

Splenic Functions in Thalassemia Major

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ABSTRACT

Platelet and factor VIII (F-VIII) storage and phagocytic functions of the spleen were studied in 15 patients with β -thalassemia major who were not splenectomized and in 7 patients with Hb-S- β -thalassemia. Eight splenectomized patients, 4 patients with β -thalassemia major, and 11 healthy children served as controls. F-VIII elevation following adrenalin was not found to be a sensitive index in the evaluation of "functional hyposplenism." No functional derangement of the organ was shown in the patients with β -thalassemia major. However, one of the tests showed that at least 30% of the patients had functional hyposplenism. Higher platelet counts were observed in the patients without palpable spleen, and the independence of the splenic functions were shown.

Key Words: Thalassemia splenic functions

INTRODUCTION

The spleen is a large mass of lymphoid and phagocytic reticuloendothelial cells with capillaries and non-fenestrated sinusoids that enhance the filtering ability of the organ (1). Among a number of functions, filtering, phagocytic function, and storage abilities are closely related to the spleen's anatomical structure.

The decrease or loss of phagocytic function of the spleen was well demonstrated in sickle-cell anemia, in spite of the enlargement of the organ (2–4). Although the phagocytic function of the spleen was demonstrated in a few cases of β -thalassemia (6), there is no study related to the organ's filtering and reservoir abilities, to the best of our knowledge.

In this study, phagocytic, filtering, and reservoir functions of the spleen for platelets and antihemophilic globulins were studied in 15 cases with β -thalassemia major.

MATERIALS AND METHODS

A total of 41 children were studied, who were divided into four groups. Group 1 comprised 11 healthy children, 4–12 years of age (2 girls and 9 boys), with an AA hemoglobin pattern. Group 2 comprised 8 children, 3–12 years of age (2 girls and 6 boys) who were splenectomized 1–3 years prior to the study because of β -thalassemia major (4 cases), idiopathic thrombocytopenic purpura (2 cases), spherocytosis (1 case), and severe α -thalassemia (1 case). Group 3 comprised 15 cases of β -thalassemia major, with the age range of 3–17 years (9 girls and 8 boys). Group 4 comprised 7 children with the age range 2.5–15 years (4 girls and 3 boys) with sickle-cell- β -thalassemia (7).

The hemoglobinopathy diagnosis was verified using starch (pH 8.6) and agar gel (pH 6.4) electrophoresis (7) in all patients and in both the parents. All children were free of infection and did not have any acute problem at the time when tests were performed.

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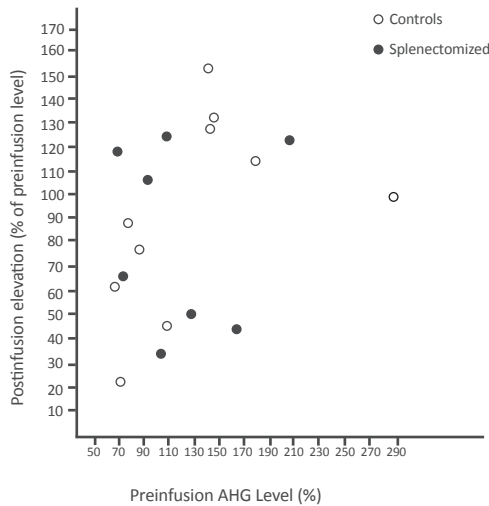


FIGURE 1: Pre-infusion F-VIII level and its post-adrenalin elevation in controls and splenectomized children.

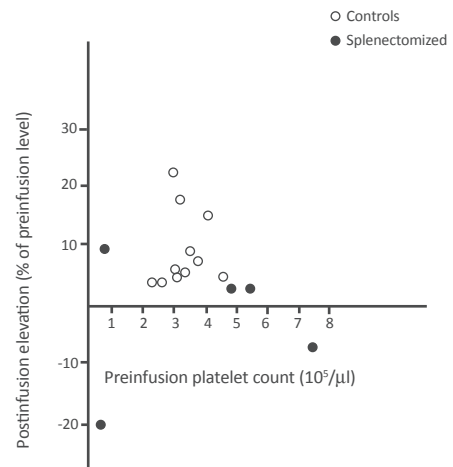


FIGURE 2: Pre-infusion platelet counts and its post-epinephrine changes in controls and splenectomized children.

The phagocytic function of the spleen was studied in the last two groups 1 hour after intravenous injection of 99m Tc-sulfur colloid (1-3m Ci) by using Anger scintillation camera pho-Gamma III No with a low-energy collimeter. The images were recorded on a polaroid film and/or a 35-mm Kodak PX 402 film in pre-set time. In addition to anterior and posterior projections, left posterior images were also obtained when previous two projections did not give a splenic image. Scans were graded as normal, decreased, and no uptake.

