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Partial splenectomy in homozygous β thalassaemia

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Abstract

Partial splenectomy was performed on 30 patients with homozygous β thalassaemia to reduce blood requirements and to avoid the risk of overwhelming postsplenectomy infections; 24 patients had thalassaemia major and six thalassaemia intermedia. Five patients received a high transfusion regimen before and after surgery and 25 a lower one. Follow up after surgery ranged from one to four years. Partial splenectomy improved the long term haematological state in the six patients with thalassaemia intermedia. Recurrence of hypersplenism occurred in nine of the 24 patients with thalassaemia major, however, and complete splenectomy was required. Serum IgM concentrations were not significantly modified by surgery. The mean (SD) residual spleen after surgery was 4·45 (2·36) cm measured by scintigraphy. No severe infections occurred after surgery; however, most patients were routinely treated with phenoxymethylpenicillin and the protective effect of the remaining spleen could not be exactly determined. Because of the possibility of recurrence of hypersplenism, routine partial splenectomy when splenectomy is needed in thalassaemia major is not advised, except in children under 5 years whose risk of overwhelming postsplenectomy infection is greatest.

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Hypersplenism is a very common complication in homozygous β thalassaemia. In regularly transfused patients it is suspected before the increased blood consumption and is sometimes associated with thrombocytopenia or leucopenia, or both. A high blood transfusion regimen usually delays this complication,[1] though it doesn't always suppress it. Splenectomy allows for the reduction of transfusional blood requirements thus reducing iron overload.[2] However, this operation exposes patients, who are mainly under 5 years of age (but also older children and even adults), to the risk of overwhelming postsplenectomy infections.[3 4] The severity of these infections has led to the search for alternative surgical techniques to replace total splenectomy so that blood requirements are reduced but the splenic contribution to the host defence against infections is preserved.

We report our experience with 30 thalassaemic patients who underwent one of these alternative techniques, partial splenectomy.

Patients and methods

Thirty patients affected with homozygous β thalassaemia were included in the study; 24 had thalassaemia major and six thalassaemia intermedia. The diagnosis of thalassaemia major and intermedia was based on transfusion requirements.[5] The patients' mean (SD) age was 7·9 (3·7) years (range 3–19 years) at the time of the partial splenectomy. Twenty five patients received a low transfusion regimen and five received a high transfusion regimen (table 1).

In all patients about nine tenths of the total hypertrophied splenic mass was ablated at operation. The size of the remaining portion was approximately half that of a normal spleen. The mean haemoglobin concentration was determined in each patient before and after partial splenectomy.

In order to determine the reduction of hypersplenism we monitored the postsplenectomy blood requirements, splenic blood flow,[6] and platelet count. Blood consumption was evaluated in thalassaemia major patients by calculating the transfusion quotient.[1] Transfusion quotient is the ratio of the annual observed blood consumption to the expected one for the transfusion scheme. Hypersplenism raises the

Table 1 Mean haemoglobin concentrations, transfusion regimen, and outcome after partial splenectomy in 24 patients with thalassaemia major

Case No	*Mean haemoglobin concentration (g/l)*	
	During year before splenectomy	*During follow up after splenectomy*
High transfusion regimen/no recurrence of hypersplenism		
1	100	122
2	115	118
3	115	128
4	105	116
5	121	123
Mean (SD)	111 (8)	121 (4)
Low transfusion regimen/no recurrence of hypersplenism		
6	80	94
7	46	57
8	70	73
9	67	73
10	72	55
11	93	63
12	84	79
13	67	63
14	96	71
15	70	68
Mean (SD)	74 (14)	69 (11)
Low transfusion regimen/recurrence of hypersplenism		
16	57	77
17	82	84
18	90	84
19	67	95
20	76	75
21	60	70
22	50	71
23	60	80
24	64	86
Mean (SD)	67 (12)	80 (8)

transfusion quotient above 1·5 to 2. All these values were determined before and after surgery. This ratio cannot be used in thalassaemia intermedia patients, therefore their annual blood consumption in relation to the mean haemoglobin concentration before transfusion was studied.

To try to assess preoperative hypersplenism, splenic blood flow was also measured in eight of our patients. This isotopic study, involving labelled platelets, evaluates the splenic blood volume per minute and relates it to the total blood volume. Results range from 3 to 6% in normal subjects and rises when hypersplenism occurs. Splenic blood flow after surgery was measured in 10 subjects.

