II. Splenectomy in Myeloid Metaplasia with Myelosclerosis

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Like many another hematologic condition, myeloid metaplasia of extensive degree in association with myelosclerosis seems to be on the increase. Certainly what used to be a very uncommon condition is now observed not infrequently on every medical service. The picture is rather well defined: (1) a variable degree of pallor, usually with icterus, (2) a marked and at times a huge splenomegaly, (3) slight to moderate leukocytosis with the presence of a variable number of early granulocytes including myelocytes and even at times occasional myeloblasts, (4) conspicuous variation in size and shape of the red cells, (5) the presence of a variable number, usually a few, nucleated red cells, (6) a variable platelet level, at times very high, at times rather low, (7) very hypocellular bone marrow aspirations, which are often difficult to obtain because of extreme hardness of the bone, (8) splenic aspirations which show "bone marrow" activity, i.e., nucleated red cells, granulocytes, and megakaryocytes, and (9) trephine bone marrow biopsies showing marked fibrosis of the marrow. Many cases have a previous history of polycythemia vera, and indeed this condition as an antecedent of the rather momentary or "snapshot" situation of myelofibrosis is always a likely possibility. In other cases, there is a history of long continued exposure to various aromatic solvents, and this may well have some etiologic significance. In any event, the highly abnormal blood picture, the increasing size of the spleen, or the development of increasing anemia requiring transfusions eventually bring the patient to study. In some cases, especially when numerous transfusions are required to keep the red cells at reasonable levels, the question of splenectomy arises.

In previous years, the one prime contraindication to splenectomy was myeloid metaplasia with myelosclerosis, and seemingly with good reason. All studies indicated that the bone marrow was nonproductive and that the chief, perhaps the only, source of blood production was in the spleen. To remove this organ under such circumstances seemed a foolhardy thing to do, inviting, it would seem, a quick and untimely demise. However, reports began to appear, chiefly in British journals, of splenectomies that had not only been performed without incident but had actually been followed by a distinct improvement in the blood picture. A re-appraisal of thinking regarding splenectomy in this disease seemed
desirable. Thus, it was quite obvious that as the spleen became larger and larger, due apparently to increasing metaplasia, the patient's anemia became increasingly severe. In other words, as more and more “marrow” was produced in the spleen, fewer and fewer red cells were found in the blood. Splenic production of blood, for one reason or another, did not appear to be very efficient, at least as regards the actual delivery of blood cells into the circulation. In some cases, too, a well defined hemolytic component, perhaps associated with the large spleen, was present, making numerous transfusions necessary. These and other considerations finally led to increasing consideration of the previously forbidden operation of splenectomy. The opinion of the above panel was therefore requested on the following questions:

In a case of myelosclerosis with myeloid metaplasia of the spleen requiring increasing numbers of transfusions, (a) would you consider splenectomy, (b) have you had experience with this operation and, if so, what are the results?

DR. CARTWRIGHT:

In cases requiring increased numbers of transfusions, we have and we will continue to consider splenectomy. To date, however, we have not splenectomized any cases in our clinic.

Two patients have been observed who were splenectomized elsewhere. One we have followed for seven years post-splenectomy and the other, nine years. So far as we can tell, the splenectomy has had no effect, either good or bad, on the course of the disease. Of course, this is a very difficult thing to evaluate. We had one patient with this condition and severe anemia who was given x-ray therapy in a dosage of 275 r to the spleen without benefit. She died twelve days after the beginning of x-ray therapy but was in a terminal state when the therapy was begun.

DR. FINCH:

Answer to question (a): Yes.

Answer to question (b): We have evaluated five patients with extensive myeloid metaplasia of the spleen. In two, red cell destruction was not increased and splenectomy was not advised. In three, there was increased blood destruction; and splenectomy, in addition to relieving symptoms, stopped the excessive cell destruction. The composite effect (decrease in blood destruction vs. removal of a blood-forming area) was an increased level of all circulating blood elements. Our experience would suggest that if the rate of blood destruction is twice normal or greater, anemia will not be adversely affected by splenectomy.

Drs. LOEB AND MOORE:

If a significant hemolytic component to the anemia can be demonstrated by careful evaluation of the erythrocyte survival time and by urobilinogen excretion studies, splenectomy should be seriously considered. A transfusion requirement in excess of 2000 cc. of whole blood per month in an adult may be used as presumptive evidence of accelerated red blood cell destruction, if there is no associated blood loss. In addition, we feel that two other observations should be made.
before splenectomy is recommended. In the first place, one should obtain evidence that blood cells are being formed in organs other than the spleen. A surgical marrow biopsy may show islands of hematopoiesis persisting in the fibrotic marrow, or myeloid metaplasia may be demonstrated in the liver. Secondly, ACTH or cortisone should be given judiciously for ten to fourteen days to see whether it will stimulate red cell production, decrease the rate of hemolysis, or both. If a favorable response to such hormone therapy is obtained, and if blood cell formation can be demonstrated in the marrow (or liver), splenectomy should be done. When the degree of hemolysis is extreme, we think it justifiable to remove the spleen even in the absence of a favorable response to steroid therapy provided, however, that erythropoiesis has been observed in organs other than the spleen.

