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Planned Splenectomy in Treatment of Idiopathic Thrombocytopenic Purpura

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Summary

The results of a policy of treatment in idiopathic thrombocytopenic purpura based on previous observations on the natural history of the disease and its response to corticosteroids are described. The results of splenectomy were better when the history was less than 100 days. Three patterns of response to splenectomy were observed: complete remission, symptomatic remission, and relapse. The prognosis can be determined by the level of the platelet count six weeks after splenectomy. Corticosteroid treatment for more than three weeks before splenectomy noticeably increased the incidence of complications after operation. Splenectomy can safely be performed in pregnancy. The decision to operate should be made on the maternal condition and its response to corticosteroids.

Introduction

In a previous paper (Watson-Williams *et al.*, 1958) we examined the natural history of idiopathic thrombocytopenic purpura (I.T.P.) and the response to adrenocorticosteroids. The disorder seemed to follow two main courses. In the first there was a long history of episodic purpura, each relapse varying in severity. Spontaneous remission was common but never permanent. Treatment with corticosteroids usually initiated a short-lived remission, which, in our experience, never lasted more than two months. Patients who followed the second course had a short history (which we defined as less than 100 days from onset till the time when some treatment was begun) and a strong tendency to spontaneous and permanent remission. When treatment with corticosteroids was considered necessary permanent remission occurred in about half the patients. Rarely, patients in this short-history group had a fulminating illness with severe bleeding sufficient to require blood transfusion. The outcome was often fatal, the main cause of death being intracranial haemorrhage.

From these observations a policy of treatment was formulated with regard to splenectomy. In patients with a long history and recurrent attacks sufficiently severe to require treatment only temporary remission can be expected from corticosteroids, and the period of this remission should be used for the performance of splenectomy. Therefore, corticosteroids are given, usually

as prednisone or prednisolone 45 mg-60 mg/day, with the aim of reducing the bleeding time and the capillary fragility and possibly increasing the platelet count as a preparation for splenectomy. In patients with a short history the same treatment is given for two weeks. If remission has not occurred within that time experience has shown that it is unlikely to do so subsequently. In this event splenectomy is indicated and corticosteroids are again looked upon as a preparation for operation.

We report here the results of splenectomy in a series of 72 patients with I.T.P., all of whom had had the operation performed more than one year earlier. The series was examined, firstly, as a whole, secondly, according to whether the history was a long or a short one, and, thirdly, according to whether or not corticosteroids were used before operation.

Progress after Splenectomy

Seventy-two patients with I.T.P. were treated by splenectomy. Of these 71 were traced and reviewed periodically from one to 29 years after operation. There was complete freedom from symptoms throughout the period of review in 60 patients and recurrence in 11 (15%). Recurrence took the form of epistaxis in four patients, melaena in three (one of whom had previously had a partial gastrectomy for gastric ulcer), purpura in five, menorrhagia in three, and a cerebrovascular accident in two. The time of the recurrent symptoms ranged from immediately after operation to 12 years later. In 10 patients the platelet count was known to be subnormal at the time symptoms recurred. It had been normal for two years after splenectomy in the 11th patient but had not been checked close to the time of her relapse. There were two deaths attributable to the bleeding abnormality, both patients dying with symptoms suggestive of intracranial haemorrhage. The first (case 1) was a woman aged 55 with a short history of purpura who died 19 days after operation from intracerebral haemorrhage, never having shown any response in symptoms or platelet count to splenectomy. The second (case 2) was a girl aged 14 who died eight years after splenectomy. Her platelet count had been consistently normal but shortly before death, which occurred at home, purpura recurred. Necropsy was not performed and death was certified as due to intracranial haemorrhage, but the possibility of meningitis cannot be excluded.

It was possible to distinguish three patterns of behaviour after splenectomy for I.T.P. (fig. 1). In the first group there was complete relief of symptoms. The bleeding time returned at once to normal, and the platelet count rose sharply in the first two weeks after operation to three or four times the normal level and then came down to and remained above 150 000/mm³.

