

## Partial splenectomy in sickle cell syndromes

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### Abstract

Partial splenectomy was carried out in four children with homozygous sickle cell disease and eight children with sickle cell  $\beta$  thalassaemia. It was performed in order to preserve splenic contribution to the host defence against infections while suppressing hypersplenism or the risk of recurrence of acute splenic sequestration. Indications for this surgical operation were acute splenic sequestration (n=1), hypersplenism (n=5), and acute splenic sequestration and hypersplenism (n=6). Surgery was uneventful in 11 patients. A significant reduction of blood requirements and a significant decrease of the number of hospitalisations/patient/year were observed after splenectomy. No recurrence of hypersplenism or acute splenic sequestration occurred and no severe infection was noticed during the follow up period after surgery (mean (SD) 4.2 (2.8) years; range 6 months-7 years). Mean haemoglobin concentration and leucocyte and platelet counts increased after surgery. The benefit of partial splenectomy compared with total splenectomy to treat acute splenic sequestration or hypersplenism in sickle cell disease is discussed.

There are several severe splenic complications that may occur in children with sickle cell disease: not only hyposplenism, which is a common event in this disease, but also acute splenic sequestration and hypersplenism. Acute splenic sequestration is defined as a fall in the haemoglobin concentration of more than 20 g/l, with evidence of marrow compensation (increased number of reticulocytes or normoblasts), and an acutely enlarged spleen.<sup>1</sup> Acute splenic sequestration is a major cause of mortality and morbidity in children with sickle cell disease younger than 5 years.<sup>2</sup> Death may occur during the first attack or during a recurrence.

A definition of hypersplenism includes: (i) a chronically enlarged spleen more than 4 cm below the left costal margin; (ii) a haemoglobin concentration less than 65 g/l; (iii) more than 15% reticulocytes; and (iv) a platelet count less than  $200 \times 10^9/l$ . These variables must have been found on at least two occasions.<sup>1</sup> Hypersplenism makes patients dependent on regular blood supplies, with repeated hospitalisations, and therefore exposes them to transfusional risks. Many authors thus recommend splenectomy in children with acute splenic sequestration or hypersplenism despite risks of infection caused by splenectomy. In order to preserve splenic contribution to the host defense against infections,

while suppressing hypersplenism or the risk of recurrence of acute splenic sequestration, we have performed partial splenectomy in 12 children affected with major sickle cell syndromes. We report here our experience of the haematological and infectious consequences of this surgical technique.

### Patients and methods

Twelve patients affected with major sickle cell syndromes were included in the study. There were four children with homozygous sickle cell disease and eight with sickle cell  $\beta$  thalassaemia. Mean (SD) age at the time of the surgical operation was: 7 (3) years (range 3-11 years). Indications for partial splenectomy for patients with homozygous sickle cell disease were: acute splenic sequestration (n=1), hypersplenism (n=2), and hypersplenism plus one episode of acute splenic sequestration (n=1). In patients with sickle cell  $\beta$  thalassaemia indications were: hypersplenism (n=3) and hypersplenism plus one episode of acute splenic sequestration (n=5).

### SURGICAL TECHNIQUE

Partial splenectomy was performed according to a previously described technique.<sup>3</sup>

### HAEMATOLOGICAL DATA

Blood supplies (expressed in litres of blood received per year) and the number of hospitalisations per year for each patient were determined the year before splenectomy and during the follow up period. Mean haemoglobin concentration and leucocyte and platelet counts were studied in the same periods. Mean values correspond to two to five determinations according to the patients.

### SPLENIC HOST DEFENCE AGAINST INFECTIONS

Spleen host defence against infections was discerned by (i) clinical survey, (ii) residual splenic mass measurement evaluated by scintigraphy or echography, and (iii) variations of serum IgM concentrations. All patients were immunised before splenectomy with a polyvalent pneumococcal vaccine. A systematic prophylactic treatment with penicillin was pursued after surgery as is usual for every child with sickle cell disease.

The follow up after splenectomy was at 4.2 (2.8) years (range 6 months-7 years).

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Table 1 Clinical results in 12 patients with major sickle cell syndromes having partial splenectomy

	Year before partial splenectomy		Follow up period	
	Homozygous sickle cell disease (n=4)	Sickle cell $\beta$ thalassaemia (n=8)	Homozygous sickle cell disease (n=4)	Sickle cell $\beta$ thalassaemia (n=8)
Mean (SD) blood supplies (l/year)	2.1 (0.3)	4.2 (1.5)	0.62 (0.70)	0.21 (0.25)
Mean (SD) No of hospitalisations	4.7 (5)	2.4 (3.2)	1.5 (1.3)	0.37 (0.7)

Table 2 Results of laboratory investigations in 12 patients with major sickle cell syndromes having partial splenectomy

	Year before partial splenectomy	Follow up period	Significance (p value)
Mean (SD) annual haemoglobin concentration (g/l)	50 (5)	83 (8)	<0.001
Mean (SD) leucocyte count ( $\times 10^9/l$ )	9 (3)	13 (3.8)	<0.001
Mean (SD) platelet count ( $\times 10^9/l$ )	134 (40)	522 (100)	<0.001
Mean (SD) IgM concentration (g/l)	16 (8)	15 (8)	NS

NS: not significant.

