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Chronic Idiopathic Thrombocytopenic Purpura
Effective preoperative preparation and long-term results of splenectomy

James C. Gruenberg, MD,* Melvin A. Block, MD,** Ellis J. Van Slyck, MD,***
and Joseph P. Abraham, MD***

A retrospective review of 98 patients seen at Henry Ford Hospital from 1953 through 1977 demonstrated that splenectomy for chronic idiopathic thrombocytopenic purpura provided a good response which usually was sustained on long-term follow-up (72% at 15 years). Although splenectomy for this condition had a low mortality, morbidity was significant in patients older than 40 years.

When compared to patients whose response to splenectomy was sustained, patients who relapsed had significantly lower platelet counts preoperatively both when they were untreated (mean: 9,194 per cc versus 18,524 per cc) and/or when they were treated with steroids (mean: 85,647 per cc versus 142,590 per cc). Another significant risk factor for relapse was a longer interval from splenectomy to the maximum postoperative platelet count.

In the immediate preoperative preparation of the patient for splenectomy, corticosteroids temporarily increased the platelet count, but high doses were necessary in many patients. A platelet count of greater than 40,000/cc usually was achieved with a dose of 60 to 80 mgs of prednisone per day for several days. Platelet infusion rarely was needed if patients were prepared adequately with steroids. There should be no hesitation to give large doses of steroids for a few days, and a delay in proceeding with the operation, once indicated, should be avoided. Because the response of the platelet count to splenectomy may be variable or fluctuating and late relapses can occur, patients should be re-evaluated periodically.

Splenectomy is often performed for the treatment of chronic idiopathic thrombocytopenic purpura (ITP). The operation is considered safe, and bleeding complications are minimized if preoperative blood platelet counts are higher than 40,000/cc, because circulating platelets in this condition are young and functionally sound (1). Our study of experience with this disorder at Henry Ford Hospital was designed to determine the dependability of short-term glucocorticoid (steroid) administration in providing adequate preoperative platelet levels and to determine the long-term effectiveness of splenectomy.

Clinical Materials

We reviewed the medical records of all patients who had been diagnosed for thrombocytopenia at Henry Ford Hospital between 1953 and 1977, and we selected 98 patients for study. Excluded were patients whose thrombocytopenia had a recognized etiology; patients, particularly children, whose idiopathic disease was acute; patients with systemic lupus erythematosus; and patients who had undergone splenectomy at another hospital. Reports of bone marrow examination were reviewed for all patients in order to verify findings typical for ITP.

In order to determine postoperative morbidity, platelet response before and after splenectomy, and the nature of relapse after splenectomy, we examined 11 variables: age, sex, duration of symptoms, duration of known thrombocytopenia, lowest preoperative platelet count, highest preoperative platelet count, clinical response to steroid therapy, spleen weight, maximum postoperative

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59
platelet count, the day of maximum platelet count, and major postoperative complications. All patients were followed from one month to 34 years, with a mean of 4.3 years. Their distribution by age and sex is shown in Figure 1.

In general, our approach to the patient suspected of having chronic ITP was to initiate a trial of steroid therapy while appropriate tests were carried out to confirm the diagnosis. Steroid medication was continued until the patient became asymptomatic and the platelet count exceeded 100,000/cc. The steroid dosage was then reduced gradually over several weeks, and the patient's platelet count was again measured.

On the basis of their preoperative response to steroid therapy, five groups of patients were identified:

1) 7 patients became asymptomatic and maintained platelet counts greater than 100,000/cc for varying periods after steroids had been discontinued.

2) 26 patients had platelet counts in excess of 100,000/cc but could not maintain this level without low doses of steroid medication.

3) 42 patients failed to reach platelet counts of 100,000/cc on high or moderate doses of steroids (greater than 20 mg of prednisone per day) or sustained a steroid complication, e.g., compression fracture or Cushingoid habitus.

4) 8 patients did not receive steroid therapy or had splenectomy before a trial of steroid therapy could be completed. For this reason, we were unable to evaluate this group of patients.

5) 15 patients did not achieve a platelet count of 40,000/cc. Within this group, nine patients received less than 60 mg of prednisone per day, four received 60-80 mg of prednisone per day, and two patients received more than 120 mg of prednisone per day.