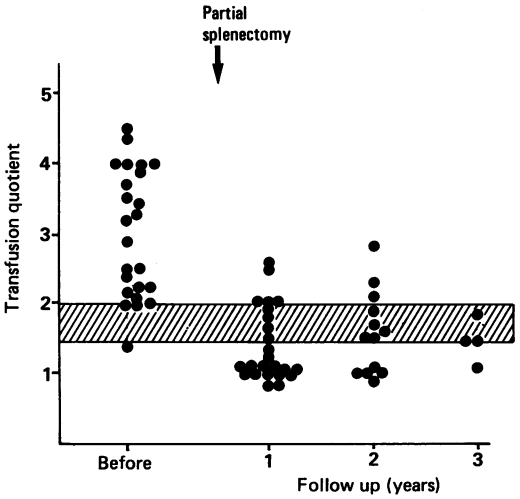

Figure 1 Transfusion quotient before and after partial splenectomy in 24 patients with thalassaemia major. The shaded area indicates the range of transfusion quotient above which is consistent with hypersplenism.

Table 2 Transfusion quotients in nine patients with thalassaemia major who had partial correction and/or recurrence of hypersplenism after partial splenectomy (indicated by transfusion quotient ≥2)

Case No	*Before surgery*	*After 1 year*	*After 2 years*	*After 3 years*
16	3·1	1·5	2·7	
17	3·5	1·2	2·2	
18	4·0	1·3	2·3*	1·5
19	2·3	1·0	2·0	
20	4·3	2·0		
21	3·8	2·0		
22	4·0	2·6		
23	3·4	2·0		
24	2·5	2·5		

The case numbers correspond to those in table 1.
*Total splenectomy performed.

Platelet counts were regularly made on all patients after surgery.

Spleen host defence against infections was determined by: (a) a clinical survey of infections; (b) measurements (by scintigraphy) of residual splenic mass in 25 patients (splenic size being considered as an indicator of splenic macrophage function); and (c) variations of serum IgM concentrations.

All patients were vaccinated preoperatively with a pneumococcal polysaccharide vaccine and most of the patients were postoperatively given prophylactic phenoxymethylpenicillin according to the proposal by Colonna and Ardjoun.[7]

Follow up after partial splenectomy was one year in 13 patients, two years in 12, three years in four, and four years in one.

Results

Surgery was uneventful in all patients.

The changes in the transfusion quotient in the 24 thalassaemia major patients is shown in fig 1. The mean (SD) value for the transfusion quotient before partial splenectomy was 3·07 (0·90) and one year after 1·42 (0·50). In five patients, however, the transfusion quotient after surgery was ≥2, which meant that there had been insufficient correction or a recurrence of the hypersplenism. Two years after surgery four additional patients presented with a recurrence of hypersplenism (tables 1 and 2). Partial correction or relapse, or both, always occurred in patients on a low transfusion regimen. Among patients on a low transfusion regimen the mean haemoglobin concentrations before and after surgery did not differ between those with and without a recurrence of hypersplenism (table 1).

All six patients with thalassaemia intermedia had reduced blood requirements (table 3). The mean (SD) haemoglobin concentration before surgery was 55·2 (7·8) g/l—with transfusion frequency ranging from one to 12 transfusions/year—and after surgery 81·2 (9·8) g/l. All patients except one are no longer being transfused after splenectomy. One patient with thalassaemia intermedia who needed three transfusions four years after surgery (reduced from 12 before) died from cardiac failure.

Mean (SD) splenic blood flow measured preoperatively was 9·5 (5·0)% and measured 15 days after splenectomy 4·2 (3·4)%. The associa-

Table 3 Results of partial splenectomy in six patients with thalassaemia intermedia

	Year before partial splenectomy		*Follow up period*		
Case No	*Mean annual haemoglobin (g/l)*	*No of transfusions during year*	*Years of follow up*	*Mean haemoglobin (g/l)**	*No of transfusions*
1	62	1	2	100 (1)	1
				80 (2)	0
2	50	12	4	80 (1)	0
				65 (2)	0
				70 (3)	0
				70 (4)	3†
3	50	6	1	90	0
4	64	4	1·5	84	0
5	45	12	2	81 (1)	0
				86 (2)	0
6	60	12	2	73 (1)	0
				73 (2)	0

*Numbers in parentheses indicate year concentration measured.
†Patient died from cardiac failure.

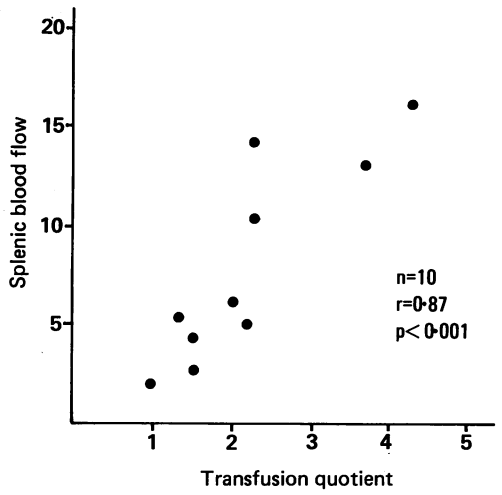

Figure 2 Correlation between splenic blood flow and transfusion quotient preoperatively.

