Dyscrasias. New England J. Med., **242**: 601, 1950.