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Discussion

Dr. A. Aufses (New York, New York): Dr. Akwari and his colleagues are to be congratulated for presenting a beautifully documented series of 100 patients operated on for idiopathic thrombocytopenic purpura (ITP) over a 10-year period.

The manuscript that I was privileged to review is replete with extensive, prospectively derived hematologic observations and the discussion section is most complete and superbly written. I recommend its reading to all of you.

I would like to limit my remarks and questions to only one aspect of this very complete review. That is, the role of the accessory spleen in the failure of response to primary splenectomy.

Autopsy studies have shown about a 10% incidence of accessory

splenic tissue. In 1969, Olsen and Beaudoin reported a large series of splenectomies performed in Ann Arbor. At operation for nonhematologic causes, the incidence of accessory splenic tissue was 4%. This incidence rose to 25% when operation was performed for either ITP or autoimmune hemolytic anemia. In that paper the authors cautiously point out that bias may have entered the picture since a more diligent search for accessory spleens was probably carried out in those patients operated on for hematologic disease.

In 1984, we reported a consecutive series of 69 patients operated on for ITP. Of 60 initial complete responders, three relapsed at 1, 2, and 5 years after operation. Nine patients were either partial or nonresponders. All 12 patients had technetium scanning and no accessory tissue was identified. We do, however, have one patient who had the primary splenectomy performed elsewhere and then relapsed after a number of years. An accessory spleen was identified by scan. This was removed by Dr. Isadore Kreel of our faculty and the patient has had a complete and sustained response.

Returning to Dr. Akwari's most interesting data, 18 accessory spleens were found at primary splenectomy in the 100 patients. Fifty-eight patients had an immediate excellent response. Of 13 patients with a poor response, five required accessory splenectomy, not recognized at the first operation, and scanning of 29 nonresponders identified seven more patients with accessory spleens of whom four were operated on. These were also not recognized at the first operation.

This gives us at least 30% of the original group of 100 patients with accessory splenic tissue, a very high percentage indeed. Might not it have been even higher?

It has been shown that it is possible in ITP to have a prolonged good response to splenectomy and still have occasional splenic tissue present. In fact, in the Duke series, four of the nine patients who had accessory splenic tissue removed at a second operation had had a response to primary splenectomy that lasted from 2 to 10 years.

My questions to the authors then are: (1) Is it not possible that some of the patients in this series as well as ours and others might still have splenic tissue remaining and be doing well? (2) Is there any explanation as to why some patients with accessory spleens will do well for prolonged periods after primary splenectomy for ITP and others do not? (3) Is it possible that some of the "accessory spleens" found at subsequent surgery were not present originally, but might represent nodules of splenic tissue developed after a fragment of spleen is spilled at the primary operation? In other words, a form of localized splenosis. Seeing the movie just now, it is hard to believe that those two lesions could have been missed at the primary operation. The first one was in the original hilum of the spleen, the second was 7 cm in diameter. Could this development of localized splenosis be the responsible agent for the late relapses? (4) Since indium-11 appears to be a more sensitive scanning isotope than technetium, should all patients who have surgery for ITP have a preoperative scan?

With a high incidence of accessory spleens, scanning might be cost effective when compared with the cost of a second operation. Certainly there is nothing more frustrating for a surgeon than to perform a splenectomy for ITP, not get the platelet response hoped for, and then worry whether an accessory spleen was left behind, or whether the patient does, in fact, have a different diagnosis?

DR. WILLIAM W. COON (Ann Arbor, Michigan): Dr. Akwari asked me yesterday to make a few brief comments concerning his manuscript. We have few differences of opinion. The immediate and sustained response rate in our recently reported series is almost identical with Dr. Akwari's. I believe one of the major points that Dr. Akwari has made, and we would certainly agree with, is that there currently is no way in a given individual to predict whether he or she will respond to splenectomy. We know some statistical bases that can help in predicting response; for example, age, as Dr. Akwari pointed out. Another observation we made is that the response rate, as you might expect, is higher in patients who respond to a burst of high-dose steroids, particularly if the platelet count goes above 100,000/mm^3. On the other hand, about half of the patients who do not get a response above 50,000/mm^3 with steroid bursts still get a response of splenectomy. Although the odds go up, there is no certainty as far as that is concerned.

We also have been unimpressed with the predictive value of platelet antibody studies. There has been no correlation in our hands between platelet antibody titers and whether the patient is going to respond to splenectomy.

One difference of opinion that we have is that we seldom believe that we need to give platelet transfusions to our ITP patients unless the platelet count at the time of operation is 20,000/mm^3 or below. In our big hematologic center we have a greater need for platelets than the supply at any given time. The ITP patient, compared with patients with other hematologic problems, has young, very hyperfunctional platelets that are circulating, and we have not encountered any bleeding problems in recent years in greatly restricting the use of platelet transfusions.

As Dr. Aufses implied, we also have been somewhat skeptical about the value of accessory splenectomy in patients who are nonresponders. Certainly there is every reason to scan a patient who responds initially to splenectomy and then relapses later. I believe there is some correlation between the size of the accessory spleen that one may encounter and the predictability of response to accessory splenectomy, and in the scan that Dr. Akwari showed, certainly with that huge splenic remnant, there would be a good chance for response, but we have performed accessory splenectomy on a number of patients without seeing any response in their recurrent thrombocytopenia.

Another observation that we have made is that, of our nonresponding patients, less than 20% are on any long-term ancillary therapy for their thrombocytopenia. Many patients will function very well with platelet counts between 50,000/mm^3 or even 30,000/mm^3 and 150,000/mm^3 without needing any subsequent treatment. The majority of those who are on any therapy are on a relatively low-dose chronic prednisone treatment.