If thrombocytopenia persisted or the patient could not be removed from steroid medication completely without a significant drop in the platelet count, splenectomy was considered. Because of the well-known risks of continuous long-term steroid administration, we preferred to proceed with splenectomy within three months of the onset of known thrombocytopenia when it became apparent that the patient could not safely be withdrawn from steroid therapy.

Results

Clinical response after splenectomy

We considered the clinical response after splenectomy to be good if the patient was asymptomatic, maintained normal platelet counts, and required no steroid therapy. As displayed by the life table method (Fig. 2), the response of our 98 patients to splenectomy was good and sustained to a remarkable degree (72% at 15 years).

Nineteen of 98 patients relapsed after splenectomy, and their response fell into one of three clinical groups. One group consisted of ten patients who experienced thrombocytopenia after splenectomy and required continuous steroid therapy postoperatively. Eight of the ten relapsed within one year after surgery, the other two at three and 15 years postoperatively. A second group of three patients had platelet counts that fluctuated between normal and thrombocytopenic. They required steroid medication intermittently and relapsed within six months after splenectomy. In the third group were six patients who had normal postoperative platelet counts but occasionally required steroid medication for brief episodes.
Idiopathic Thrombocytopenic Purpura

Response to Splenectomy

Fig. 2
Cumulative patient survival without relapse after splenectomy.

of thrombocytopenia. Two of these six relapsed within one year after splenectomy, the other four at two, three, seven, and 18 years postoperatively.

Platelet response after splenectomy

Before splenectomy, a series of platelet counts was taken for each patient in the study, which ranged from a minimum of three to as many as 40 in a few cases. The rise in the platelet count was plotted for each patient, and these elevations were then compared among patients.

Each patient's lowest preoperative platelet count, usually obtained at the time of initial presentation, was higher (mean: 18,524/cc) in patients whose response to splenectomy was sustained than in those patients who relapsed (mean: 9,194/cc) (P=0.0246), although the statistical variance was large in each group. Similarly, each patient's highest preoperative platelet count, usually obtained when the patient was receiving steroid medication, was higher in those patients who did not relapse after splenectomy (mean: 142,590/cc) than in those who did (mean: 85,647/cc) (P=0.0284). This difference was more significant at lower platelet counts (P=0.0162 at 40,000/cc versus P=0.0527 at 100,000/cc), indicating that the risk of relapse was greatest for patients who had the poorest response to steroid therapy as measured by platelet counts. Thus, our group of 15 patients whose preoperative platelet count did not reach 40,000/cc was more likely to relapse after splenectomy (Table I), and the type of relapse was more likely to be severe and persistent, as clinically defined (Table II).

After splenectomy, only two patients did not have an increased platelet count, and three patients could not be removed from steroid medication because of persistent thrombocytopenia. There was no statistically significant difference in the maximum platelet count reached after splenectomy between those patients who subsequently relapsed and those who did not. However, in those patients who sustained a good clinical response to splenectomy, the platelet count reached its maximum level earlier than in those patients who relapsed (mean of 7.6 days versus mean of 9.5 days) (Fig. 3). Those patients whose maximum platelet count occurred later after splenectomy (P=0.0003 at 15 days) had a particularly high risk of relapse.

Postoperative complications

Of 98 patients, 23 developed 39 major postoperative complications. The 11 wound complications included evisceration (one patient), incisional hernia (two), and major wound infections (eight). The major pulmonary complications of six patients included labor consolidation and persistent infiltration with fever. No patient had a pulmonary embolus, and of the two patients who had a deep venous thrombosis, one also had an episode of deep venous thrombosis in the same leg years before chronic ITP had been diagnosed. In addition to 11 other major complications, there were four patients with a

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**TABLE I**

<table>
<thead>
<tr>
<th>Highest Preoperative Platelet Count</th>
<th>Relapse</th>
<th>Sustained Response</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>&lt;40,000</td>
<td>6</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>≥40,000</td>
<td>10</td>
<td>65</td>
<td>75</td>
</tr>
<tr>
<td>Not evaluable</td>
<td>3</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>79</td>
<td>98</td>
</tr>
</tbody>
</table>

Chi-square = 6.08; Significance = 0.013
Fisher Exact Probability = 0.0236

**TABLE II**

<table>
<thead>
<tr>
<th>Highest Preoperative Platelet Count</th>
<th>Clinical Relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I</td>
</tr>
<tr>
<td>&lt;40,000</td>
<td>3</td>
</tr>
<tr>
<td>≥40,000</td>
<td>6</td>
</tr>
<tr>
<td>Not evaluable</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
</tr>
</tbody>
</table>

Chi-square = 6.48; Significance = 0.0370
subphrenic abscess, two with cardiac difficulties, two with pancreatitis, and one with chronic hepatitis.

