

Splenectomy in agnogenic myeloid metaplasia: factors of possible prognostic significance

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Summary

The available data of 338 cases of splenectomy in agnogenic myeloid metaplasia published since 1940 were retrieved from the literature and analysed. Postoperative survival was significantly shorter in patients with anaemia, massive splenomegaly or elevated serum alkaline phosphatase. Younger age or normal platelet counts were associated with a longer postoperative survival than that in older patients and in patients with low platelet counts respectively. The shortest median postoperative survival was found in patients in whom serum alkaline phosphatase exceeded twice the upper limit of the normal; patients with anaemia (less than 10 g/dl haemoglobin) and massive splenomegaly (above 3 kg); and patients with anaemia and a splenic weight less than one kg.

Introduction

Advanced agnogenic myeloid metaplasia (AMM) is characterized by massive splenomegaly, which produces pain, pressure symptoms and contributes to the development of anaemia, thrombopenia and portal hypertension. Splenectomy has been repeatedly reported as relieving these manifestations (Mulder, Steenbergen and Haanen, 1977; Silverstein and ReMine, 1979). The operation carries a relatively high mortality rate and is therefore recommended only for selected cases of AMM in whom the benefits of splenectomy appear to outweigh its risk (Silverstein, 1975; Silverstein and ReMine, 1979; Ward and Block, 1971).

The accepted indications for splenectomy in AMM are painful splenomegaly, portal hypertension, refractory anaemia and thrombopenia (Silverstein and ReMine, 1979). The operation is regarded as contra-indicated in patients with disseminated intravascular coagulation (Silverstein and ReMine, 1979) and thrombocytopenia

(Ward and Block, 1971). A shorter postoperative survival of male patients has been reported (Silverstein and ReMine, 1974) but not confirmed (Benbassat and Penchas, 1980). The difficulty in selecting patients with AMM for splenectomy is compounded by the finding that the indications for splenectomy are of themselves also manifestations of advanced AMM and consequently predict poor survival (Benbassat, Penchas and Ligumski, 1979).

The authors have recently surveyed the literature on splenectomy in AMM and reported a preliminary analysis of the prognostic significance of several clinical and laboratory variables at splenectomy (Benbassat *et al.*, 1979). In this paper a further evaluation is presented of the patients' age, haemoglobin level, platelet count, splenic size, serum alkaline phosphatase and combinations thereof as predictors of postoperative survival.

Methods

Reports on splenectomy in AMM published between January 1940 and December 1978 were retrieved from the medical literature as detailed previously. Altogether, 79 articles reporting a total of 332 cases were collected, and to these were added 6 cases from the records of the Hadassah University Hospital in Jerusalem. When available, clinical, laboratory and follow-up data were compiled for each individual case according to a predesignated format, and a digital computer was used for the analysis of the data. Breakdown of postoperative survival by date of publication showed that postoperative survival has not changed significantly during the last four decades (Benbassat *et al.*, 1979).

Survival functions were processed by the biomedical computer programs, P-series of the University of California Press, 1979 (BMDP-79). The authors selected the Berkson and Gage (1950) option

for actuarial survivorship curves. The differences between the survival curves were tested by the analogues of non-parametric rank tests provided by the program—the Mantel-Cox and the Breslow tests. Both statistics are asymptotically distributed as χ^2 . The Breslow test gives greater weight to early observations, and is less sensitive to late events which occur when few study patients remain alive (Breslow, 1975; Mantel, 1966; Peto *et al.*, 1977). The significance of the differences in mortality was determined by the χ^2 or Fisher exact tests.

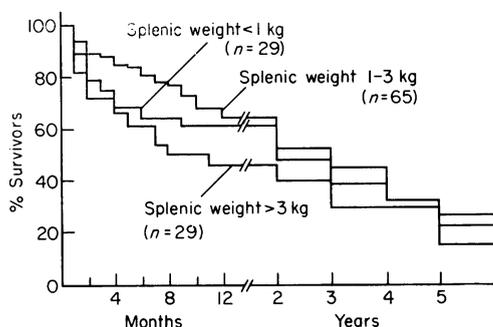


FIG. 1. Splenectomy in AMM. Actuarial postoperative survival in 123 cases by splenic weight. The differences between the survival of patients with splenic weights one–3 kg and those of patients with splenic weights above 3 kg were significant to the level of $P=0.0243$ (Breslow) and 0.0869 (Mantel-Cox).

Results

Splenic weight (Fig. 1), haemoglobin level (Fig. 2) and serum alkaline phosphatase (Fig. 3) at splenectomy were the best predictors for postoperative survival of patients with AMM. Younger age and higher platelet counts were associated with a statistically non-significant longer postoperative survival (Table 1).

The prognosis of patients with high serum

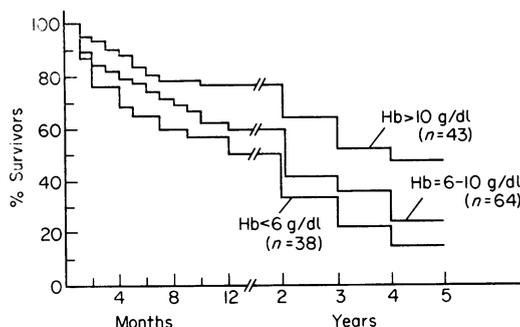


FIG. 2. Actuarial postoperative survival of 145 cases of AMM by haemoglobin level at splenectomy. $P=0.0125$ (Breslow) and 0.0153 (Mantel-Cox).