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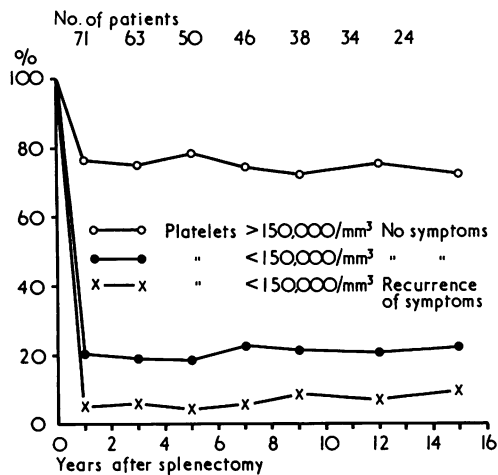

FIG. 1—Three patterns of progress after splenectomy in patients with idiopathic thrombocytopenic purpura. 100% represents total number of potential survivors at each time period less number of deaths from intercurrent and non-attributable causes.

The greatly reduced survival time of the platelets also returned to or near normal (Donaldson, 1965). Once this pattern was established it tended to persist. This pattern was found in 54 of the 71 patients who were traced for one year after splenectomy (76%), in 34 out of 46 who were traced for seven years (74%), and in 17 out of 24 for 15 years (71%). There were only two possible exceptions. One of these, in which the evidence is inconclusive (case 2), has been reported above. In the second (case 3), a 45-year-old woman with a short history, thrombocytopenia and purpura recurred after the onset of thyrotoxicosis nine years after splenectomy. There was complete remission, which at the time of study had lasted more than nine years, on treatment with ^{131}I and prednisolone.

In the second group the platelet count started to rise immediately after splenectomy but either flattened out at a persistently subnormal level or fell below normal within four to six weeks. The level of the platelet count six weeks after splenectomy was found to be a reliable indicator of its future behaviour. If thrombocytopenia had recurred by this time it almost always persisted. This group comprised 14 of the 71 cases at one year after splenectomy (20%), 10 of the 46 at seven years (22%), and five of the 24 at 15 years (21%). A remarkably constant proportion of this group (about 80%) was symptom-free throughout the period of follow-up. In eight patients abnormal bleeding recurred at varying periods between two months and 12 years after splenectomy, but the incidence was so scattered that it did not affect the proportion remaining symptom free. Relapse usually occurred without any change in the blood picture or apparent precipitating cause. Two of this group had tooth extractions performed, one with and one without corticosteroid cover, without abnormal bleeding, and two women were delivered of six babies (one by caesarean section) without mishap.

In the third pattern of behaviour neither an increase in platelet count nor any remission in symptoms occurred. It was seen in three patients. Death is likely in the postoperation period from bleeding into a vital area such as the brain, as in the patient in case 1, or from uncontrollable haemorrhage from the site of operation.

Mortality.—Thirteen patients died during the period of review. The cause of death in two patients who died six and 15 years after splenectomy is not known. Of the others only two deaths were attributable to the disease (cases 1 and 2) and none to the operation itself.

Duration of Symptoms before Splenectomy

There were 24 patients with a history of less than 100 days

(short history) and 48 patients with a history of more than 100 days (long history). All the long-history patients and 23 short-history ones were reviewed repeatedly over periods from one to more than 20 years after splenectomy. It is evident from fig. 2 that there was a difference in the response to splenectomy between short- and long-history patients. Relief of symptoms and a normal platelet count were present in 20 of the 23 short-history patients one year after splenectomy (87%), in 12 out of 13 (92%) at seven years, and in five out of six (83%) at 15 years. Only two patients had a platelet count below 150 000/mm^{3} after operation. One patient suffered from epistaxis at two months and one patient suffered from purpura eight years after splenectomy, and one of these had a recurrence nearly nine years afterwards, apparently secondary to thyrotoxicosis (case 3). One patient (case 1) died in the postoperation period without any change in symptoms or platelet count.

