RECURRENT PRIMARY THROMBOCYTOPENIC PURPURA WITH ACCESSORY SPLEENS*

Review of the Literature

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WERLHOF in 1731, laid the foundation for our present concept of the disease which bears his name, and which also is described as "purpura hemorrhagica." However, in the eighteenth century, the spleen was unsuspected of being associated with thrombocytopenic purpura. In 1916, Kaznelson,[2] while still a medical student, favored the theory that hypersplenism was responsible for lowered platelet counts. This resulted from an observation which he made, namely, that in three of four cases of thrombocytopenic purpura, he found a splenomegaly. At his insistence, he persuaded Shloffer of Prague to do a splenectomy on a patient suffering from chronic thrombocytopenic purpura; this resulted in a dramatic response. In 1921, Finkelstein[3] was probably the first to call attention to the fact that accessory spleens might be responsible for the recurrence of symptoms in postsplenectomy essential thrombocytopenia, and in 1928, Morrison, Lederer and Fradkin[4] reported two cases of accessory spleens associated with this condition. The role played by unremoved accessory spleens following splenectomy for primary thrombocytopenic purpura has been stressed by Curtis and White,[5] Vaughan,[6, 7] Robertson,[8] Maingot,[9] Curtis and Movitz,[10, 11] and Watson and Moir.[12]

Despite the fact that such significance has been placed upon unnoticed splenicules, few cases are reported. Watson and Moir[12] record recurrent purpuric manifestations in a case following therapeutic splenectomy in which a 2.5 cm. diameter accessory spleen was found at necropsy. A similar case appears in the article of Curtis and Movitz.[11] These latter two authors have established the importance of accessory spleens in showing that in 174 consecutive cases of splenectomy, and in four abdominal explorations, they found 131 accessory spleens in 56 patients, an incidence of 32 per cent. The number of accessory spleens varied from one to ten.

Recurrence of primary thrombocytopenic purpura is reported by Giffin and Holloway[13] as 14 per cent, and Vaughan[7] as 17 per cent. What percentage of such recurrences results from accessory spleens is unreported, but it is suggested by Watson and Moir,[12] that the incidence of the recurrences closely resembles that of accessory splenic tissue reported by pathologists. Adami and Nichols[14] report 11 per cent in their necropsies; the incidence at Cook County Hospital is 10 per cent; Emmet and Dreyfuss[15] record 10 per cent and Morrison et al[4] report 35 per cent after adoption of a systematic search. Increased incidence of accessory tissue in primary splenic disease is reported

* Submitted for publication, April 1948.

by Maingot[16] (44.4 per cent), Curtis and White[5] (20 per cent), McLaughlin[17] (24 per cent), and Curtis and Movitz[11] (31.4 per cent).

Splenic "seeding" should be considered during the removal of the spleen for such diseases as primary thrombocytopenic purpura and congenital hemolytic icterus, especially when recurrence follows. Such accidental "seeding" is suggested by Curtis and Movitz.[11] McLaughlin[17] has reported a case of recurrent congenital hemolytic icterus in a splenectomized patient, in whom generalized so-called abdominal "hemolymph" glands were found enlarged at necropsy; it was thought that these were splenic type tissue. The successful transplantation of such tissue into subcutaneous and muscle layers by Putschar[18] and Perla,[19] and the observation by several writers[20-29] of multiple intra-abdominal splenic tissue islets following trauma to the spleen, suggests the possibility of relapse by gradual assumption of splenic functions by these new growths. No instance, however, is reported in which such nodules following surgery for rupture of a normal spleen have resulted in primary splenic disease.

Buchbinder and Lipkoff[29] have termed the "seeding" of multiple splenic transplants through the abdominal cavity following splenic trauma as "splenosis," and this condition technically should be differentiated from the presence of true accessory splenic tissue. It is probable that the 400 accessory spleens reported in 1896 by Albrecht[20] and the case he cites by Orth were of this category.