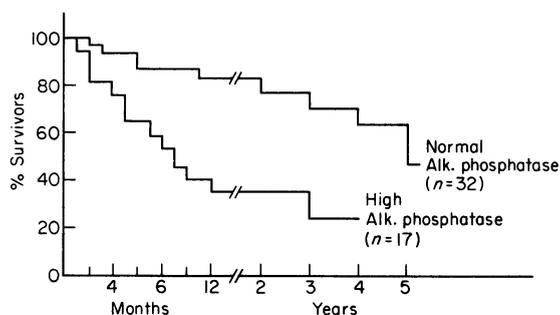


FIG. 3. Actuarial postoperative survival of 49 cases of AMM by level of serum alkaline phosphatase at splenectomy. 'High' alkaline phosphatase refers to concentrations exceeding twice the upper limit of the normal. $P=0.0026$ (Breslow) and 0.0062 (Mantel-Cox).

alkaline phosphatase was poor irrespective of splenic weight. The longest median postoperative survival was observed in seven patients with normal alkaline phosphatase and a splenic weight of less than one kg, whereas patients with normal alkaline

TABLE 1. Splenectomy in agnogenic myeloid metaplasia. Breakdown of postoperative survival by age and platelet number at splenectomy

	Number of cases with available data	Median survival (months)	Mortality after 3 months %
Age (years)			
< 45	29	38.6	10.3
45–65	123	17.8	18.7
> 65	32	23.8	21.9
		n.s.*	n.s.*
Platelets ($\times 10^9/l$)			
< 100	76	18.3	22.4
100–400	33	25.4	18.2
> 400	11	59.0	0
		n.s.	$P < 0.01$

*n.s. = not significant ($P > 0.06$).

TABLE 2. Splenectomy in agnogenic myeloid metaplasia. Breakdown of postoperative survival by splenic weight and serum alkaline phosphatase concentration at splenectomy

Variables		Number of cases with available data	Median survival (months)	Mortality after 3 months (%)
Splenic weight (kg)	Serum alkaline phosphatase			
< 1	normal	7	> 70.0	0
< 1	high*	1	—	—
1-3	normal	17	67.6	0
1-3	high	10	9.7	20.0
			$P=0.0536$ (Breslow)	n.s.**
			$=0.1442$ (Mantel Cox)	
> 3	normal	7	51.4	14.3
> 3	high	6	6.9	0
			n.s.	n.s.

*'High' alkaline phosphatase refers to concentrations above twice the upper limit of the normal.
 **n.s.=not significant ($P>0.06$).

phosphatase had a relatively long median survival even with splenic weight above 3 kg (Table 2). Splenic weights of less than one kg were associated with a shorter median survival than that of patients with spleen weighing between one and 3 kg (Fig. 1). The survival curve of patients with spleens of less than one kg depicted a heterogeneous population consisting of short- and long-lived groups of patients. Further breakdown of this survival curve by haemoglobin level suggested that its short-lived component consisted of patients with less than 10 g/dl haemoglobin at splenectomy (Table 3).

Discussion

This survey identified two groups of patients with AMM who after splenectomy had a significantly shorter median survival than that of the remaining cases, and who should be considered as poor

candidates for surgical treatment. The first group consisted of patients with very advanced AMM as judged by high concentrations of serum alkaline phosphatase, or splenic weights above 3 kg with less than 10 g/dl haemoglobin. Patients in whom the concentration of serum alkaline phosphatase exceeded twice the upper limit of the normal had a median postoperative survival of 9 months, and their prognosis was even poorer in the presence of splenic weight of 3 kg or more. Patients with massive splenomegaly (more than 3 kg) and anaemia had a median survival of 7.4 months only. The second group of poor risk patients had at splenectomy a splenic weight of less than one kg, but also anaemia of less than 10 g/dl haemoglobin. Their median postoperative survival was 8.4 months and their postoperative mortality was 40% within the first three months. These patients may have belonged

TABLE 3. Splenectomy in agnogenic myeloid metaplasia. Breakdown of postoperative survival by splenic weight and haemoglobin concentration at splenectomy

Variables		Number of cases with available data	Median survival (months)	Mortality after 3 months (%)
Splenic weight (kg)	Haemoglobin (g/dl)			
< 1	< 10	15	8.4	40.0
< 1	> 10	9	34.9	11.0
			$P=0.0876$ (Breslow)	n.s.*
			$=0.0584$ (Mantel-Cox)	
1-2	< 10	37	20.7	13.1
1-2	> 10	15	38.0	13.3
2-3	< 10	14	22.0	21.4
2-3	> 10	7	30.0	14.3
> 3	< 10	13	7.4	7.6
> 3	> 10	9	49.9	33.3
			n.s.	n.s.

*n.s.=not significant ($P>0.06$).

to the entity of acute (malignant) myelofibrosis (myelosclerosis), which is characterized by anaemia, myelofibrosis, peripheral leucoerythroblastosis, a splenic weight of less than one kg and a rapidly fatal course (Lubin, Rozen & Rywlin, 1976).

The validity of the present observations is limited by their retrospective nature. However, the data used, although imperfect, are the best available at present. In the absence of prospective studies several tentative conclusions may be drawn. It is suggested, that in addition to thrombocythaemia (Ward and Block, 1971) and disseminated intravascular coagulation (Silverstein, 1975) the following manifestations should be regarded as relative contra-indications for splenectomy in AMM: high concentrations of serum alkaline phosphatase; anaemia in the presence of an estimated splenic weight of 3 kg or more; and anaemia with an estimated splenic weight of one kg or less.

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