The reservoir function for platelets and F-VIII procoagulant activities were evaluated before and 10 minutes after the intravenous injection of adrenalin (5 γ/kg epinephrine was diluted in 10 mL 5 % glucose, which was infused in 10 minutes). Platelets in the blood emerging from a finger prick were examined under phase contrast microscopy (8) and the F-VIII procoagulant activity in the same blood was determined according to the study by McMillian et al. (9) on fresh frozen samples of plasma that were stored at -30°C for no more than 3 weeks.

For evaluating the filtering function of the spleen, the presence of Howell-Jolly bodies per 500 red blood cells were determined.

RESULTS

In the case of healthy controls, platelet and anti-human globin (AHG) levels significantly elevated following epinephrine perfusion ($P < 0.001$ and $P < 0.0001$, respectively) without exhibiting any relation to the age and sex. The mean baseline

platelet counts and AHG levels were $320.363/\mu\text{L}$ (SD ± 71.631 , range 220.000–464.000) and 132.8% (S.D. $\pm 71,19$, range 62–286%), respectively. The elevation of platelets was 8.82% (the range 3.5–22.05%) and the mean AHG elevation was 93.1% (the range being 23.18–151.9%) (Figures 1 and 2). The changes in the platelet count was evaluated in five cases in Group 2 following epinephrine infusion, and the minimal change observed was most likely due to the technique used (Figure 2). This group was not homogeneous in terms of their platelet counts and, therefore, the statistical evaluation was not carried out. The baseline AHG level was normal (mean 110.8%; range 56–194%), and its elevation after epinephrine perfusion was carried out in all eight cases; the elevation was found significant ($P < 0.01$). The mean elevation of AHG was 70.66% with the range of 24.2–120.6%.

Spleen scanning and the evaluation of platelet counts were performed in all 15 cases with β -thalassemia major. The spleen was found enlarged in all cases as was clinically evident; only in 1 case, hypoactive areas were seen.

The baseline platelet count (mean $224,266/\mu\text{L}$ with the range of 100.000–304.000/ μL) in this group did not differ from that in the controls ($P > 0.05$). The evaluation of post-infusion platelet counts of all 15 cases were statistically significant ($P < 0.01$, Table 1, Figure 3). The mean pre-infusion F-VIII procoagulant activity (151%) was higher in this group than that in the controls, and the activity significantly elevated following adrenalin perfusion ($P < 0.001$) (Table 1/ Figure 4).

TABLE 1: Initial platelet and F-VIII levels with their elevation following adrenalin perfusion, spleen size, and scanning results in patients with β -thalassemia major.

Patient's initials	Age / Sex	Spleen (cm)	Platelets		F-VIII		Splenic* scanning
			Initial ($\times 10^3/\mu\text{L}$)	Elevation (%)	Initial ($\times 10^3/\mu\text{L}$)	Elevation (%)	
ZT	3, F	4	100	16.0	210	61.2	N
HT	3, F	6	224	8.92	145	80.68	N
EE	4, M	2	284	5.63	121	50.41	N
AK	4, F	3	172	7.0	101	72.27	N
ET	5, F	3	272	4.41	165	63.00	N
AY	5, M	3	288	19.44	152	31.57	N
AP	5, M	7	304	3.94	106	62.26	N
HY	5, F	7	276	8.69	142	79.57	N
GY	6, F	8	236	11.86	208	73.00	N
MK	6, F	6	296	14.86	172	100.58	N
FK	7, F	4	148	21.62	106	37.73	N
AK	9, F	7	156	5.12	164	98.17	N
AK	10, M	4	152	5.26	116	50.00	N
MP	12, M	10	160	25	214	61.02	H
MS	17, M	2	296	9	143	87.4	N
Mean :		224	9.28	151	67		

* N: Normal H: Hypoactive, Areas

With one exception, all the patients in Group 4 had Hb-S- β^0 -thalassemia. The spleen could not be visualized in one of the patients with splenomegaly, and the phagocytic dysfunction of the organ was shown in two cases (no uptake in one and decreased in one) without clinical splenomegaly (Table 1). Although the platelet elevation following adrenalin infusion was significant ($P < 0.05$), no response was found in three patients whose splenic ^{99m}Tc uptake was abnormal. In spite of lower pre-infusion thrombocyte counts in patients with palpable spleen, post-perfusion rises were more marked in them (Table 2 / Figure 3). The mean pre-infusion AHG activity in Group 4 (165.5%) was higher than that in the controls; after adrenalin infusion, the AHG activity was statistically significant ($P < 0.01$) but the elevation of F-VIII activity (37.82 %) among the groups was the lowest.

Howell-Jolly bodies were present in the peripheral blood of all splenectomized children and patients with Hb-S- β -thalassemia but were not present in that of normal controls and patients with thalassemia.

DISCUSSION

Although "functional hyposplenia" has not been reported in blacks with Hb-S- β -thalassemia (2, 6), at least two of our seven patients had this disorder (28.6%). With one exception, all of our Hb-S- β -thalassemia combinations had β^0 -thalassemia; their Hb-S concentrations were comparable to our patients with Hb-SS disease and their Hb F values were not significantly different from our sickle-cell anemia patients (10). Their Hb and Hct values and ages were also comparable to the patients with sickle-cell anemia. Therefore, only decreased ^{99m}Tc -sulfur colloid uptake is correlated to Hb S concentrations; it would be expected in more of our patients with Hb S- β -thalassemia.