While "splenosis" as described above follows no general plan, there are certain generalities to be noted concerning the locations of true accessory spleens. Since minuteness in no way eliminates the tissue as a cause of future recurrence, a definite plan of search should be followed to remove these offenders. Schilling[21] lists the possible sites in this order of frequency: (1) splenic hilus, (2) gastrosplenic omentum, (3) great omentum, (4) edge of the omentum, (5) splenocolic ligament, (6) pleurocolic ligament, (7) peritoneum along the splenic vessels, and (8) pancreas. Curtis and Movitz[10, 11] list: (1) the hilus of the spleen, (2) the pedicle of the spleen, (3) the retroperitoneal region around the tail of the pancreas, (4) the omentum, especially at the greater curvature of the stomach, (5) splenocolic ligament, (6) the mesentery of both small and large bowel, and (7) the left adnexa in females. The latter authors surprisingly found that 85 per cent of patients with accessory spleens had them in a single location, and that in no instance were more than two locations found. In addition, where such was the case, one of the double sites was always hilar. Even in unusual cases, such as Olken's,[30] a second hilar accessory was found in addition to a left scrotal splenicule.

EMBRYOLOGY

Splenic anlagen first appear in the 8 mm. embryo,[31] on the left side of the dorsal mesogastrium, as an accumulation of mesenchymal cells, just beneath the surface (peritoneal) epithelium. These appear as several small "hillocks" whose subsequent fusion forms a single organ. The survival of one of these may result in a lobulated or accessory spleen. Whether this abnormality occurs

cephalad, caudad or ventrad to the main mass, and whether it arises early or late in embryonic life determines roughly the location of the splenicule.

Curtis and Movitz[11] have given an excellent review of the underlying embryologic principles and consider five phases of splenic development sufficient to explain all accessory spleens. They are the following: (1) the manner of formation of the major spleen with its notches and lobulations by fusion of the separated splenic masses; (2) the formation of accessories by failure of fusion of the separate anlagen; (3) the formation and development of the subjacent dorsal mesogastrium into the various ligaments and bursae carrying along the accessory spleens to their various distant future locations; (4) the development of the splenic artery and its branches providing a similar blood supply to the splenic lobules and the accessories, with the accessory merely representing a greater degree of "fusion failure" than the lobule; (5) the embryonic contiguity of splenic anlagen to the genital ridge (on medial side of the mesonephros) permitting an accessory spleen to become attached to the left gonad.

Although the spleen is part of the blood system of the body, Keith[32] considers its development with organs of digestion since he thinks it must originally have been part of the alimentary system. Its origin is connected with the stomach, and its blood like the alimentary tract enters the portal circulation. The spleen grows from the left surface of the dorsal mesogastrium above the cardiac end of the stomach. It appears at the beginning of the sixth week as a localized growth of mesoderm. In the third month, the dorsal splenic surface is nodular and deeply fissured, and at the middle of fetal life these fissures begin to disappear but only persist on the anterior (gastric) border.

PATHOLOGIC PHYSIOLOGY

C. A. Doan[33] has done much to clarify the modern concept of the physiology of the spleen from an organ of complete mystery to one of understandable functions. Although much information concerning the spleen is controversial, certain facts seem fairly well established. This organ seems to have the following three structures: (1) a reticulo-endothelial system; (2) a vascular system; (3) a lymphoid system. The smooth muscle in the capsule and trabeculae together with the vascular system serve as the structural basis for the blood reservoir function of the spleen. The reticulo-endothelial system is made up of "specific endothelia," and a reticulum endowed with special phagocytic powers.

The normal spleen is concerned with blood cell destruction, formation and sequestration. A delicate splenic equilibrium results which may be upset by either congenital or acquired causes, resulting in diminution or accentuation of these physiologic processes. By means of supravital studies on splenic parenchyma, it has been shown that the spleen may become hyperactive with a resulting increase in number and phagocytic power of the macrophage. This has been referred to as hypersplenism. If this overactivity focuses on the red blood cells, congenital hemolytic icterus results; if it focuses on the thrombo-

cytes, then essential thrombocytopenic purpura results; and if the granulocytes are affected by the destructive process, a condition designated as primary splenic neutropenia results.[84]

When such a spleen becomes hyperactive, the bone marrow tries to compensate for the destruction and loss of blood elements. However, the spleen usually gains the upper hand and the involved blood cells are kept at a pathologic low level. Should an overactive spleen fail to discriminate between the elements which pass through it, red cells, granulocytes and platelets all may be destroyed simultaneously, resulting in a condition called pansplenic hematocytopenia. In such patients, a marked compensatory hyperplasia of the bone marrow results.