## Results

Surgery was uneventful in 11 patients. A bilateral pneumonia occurred in one patient on the third postoperative day. Bacteriological investigations were negative and the patient promptly recovered with antibiotic treatment.

A reduction of blood requirements and a decrease of the number of hospitalisations/patient/year was observed after splenectomy (table 1). No recurrence of hypersplenism or acute splenic sequestration occurred.

Mean haemoglobin concentrations and leucocyte and platelet counts before and after surgery are shown in table 2 (the data for both groups of patients were combined because they do not differ significantly). All three of these variables were significantly increased after splenectomy ( $p < 0.001$ ). Platelet count immediately after surgery was  $540 (273) \times 10^9/l$ . No thrombosis occurred and platelets returned to normal in all patients within one year.

No severe infection was observed during the follow up period.

Mean residual splenic size was 4.6 (0.7) cm in six patients according to scintigraphic data and 4.6 (1.7) in seven others according to the echographic data; mean splenic size before surgery was 13 (2.7) cm. Mean IgM concentrations did not differ before and after splenectomy (16 (8) and 15 (8) g/l respectively).

## Discussion

The underlying mechanisms leading some sickle cell children to have an hypertrophic spleen, responsible for red blood cell sequestration and destruction, instead of an atrophic unfunctional spleen usually observed in this disease, are not known.

Splenic sequestration may occur in all major sickle cell syndromes: homozygous sickle cell disease, sickle cell haemoglobin C disease, and sickle cell  $\beta$  thalassaemia. Our series included twice as many children with sickle cell  $\beta$  thalassaemia than with homozygous sickle cell disease; this is in agreement with the higher prevalence of splenomegaly in the former. Hypersplenism and acute splenic sequestration could be the chronic and acute expressions of the same process. It has already been shown that hypersplenism was much more common in

patients with a history of acute splenic sequestration than in others ( $p < 0.001$ ).<sup>4</sup> It is also possible that episodes of acute splenic sequestration may be found with hypersplenism,<sup>4</sup> as it occurred in six out of 12 of our patients.

A prospective study of a cohort of Jamaican children with sickle cell disease who had been followed up from birth indicates a prevalence of acute splenic sequestration in a 10 year period of 8.2/100 patient years of observation.<sup>5</sup> The first attack can occur from 3 months to 6 years of age. Recurrences may happen in about half the cases, and the overall case fatality rate is 9.8/100 attacks, concerning mostly the children under 2 years.

Two methods of treatment have been proposed for children surviving their first attack of acute splenic sequestration: a short term transfusion programme and splenectomy. A recent study has shown that blood transfusion did not prevent recurrent sequestration as four out of 12 patients who were transfused experienced a new attack on treatment.<sup>6</sup> Furthermore, the risk of recurrent sequestration is highest soon after the transfusion programme is discontinued. Regular blood supplies expose children to viral contamination, alloimmunisation, and iron overload. Thus splenectomy seems the appropriate treatment for children having experienced acute splenic sequestration or exposed to the same complications on account of their hypersplenism. This intervention is nevertheless to be avoided in very young infants because of the immunological impairment it induces. The spleen has a major role in phagocytosis for blood borne antigens in the presence of low concentration of antibodies,<sup>7</sup> it synthesises specific IgM antibodies and opsonins such as tuftsin and properdin,<sup>8</sup> and intervenes in the alternative complement pathway.<sup>9</sup> This anti-infectious role of the spleen remains important in children with sickle cell disease since severe infections have been reported in a cohort of 60 children with sickle cell disease who underwent splenectomy: two deaths resulting from sepsis after splenectomy and 17 acute chest infections occurred, mainly in children under 2 years.<sup>1</sup> Partial splenectomy could be thus a possible alternative as it reduces splenic hypertrophy while preserving some immunological function of this organ. The ability of partial splenectomy to reduce hyper-

splenism has already been shown in thalassaemic patients.<sup>10</sup> It is clearly shown in our series of patients with sickle cell disease as we found significantly higher concentrations of haemoglobin and lower blood requirements with a follow up of more than five years in eight cases. No recurrence of acute splenic sequestration or hypersplenism occurred, there was no severe infection, and the IgM concentrations remained stable after the intervention. Although only a few patients were involved, we conclude that partial splenectomy can be of benefit in treating acute splenic sequestration or hypersplenism in children with sickle cell disease. A rigorous follow up must be maintained to observe the long term consequences of this intervention.

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