I believe we can limit the use of cyclophosphamide or vincristine with all their potential toxic effects because even the nonresponders seldom need it.

DR. CHARLES L. WITTE (Tucson, Arizona): I congratulate the authors on their remarkable series and on an ingenious method to detect these spleens at operation. On the other hand, as some of the other discussants implied, I also interject a word of caution about the real implications of these accessory spleens. Some years ago Crosby suggested (N Engl J Med 1972; 286:1252–1254) that small remnants play little or no role in ITP, which displays great clinical variability in terms of platelet response as well as need for prolonged follow-up to ensure that these small remnants or their removal truly exert an impact on the peripheral platelet count. We are all familiar with the improved response of children over adults to splenectomy. When an IgM protein coats the peripheral platelets, as in adults, both the liver and the spleen prematurely extract platelets from the blood circulation, whereas when platelets are coated by IgG alone, as in children, splenectomy is usually highly effective.

I would like to describe three patients with ITP from my experience whose findings cast doubt on the importance of small accessory spleens in influencing the peripheral platelet count. Although I would not recommend the first approach, it nonetheless is noteworthy that one of my colleagues, a pediatric surgeon in Tucson, some years ago in a 5-year-old boy with a very low peripheral platelet count opted to do a splenectomy, which was entirely appropriate, and then placed small autoremnants into the anterior abdominal wall as an implant, presumably to protect against overwhelming sepsis. A technetium sulfur colloid scan at 2 months failed to reveal remnant tissue, and the peripheral platelet count was normal. About 2 years later, the mother returned and inquired about a palpable nodule in the boy's abdominal wall. A radionuclide heat-damaged red cell scintiscan was then obtained (slide), and on the lateral view right beneath the skin a splenic remnant is clearly visible. The child's platelet count was still 350,000/mm^3, and 4 years thereafter the platelet count remained normal despite persistence of the splenic nodule. Unfortunately over the past 1.5 years he has disappeared from follow-up.

A second patient was a 5-year-old girl (slide) in whom I tried some years ago to regulate splenic function by ligating the splenic artery close to the hilum. Subsequently I have learned that because of a rich peripancreatic and gastric collateral circulation, the effectiveness of this

procedure is only temporary. Nontheless, her peripheral platelet count, which had been less than 20,000/mm^3 for over 1 year, rose promptly after operation but thereafter fluctuated widely. Four months after splenic artery ligation she demonstrated a normal splenic image on radionuclide scintiscan and her blood platelet count 12 years later is now 300,000/mm^3. She menstruates without excessive bleeding.

The final patient is a young man with Evans syndrome, which is both an autoimmune hemolytic anemia and thrombocytopenic purpura. He initially did well after splenectomy, but returned 15 years later with recurrence of thrombocytopenia, and a prominent splenic remnant was detected. This splenic fragment was removed and again he had a prompt rise in the blood platelet count. Within 6 months, however, the peripheral platelet count again dropped to 22,000/mm^3 despite lack of a residual spleen.

These patients with ITP highlight the variable nature of peripheral platelet count with and without remnant spleens and suggest that we should exert extreme caution in ascribing the clinical outcome to small residual splenic fragments after splenectomy. They also emphazise again the need for prolonged follow-up given the wide fluctuation in platelet count and even spontaneous remissions that may occur in ITP.

DR. ONYE E. AKWARI (Closing discussion): I am most grateful to the discussants. The points raised are all most interesting and reveal our ignorance in this disease.

One can say that ITP, an immune disorder, is not primarily a surgical disease, and requires close collaboration between the surgeon and the hematologist for optimum management. We continue to learn a lot from this team approach.

Dr. Aufses, I believe that splenosis is well documented in the literature, and as I remarked in my presentation, we do exercise great care not to spill any splenic tissue because of that eventuality, and the possibility of iatrogenic splenosis. I do not know, however, that there is proof that splenosis *per se* relates to recurrence of this disease. I know of no specific evidence that splenosis tissue is immunologically viable or can lead to the phenomena that are observed in this disease.

It is true that a large number of the patients have relatively large accessory spleens, but in some of these patients we found accessory spleens less than 1 cm in greatest diameter. Still when the splenic tissue was removed, the patients had a sustained response, with normal platelet counts during several years of observation. All we can conclude is that the accessory spleen must have had something to do with the disease in these patients, but the exact mechanism of its function remains to be fully elucidated.

The 30% incidence of recurrent ITP observed in this series is high. I believe it is because we search unusually meticulously for accessory spleens. I have no further explanation for that.

Dr. Coon raised many good points, and I would agree with him that currently we do not have any way of predicting response in any one patient, but therein, I believe, lies a challenge for the future.

I enjoyed seeing the transplanted splenic tissue in the abdominal wall, and was pleased to learn that the patient is doing well. I would agree with you that one would not advise doing that on a routine basis. I believe, however, that our data would suggest that the patient in question merits close observation.

Recurrence of ITP after previous accessory splenectomy occurred in one of our patients, and this was before we established our current techniques of intraoperative localization. In that patient, I believe it was patient No. 5 in our series, we identified additional accessory splenic tissue on a subsequent scan and performed repeat accessory splenectomy. The patient now enjoys a total response. One would have to conclude, cautiously, that in cases of initial failure, re-examination and repeat accessory splenectomy may be helpful in those selected cases in whom unequivocal evidence of additional splenic tissue is found.