CASE REPORT

J. H. (46-58183), a 22-year-old white married female, entered Cook County Hospital November 25, 1946, complaining of an aching pain in the "right side" for 4 days, which was accompanied by vomiting and constipation.

History. History revealed that the patient, in her youth, suffered severe epistaxis once every two months, and also had marked gingival bleeding. After menarch at 14 years, she experienced prolonged menstrual periods which always lasted from one to two weeks with onset at 30-day intervals. These were described as not excessive but merely prolonged.

In April 1943, a slight injury resulted in a large bruise over the anterior forearm and arm. She consulted her family doctor who immediately had her hospitalized for observation. She recalls the diagnosis as "purpura" and states that she received "shots" in the deltoid area; however, she stopped these voluntarily.

In August 1943, following severe vaginal bleeding, the patient consulted a gynecologist and was immediately hospitalized. She received 6 transfusions, and a splenectomy was performed. She remained in the hospital for about 2 weeks, her vaginal bleeding stopped, and the small red spots which were present on her legs gradually disappeared. Postoperative platelet counts unfortunately were not done.

Thirty days after the preceding hemorrhage, another severe vaginal hemorrhage occurred and following its cessation, in approximately 10 days, the patient received radium therapy via a vaginal pack. Although her ecchymoses and gingival bleeding persisted and the small red spots continued to appear, she had no vaginal bleeding until May 1945, when she had a scant three-day flow. These facts should have made one suspicious of the presence of accessory splenic tissues.

In May 1946, the patient consulted her local doctor because of severe pain in the left side and back and was told she might be pregnant. In the latter part of April, the vaginal bleeding recurred and the fourth day after its onset, May 2, 1946, she entered the Cook County Hospital as a threatened abortion case. She was treated for shock and severe anemia by multiple transfusions of whole blood. A blood count done on May 3, 1946, revealed RBC 1.06, WBC 33,700, Platelets 252,290 and Reticulocytes 4.9. A marrow smear was reported as not unusual, and it was the impression of the hematologist that local genital pathology was the cause of the prolonged hemorrhage. On May 11, 1946, a currettement was done with negative gross and microscopic findings, and on May 22, 1946, she was operated upon and the left tube and ovary were removed. Diagnosis: hematosalpinx and hemorrhage into an ovarian cyst. No further platelet counts were done and the patient left the hospital on the twenty-ninth day.

At the present admission, she complained of pain just above the right iliac crest which was present for 4 days, and was dull and aching in character. She was awakened during this period each morning at 4:00 A. M., by a pronounced desire to defecate but was unable to have a bowel movement. Nausea and vomiting of clear fluid relieved the

urge to defecate without alleviating the pain. This sequence was repeated once each afternoon during the present illness with no relation to hour, food intake or activity. Voluntary dietary restrictions were imposed. On the day of admission, she was again awakened with the desire to defecate, but had relief following a small clear liquid emesis which this time contained specks of blood. Upon admission to the Cook County Hospital the