We have studied six patients with myelosclerosis and myeloid metaplasia who fulfilled the above criteria. One woman responded so satisfactorily to cortisone over a 12 month period that splenectomy was not done; no follow-up is available on this patient. Of the remaining five patients whose spleens were removed, three have expired. One elderly woman died in the immediate postoperative period as the result of cerebral thrombosis and another patient with massive extramedullary hematopoiesis died shortly after removal of a 3200 Gm. spleen. A third patient required no transfusions for seven months after the operation; during the eighth month, megakaryocytes appeared in abundance in the peripheral blood and she died from portal and pulmonary vein thromboses. The remaining two patients have been observed for 14 and 43 months. In both instances the postoperative period was complicated for varying periods of time by a striking thrombocytosis, the presence of megakaryocytic fragments in the peripheral blood, and by thrombotic episodes or phlebothrombosis which persisted for as long as one year. Transfusion requirements have been markedly reduced, however, and in one patient the red blood cell count has been maintained at fairly normal levels without any additional transfusions. In no instance has a leukemic change occurred. The woman, who is now 43 months post-splenectomy, remained quite comfortable for the first two and one-half years, but has now developed a striking hepatomegaly. Her heart has also enlarged, possibly because of areas of myeloid metaplasia in the myocardium. In the three patients who survived the operation, life has been made more comfortable, and probably has been prolonged.

DR. SINGER:

Splenectomy in severe symptomatic hemolytic anemia associated with myelosclerosis and myeloid metaplasia of the spleen should certainly be considered. In such instances we first give large doses of cortisone, starting with 250 to 300 mg. daily, and observe whether the reticulocyte count increases and the requirement for transfusions to maintain a level of about 5 to 6 Gm. hemoglobin decreases. If that is the case we advise splenectomy following pre-treatment with cortisone for several weeks. After operation, the cortisone doses are gradually diminished. We have observed two such cases with gratifying results. In the first, a 51 year old male, a severe hemolytic process with positive Coombs test existed; Hb 6.0 Gm. RBC 1.9 M. Under cortisone treatment the reticulocyte
output increased from one per cent to eight per cent, the requirement for transfusions diminished, and splenectomy was performed three weeks afterwards. Histologically, the spleen showed myeloid metaplasia. Following operation, the patient had a Hb varying from 10 to 11 Gm. with a continuous high reticulocyte output (8 to 10 per cent), the Coombs test remained positive, but no transfusions were required any more. The patient died one year later from pneumonia.

The second patient, a 34 year old female, showed a similar picture which was, however, complicated by a severe thrombocytopenia (20,000 platelets), prolonged bleeding time (over 15 minutes), leukopenia (2 to 3000 WBC) in addition to a normochromic normocytic anemia of about 5 Gm. with one per cent reticulocytes. She had received about 3 transfusions (500 cc.) weekly to maintain this Hb level for almost 2 months prior to admission. Two weeks after intensive cortisone treatment (300 mg./day) the bleeding time had become normal, although the platelet level had not changed. The reticulocyte count became elevated to about 7 per cent, and only one transfusion per week was required to maintain a hemoglobin level of about 7 Gm. When splenectomy was performed the platelet count became normal, the leukopenia disappeared, the hemolytic anemia improved markedly, and no further transfusions were required to maintain a hemoglobin level of about 10 Gm.

Green et al. (New England J. Med., 248: 211–219, 1953) gave an excellent summary of the effect of splenectomy in 29 patients with agnogenic myeloid metaplasia. From their data it is clear that the operation rarely has a deleterious effect on the hematologic status and may sometimes result in marked improvement of the symptomatic auto-immune hemolytic anemia and/or thrombocytopenia. Much more experience is needed to evaluate whether the response to cortisone may indicate the possible effect of splenectomy. It goes without saying that the general state of the patient must also be considered before decision to perform this operation is made.

**Moderator’s Comment**

It is apparent that all members of the panel agree that splenectomy should be seriously considered in at least some cases of myelosclerosis and myeloid metaplasia. If the patient’s condition is a static one, and the blood picture reasonably good without any transfusions, splenectomy would seem to be inadvisable, as one would hardly expect to modify the resultant course of the disease by the operation. On the other hand, if the patient requires ever-increasing numbers of transfusions, indicating the likelihood of a hemolytic component, splenectomy must be seriously considered. Further considerations should involve the patient’s age, general condition, the size of the spleen, etc. A huge spleen occupying almost the entire abdomen in an elderly individual with impending heart failure is hardly a good surgical risk. An important limiting factor, too, may be the platelet level. Many patients with this condition have platelet counts of 1.0 to several million and splenectomy in such cases may be followed by an extraordinary thrombocytosis up to 8–10 million which may lead to multiple thromboses and even to fatal termination. This happened in two of our cases. In two others splenectomized elsewhere, the patients survived the operation but eventually developed extraordinary degrees of thrombocytosis associated with either throm-
botic or hemorrhagic manifestations—the latter a not uncommon paradoxical effect of thrombocytosis. The most ideal case for splenectomy is a relatively young individual with a marked but not striking splenomegaly who has need for numerous transfusions but whose leukocyte and particularly platelet counts are lower than normal. In three such patients, splenectomy was followed by complete freedom from further transfusion requirements during the follow-up period (4 to 10 months), whereas previously, transfusions were needed every two or three weeks. One patient, previously requiring frequent transfusions, actually developed polycythemic blood levels and was venesected twice by her physician because of headaches. The ultimate course of those patients benefited by splenectomy remains to be determined, although in some cases there is apparently no effect, and in others, as in the case of Loeb and Moore recorded here, there has been increasing size of the liver and evidence of impending heart failure. Certainly, splenectomy is not to be entered into lightly and is best postponed until one is sure that all conditions are "right." It should also be fully realized that splenectomy is by no means curative of the fundamental myeloproliferative disease, which may eventually terminate in one of several directions.
Panels in Therapy. II. Splenectomy in Myeloid Metaplasia with Myelosclerosis

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