Of the 48 patients with a long history 34 (71%) were symptom free and had a platelet count of more than 150 000/mm^{3} one year after splenectomy, 22 out of 33 (67%) were thus at seven years, and 12 out of 18 were well at 15 years (67%). Thrombocytopenia was present in 14 patients at one year, in 11 patients at seven years, and in five patients at 15 years. Seven of these patients had recurrent symptoms and one died eight years after splenectomy from a presumed intracranial haemorrhage (case 2).
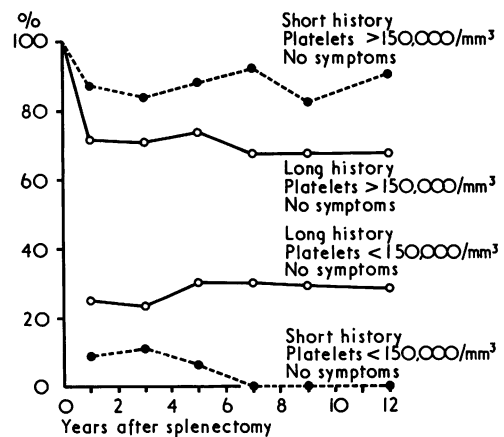

FIG. 2—Progress after splenectomy in short-history and in long-history patients. 100% represents total number of potential survivors at each time period less number of deaths from intercurrent and non-attributable causes.

Preliminary Treatment with Corticosteroids

Whether or not patients had corticosteroids before splenectomy was determined almost entirely by the date of the introduction of these drugs into clinical practice. Altogether 31 patients were operated on without steroid cover and 40 had preliminary treatment which varied in duration from a few days to more than a year. The incidence of postoperation complications and the subsequent progress of these patients are shown in the table. In the patients not on steroids one patient died after operation and one was lost to follow-up. Corticosteroid therapy was followed by more complications after splenectomy but the higher incidence was confined to patients who were given the drugs for longer than three weeks before operation. Of the 10 complications in this group four were directly attributable to the corticosteroids and four were due to infection. By contrast, there were no infective complications in those who did not receive steroids before operation. Purpuric symptoms recurred at some time after splenectomy in nine of the 31 who had no preoperative treatment, and in only two of the 40 who did.

I.T.P. and Pregnancy

In three patients splenectomy was performed at about the fourth month of pregnancy. In two of these three patients the pregnancy

Incidence of Postoperative Complications and Subsequent Progress of 71 Patients who Underwent Splenectomy according to Steroid Treatment. Results are Numbers of Patients

History	No. of Patients	Postoperative Complications	Progress		
			Uncomplicated	Symptomless Thrombocytopenia	Bleeding
Patients not on Steroids					
Short..	8	2	5	0	2
Long ..	23	2	12	3	7
Patients on Steroids <21 Days					
Short..	10	0	8	1	1
Long ..	14	3	9	4	1
Patients on Steroids >21 Days					
Short..	5	2	5	0	0
Long ..	11	8	10	1	0

went to full term, and one terminated with an accidental haemorrhage at 34 weeks when the maternal platelet count was 300 000/mm³. Neither of the full-term children were purpuric, but platelet counts were not recorded. Fifteen pregnancies occurred in six patients after splenectomy. All went to full term except one which terminated at three months. In one 31-year-old patient whose platelet count varied during pregnancy between 90 000 and 200 000/mm³ a caesarean section was performed at term and the bleeding at and after operation was recorded as excessive. She subsequently had two more children by vaginal delivery without undue loss. Delivery in every other case was normal and without incident.

Four infants had skin purpura with ecchymoses. In one case the maternal platelet count was 50 000/mm³ at the time of delivery, but in the others it was normal. Platelet counts were recorded in only three infants and in each case were less than 50 000/mm³. The patient reported below had a child with purpura and thrombocytopenia both before and after splenectomy.