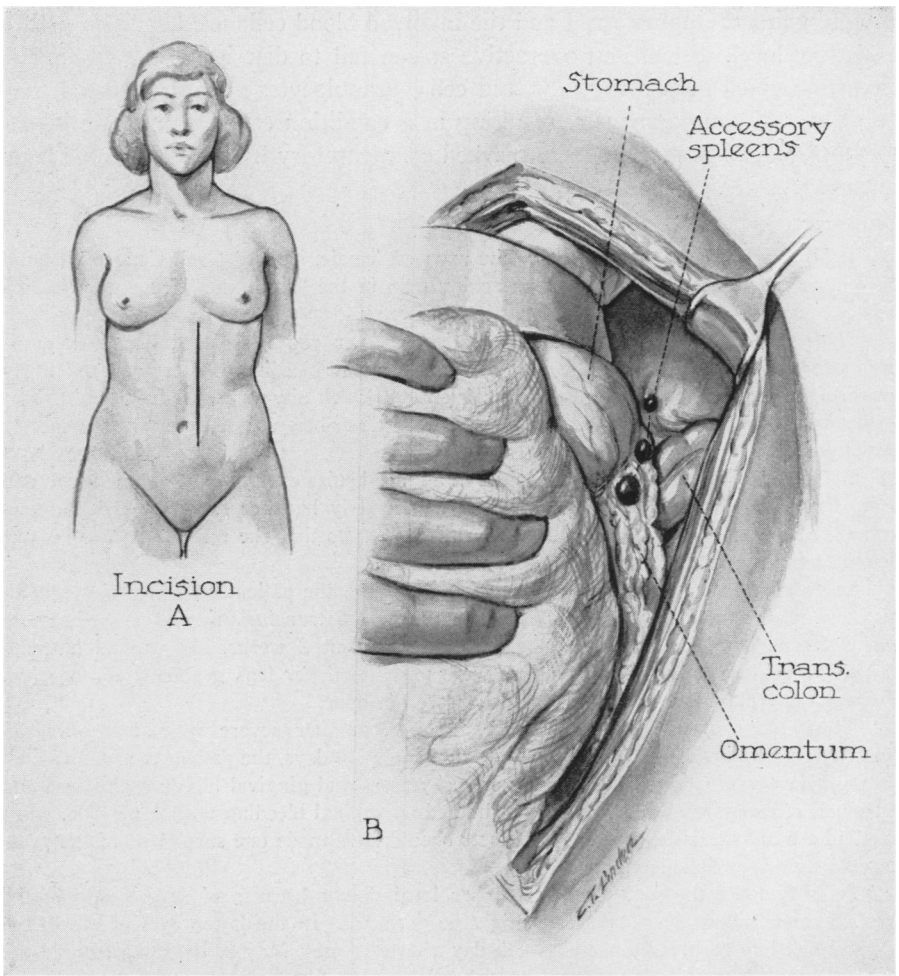

FIG. 1. (A).—Longitudinal left transrectus incision gave adequate exposure.
(B).—The three accessory spleens as seen at surgery.

patient gave no history of drug or medication ingestion nor of recent illnesses. The family history was essentially negative and venereal disease was denied.

Physical Examination. Physical examination revealed a pale, thin white female who did not appear acutely ill. Blood pressure 110/80, pulse 90, respirations 18, and the rectal temperature was 99.8. Several large ecchymotic patches were found over the body unassociated with trauma. The abdomen was soft, not tender, and no masses could be palpated. Bowel sounds were somewhat hypo-active. Left subcostal and Pfannensteil scars were well healed. The pelvic examination was non-contributory except for a very firm, regular cervix and vault, and adnexal adhesive distortion. A Rumpel-Leeds test was negative.

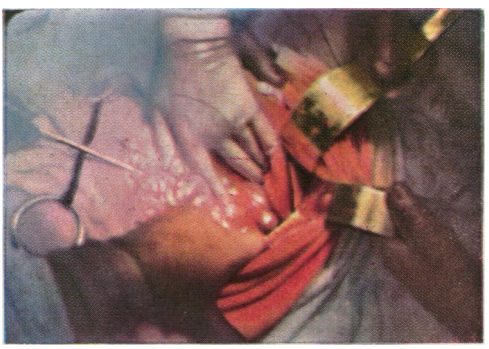

FIG. 2.—The largest of the three accessory spleens located in the omentum near the previously ligated splenic pedicle.