Those patients who developed major postoperative complications were older (Table III), had larger spleens (Fig. 4), and experienced platelet counts that reached maximum levels later after splenectomy. This difference in the maximum level was more significant earlier in the postoperative period ($P=0.0058$ at 8 days versus $P=0.0432$ at 11 days).

**Operative mortality and morbidity**

Three patients died early in the postoperative period from complications not specifically related to thrombocytopenia. All three had responded well to splenectomy as determined by a good platelet response postoperatively. Ten patients died between seven months and 17 years after splenectomy. Five experienced no recurrence of thrombocytopenia, and of the five who relapsed, thrombocytopenia was a contributing factor in the death of only one.

**Discussion**

Of the 11 variables we measured with respect to postoperative morbidity, platelet response, and nature of relapse, there was a correlation between postoperative morbidity and increasing age, larger spleen weight, and delay in reaching maximum platelet counts. There was no correlation among any of the other variables.

Our study confirmed previous reports which indicate that splenectomy gives good results for the treatment of chronic ITP (2-8). Furthermore, we found that long-range patient follow-up is essential to provide accurate data, as the response to splenectomy may be delayed or incomplete, and an occasional late relapse occurred. Our study also emphasized that it was possible to achieve satisfactory preoperative platelet counts for nearly all patients with chronic ITP, if sufficiently large doses of steroids were administered. We recommend that after the decision has been made to perform splenectomy, it should be carried out as soon as feasible. The patient should be given large doses of steroids, and once the platelet count reaches $40,000/cc$ or higher, any
further delays should be avoided. In general, we believe that platelet transfusions are not useful in preparing patients with ITP for splenectomy, since, even if the patient has received a large dose of steroids, donor platelets are rapidly consumed in the recipient with chronic ITP. Preoperative plasmapheresis is a new technique that has been developed since this series concluded (9).

Many authors have suggested that the patient's initial preoperative response to steroids will determine the effectiveness of splenectomy as treatment for chronic ITP (1,3,6,8,10-13). Although uniform criteria for response to steroids do not exist, and comparisons among different series are thus not practical, our study did not confirm this reported relationship. While 15 patients in our series had a poor clinical response to steroids as manifested by a maximum preoperative platelet count of less than 40,000/cc, nine of them had a good response to splenectomy. Nevertheless, these 15 patients, who were receiving large doses of steroids, appeared at higher risk for relapse after splenectomy.

Similarly, previous reports have indicated that the longer the duration of the disease, the poorer the patient's response to splenectomy, to steroids, or to other immunosuppressive therapy (6,13,14). In our series, the duration of the disease, as defined by the duration either of symptoms or of known thrombocytopenia, did not correlate with the response or relapse after splenectomy.

The pattern of the relapse correlated with the highest preoperative platelet count induced by steroid therapy, with the lowest preoperative platelet count, and with the day of the maximum platelet count postoperatively, but with none of the other variables. Others have reported that in those patients with chronic ITP who did not respond well to splenectomy or who relapsed after an initial good response, the maximum platelet count was delayed (10,13,15); our study confirmed this observation. However, in our patients the magnitude of the maximum postoperative platelet count was not predictive of response or relapse. Also, while others have noted that those patients who had high platelet counts before splenectomy have a greater chance of a subsequent good response to splenectomy (12), this was not true in our series.

In our patients who had significant postoperative complications, the maximum peak in the postoperative platelet count was reached later, but this may reflect only the tendency of most acute illnesses to lower an individual's platelet count. It is noteworthy, however, that both patients with as well as those without postoperative complications reached the same maximum platelet counts after splenectomy.

The additional morbidity associated with larger spleens was surprising, as the largest spleen in our study (482 gms) and in the other ITP series is still much smaller than the spleen sizes reported in the literature on the morbidity of splenectomy for splenomegaly (16).

While mortality is low in splenectomy series, morbidity has been commented on only casually in other reports (3,5,7,11). The increased morbidity in older age groups, we feel, reflects the surgical procedure rather than the underlying disease process, as the significant morbidity is not unusually high for the same procedure in younger age groups.

Acknowledgment

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References