Case 4.—This 20-year-old patient was first seen when seven months' pregnant. She had a five-year history of menorrhagia and easy bruising, and her platelet count was 25 000/mm³. A full-term child was spontaneously delivered on 27 September 1949. She bled freely during labour, and a one-litre blood transfusion was given. Because of purpura and continued loss per vaginam and a bleeding time of over 20 minutes splenectomy was performed on 3 November 1949. Symptoms and bleeding time returned at once to normal, but platelets never exceeded 100 000/mm³. The baby was purpuric at birth, with a platelet count of 30 000/mm³. Purpura and thrombocytopenia continued until the baby was taken off breast feeding. On 8 December 1949 the baby's platelets were 310 000/mm³. A second child was born on 23 December 1950. It also had purpura with a platelet count of 60 000/mm³ and a normal bleeding time. On 3 January 1951 the baby's platelet count was 50 000/mm³. A third child was born without incident on 22 November 1954, when the maternal platelet count was 15 000/mm³. The baby did not have purpura, but the platelet count was only 20 000/mm³. Five weeks later it had risen to 365 000/mm³.

Discussion

The overall results of splenectomy in our patients were similar to those of other large series (Elliott and Turner, 1951; Charlesworth and Torrance, 1968). What has been shown by repeated review is that a normal platelet count and freedom from purpura have been continuously observed in about 75% of patients for up to 20 years after operation. A further 20% "benefited" from splenectomy in that they were symptom free throughout most of the period of follow-up but the platelet count was persistently subnormal. The relapse rate at any time after splenectomy in this group was about 20%. Into which of these two groups a patient would fall could be determined at six weeks after operation, a point also noted by Charlesworth and Torrance (1968).

The finding of a platelet count which was subnormal at this time has proved to be a reliable indicator that thrombocytopenia would persist.

Previous studies (Watson-Williams et al., 1958) have shown that the duration of symptoms before medical treatment was begun greatly influenced the incidence and the duration of both spontaneous and corticosteroid-induced remissions. The effect on the results of splenectomy is similar. Relief of symptoms and a normal platelet count result from splenectomy in about 90% of patients with a short history but in only 67% with a long history. The explanation of this difference seems to lie in the demonstration by Aster and Keene (1969) that parts of the reticuloendothelial system other than the spleen become increasingly involved in the processes of platelet destruction the longer splenectomy is delayed.

When corticosteroids were given, prednisone or prednisolone 45-60 mg daily, for three weeks or less before operation morbidity in the postoperation period was similar to that after splenectomy without steroid cover. When the period of pre-operation corticosteroid therapy was extended, however, the complication rate, and especially the infection rate, rose sharply. This finding emphasizes the advisability of restricting treatment with corticosteroids to the minimum necessary to bring the bleeding time and capillary fragility nearly to normal and of performing splenectomy at this "optimum" time. Recurrent purpura after splenectomy was much less frequent in the patients who received corticosteroids before operation, but there is no obvious explanation for this observation.

It is evidently safe to perform splenectomy for I.T.P. in the middle trimester of pregnancy. The decision to operate should be made on the maternal condition and its response to treatment with corticosteroids. Two of the 18 pregnancies did not go to full term. All the other 16 babies survived and only four had purpura. This incidence is less than that collected from the literature by Epstein et al. (1950), who recorded 25% infant mortality and the occurrence of purpura in 19 out of 36 survivors (56%). I.T.P. may occur in the baby whether or not the spleen has been removed, and it seems to depend on the migration across the placenta of antibodies which have a limited duration of action after birth. The symptoms disappeared and the platelet count returned to normal within three to four months of delivery in both the five cases of Epstein et al. (1950) and in our series.

At the time of splenectomy 11 histologically proven spleniculi were found and removed in nine patients. All were situated either in the lienorenal or the gastrosplenic ligaments. This incidence is half that reported by Elliott and Turner (1951). Exploration for a possible missed spleniculus was not undertaken in any patient with relapse because in no case were the symptoms sufficiently severe or prolonged to warrant it. Furthermore, Elliott and Turner reported two laparotomies and one necropsy in which nothing abnormal was found in three patients with relapses, which suggests, together with the observation that the future of the platelet count can be predicted by its level four to six weeks after operation, that the importance of the spleniculus in causing relapse in I.T.P. may have been exaggerated. It may be possible to throw light on this problem by the use of scanning after the injection of ⁵¹Cr-labelled, heat-denatured erythrocytes to show the presence of enlarged spleniculi.

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