Treatment. The patient was placed on a high-protein, high-carbohydrate diet with supplemental vitamin and iron therapy. On November 27, 1946, the second day of hospitalization, a platelet count was 77,280. It was at this time that the possibility of accessory splenic tissue presented itself. On November 30, 1946, platelets numbered 6,850 and a normal cell count and differential were recorded. Vigorous intravenous therapy was started, giving at least 500 cc. of blood daily in addition to other parenteral fluids. An elimination diet was begun, all medication stopped, and the patient held in readiness for emergency exploratory laparotomy in search of accessory splenic tissue if significant increase in peripheral platelets did not occur. A sternal puncture at this time revealed a marrow with slightly increased granulopoieses and a right shift, but with megakaryocytes and eosinophiles in normal numbers; findings were compatible with the clinical diagnosis of recurrent thrombocytopenic purpura. Chest plate and barium studies revealed no pathology. Preoperative bleeding time was 8 minutes 5 seconds; coagulation time was 4 minutes 10 seconds. Elimination diet was discontinued since the thrombopenia was apparently not on an allergic basis; on December 4, 1946, the Rumpel-Leede test was positive.

On December 5, 1946, under pontacaine spinal anesthesia, an exploratory operation was performed, by Dr. P. T., through a longitudinal left transrectus incision. It was noted during the entire course of the operation that there was a marked tendency to bleed. Three accessory spleens were found (Fig. 1). The largest approximately the size of a cherry (Fig. 2), the second about the size of a pea and the third that of a pinhead. The first two were close to each other and were located in the omentum near the previously ligated splenic pedicle. The smallest spleen was found along the upper border of the tail of the pancreas. Macroscopically it was difficult to differentiate the latter from a tiny lymph node. Microscopic sections on all three specimens definitely established each as being an accessory spleen with the following description: the section revealed dilated sinusoids with a slightly hemorrhagic pulp and marked proliferation of mononuclear cells and a few polymorphnuclear leukocytes. The malpighian corpuscles were large. The pathologist concluded that these findings were in keeping with a diagnosis of thrombocytopenic purpura.

Following the removal of these masses, there was no dramatic cessation of bleeding; in fact, gingival hemorrhage of a moderate sort continued for two postoperative days despite whole blood transfusions. On the second postoperative day her clotting time was 9 minutes 17 seconds and bleeding time was 6 minutes. On the third postoperative day, all gum bleeding stopped, even though menstruation which began on December 2, 1946, continued. On the fifth postoperative day, December 10, 1946, the bleeding time was normal, platelets numbered 95,200 and the patient was up and about; menstruation ceased. Clinical improvement paralleled subsequent platelet increases and the patient left the hospital on December 21, 1946, with a platelet count of 750,000 to be followed as an out-patient.

The patient did remarkably well until January 8, 1947, when she again noted petechial hemorrhages and bleeding from the mouth. This increased in severity. She was readmitted. Repeated platelet counts varied between 0 and 14,000. She was reexplored on another surgical service January 14, 1947, and no additional splenic tissues could be found. However, on January 22, 1947, her platelet count had risen to 92,360. The patient gradually improved, her bleeding stopped and upon discharge from the hospital was clinically improved. She will be followed in the out-patient department. Whether or not tissue damage following surgery may stimulate platelet formation or not is theoretical. It seems more logical to conclude that splenic "seeding" might have occurred, or that ectopic splenic tissue still may exist in some very remote anatomical recess.

Many other methods of therapy have been advocated, especially in chronic cases, such as snake venom, cevitamic acid, roentgen-ray, viosterol, parathyroid extract and rutin, but these usually fail to produce the desired results.

The treatment for purpura hemorrhagica is splenectomy. This is an emergency procedure in the acute cases, and may be elective if the condition is chronic. The possibility of accessory spleens must be kept in mind, a search made for these, and if found they must be removed. Repeated transfusions with freshly removed matched blood (not bank blood) supply effective platelets. Hemorrhagic manifestations usually disappear while the patient is still on the operating table, and the platelet count rises immediately.

SUMMARY

1. A case of recurrent primary thrombocytopenic purpura associated with the removal of three accessory spleens is reported.
2. The literature is reviewed.
3. The importance of searching for accessory splenic tissue at the time of operation is emphasized.
4. The pathologic physiology of the spleen is reviewed.

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