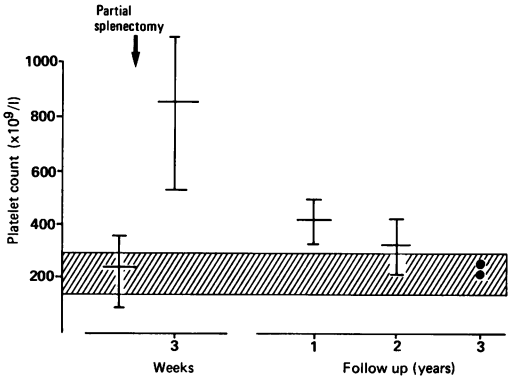

Figure 3 Mean (SD) platelet count before and after partial splenectomy in 30 patients with thalassaemia. The shaded area indicates the normal range.

tion between transfusion quotient and splenic blood flow was strong, as shown in fig 2 ($r=0·87$; $p<0·001$).

Figure 3 illustrates the effects on platelet counts: before surgery nine patients had thrombocytopenia (platelets under 150×10^9/l) and the mean (SD) value for the 30 patients was 206 (103)$\times10^9$/l. In the third week after surgery thrombocytosis occurred (mean (SD) platelet count 831 (268)$\times10^9$/l, n=30) with no complications resulting. One year after surgery the mean (SD) platelet count had fallen to 411 (109)$\times10^9$/l (n=21), and after two years it fell within the normal range: 319 (107)$\times10^9$/l (n=11).

No severe infection was noted after surgery. The mean (SD) postoperative residual splenic size, as determined by scintigraphy, was 4·45 (2·36) cm. Serum IgM concentrations were not significantly modified by surgery. The mean (SD) concentration before partial splenectomy was 16·4 (7·8) g/l. It rose to 19·6 (13·2) g/l three weeks later and remained at 17·8 (9·4) g/l one year later.

Discussion

In thalassaemic patients hypersplenism is most probably due to hypertrophy of the reticuloendothelial system. It is suspected before splenomegaly, leucopenia and/or thrombocytopenia, and chiefly by an increase in transfusion requirement to maintain a normal haemoglobin concentration. This results in an increased iron overload in hypertransfused patients. Despite chelation treatment, iron balance is positive in most of these subjects, exposing them to the morbidity and mortality of haemosiderosis: hepatic and endocrine complications and cardiac failure. Splenectomy reduces blood consumption and with desferrioxamine treatment allows iron balance to be achieved.[2] Splenectomy is beneficial against transfusional haemosiderosis even if it suppresses a reticuloendothelial iron store.[1] Splenectomy also exposes the patient to an important risk of infection: overwhelming postsplenectomy infections are frequent in children under 5 years but also found in adults.[3] These infections mainly occur during the first months after surgery, but some severe infections have been observed many years after surgery. The most commonly involved organisms are *Streptococcus pneumoniae* (about 50% of cases), *Haemophilus influenzae*, and *Neisseria meningitidis*.[3 8]

The spleen has several immunological functions: it may phagocytose blood borne antigens in the presence of low concentrations of antibodies, participate in opsonisation, and generate specific antibodies; it maintains the integrity of the alternative complement pathway and has an 'immune memory'.[9 10] To preserve these functions, alternative techniques to total splenectomy have been proposed in thalassaemia patients: partial splenic embolisation,[11] partial vascular disconnection of the spleen,[12] or partial splenectomy.[13] Hypersplenism is reduced in many cases, but not consistently: relapses are sometimes observed after an excellent initial result. The total number of patients treated with each of these techniques is low, however, and in some cases follow up periods have been short. No definite conclusions can be drawn from our results regarding the absence of severe infection after surgery for several reasons. Most patients followed up in Algeria were routinely given phenoxymethylpenicillin to protect them against infections, but the number of patients who had a splenectomy was low and therefore conclusions cannot be drawn on the anti-infection protective effect of the residual spleen. Serum IgM concentrations did not decrease after splenectomy, however.

Concerning the correction of hypersplenism in terms of blood requirements, we noted a positive effect of partial splenectomy in most of the patients during the follow up period of the study. The influence of the blood transfusion regimen is important because no relapse occurred in patients on a high transfusion regimen; on the contrary a partial correction or relapse was observed in almost half of the patients on the low transfusion regimen. This finding discourages us from routinely performing partial splenectomy when splenectomy seems needed in patients on a low transfusion regimen, and no definite conclusions can be drawn in patients on a high transfusion regimen, but further studies

would be useful. We suggest that partial splenectomy be limited to children under 5 years, whose risk of severe infection is greatest; this leaves the option of total splenectomy should relapse occur.

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