The platelet storage of the spleen after adrenalin infusion was normal in patients with Hb-S- β -thalassemia. However, the increase of F-VIII level, although significant, was the lowest among the groups. These results indicate the relative dissociation of the splenic function of these patients as was indicated by

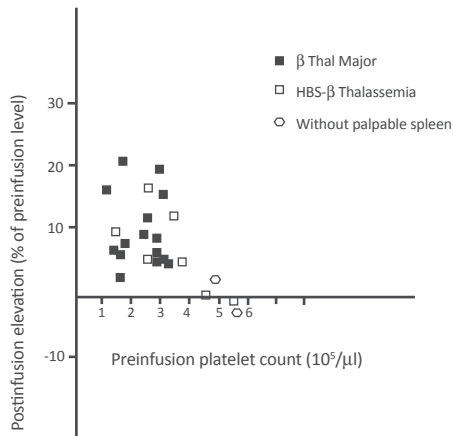


FIGURE 3: Pre-infusion platelet counts and its post-adrenalin changes with β -thalasemia major and Hb-S- β -thalassemia.

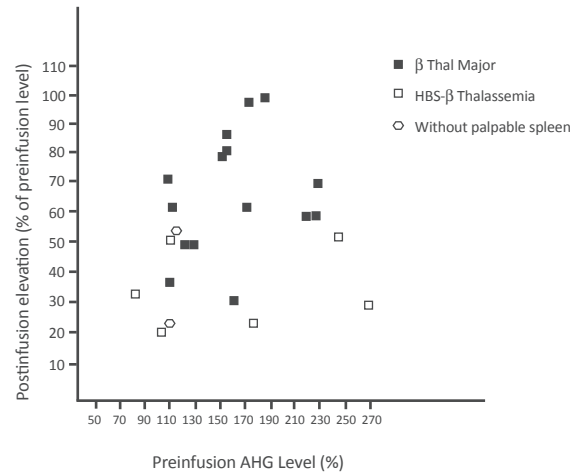


FIGURE 4: Baseline F-VIII level and its post-adrenalin elevations in β -thalasemia and Hb-S- β -thalassemia.

Schwartz (6), Flater et al. (4), and us (11) in sickle-cell anemia cases. The platelet elevation following epinephrine perfusion was marked more in patients with enlarged spleen as indicated by Libre et al. (12) Aster and his colleagues (13), and Branchög et al. (14). Libre et al. (12) mentioned that the elevation of F-VIII level did not seem to be dependent on the concomitant platelet rise following adrenalin infusion, which was also observed in our cases.

In patients with β -thalasemia major, the functional derangement of the organ was shown with none of these tests. Although the presence of Howell-Jolly bodies were reported in β -thalasemia major in a study by Forget and Kan (15), these were not found in any of our cases.

Howell-Jolly bodies were observed in all our patients with Hb-S- β -thalassemia, Hb SS disease (11), and all splenectomized cases in this study, but these were observed neither in normal controls nor in patients with thalassemias.

The AHG elevation in splenectomized individuals in this study is not in agreement with the results of Libre and his colleagues (12). But Flater et.al. (4) also showed AHG elevation after epinephrine infusion in splenectomized individuals; therefore, the elevation of AHG may cautiously be interpreted as showing the presence of splenic function in at least in our way of perfusion studies.

Penny and coworkers (16) reported that the spleen contains about one-third of the platelet mass. Aster (13) and Branchög et al. (14)

TABLE 2: Initial platelet and F-VIII levels with their elevations following adrenalin perfusion, spleen size, scanning, and Hb F levels in patients with Hb S- β -Thalassemia

Patient's initials	Age / Sex	Spleen (cm)	Hb F (%)	Platelets		F-VIII		Splenic* scanning
				Initial (ml)	Elevation (%)	Initial (%)	Elevation (%)	
MG	2.5, M	3	14	352.000	3.4	235	53.61	N
HK	8, F	3	19	328.000	12.2	215	46.04	N
AA	9, M	4	6.3	244.000	4.9	77	33.76	NU
EH	15, F	15	22	124.000	9.67	258	32.17	N
GS	15, F	4	18	240.000	16.66	170	25.29	N
YG	9, M	NP**	11.3	456.000	0.87	104	52.88	D
FS	10, F	NP**	20	560.000	0.7	100	21	NU
Mean :		15.8	329.142	6.71	165.5	37.62		

* N: normal, D: decreased, NU: no uptake ** NU: not palpable

showed that the pooled platelets in the spleen are exchangeable and available to the circulation with epinephrine infusion, which is abolished by splenectomy as in our splenectomized controls. Also, statistically significant platelet elevation was not observed after epinephrine perfusion in three patients with Hb-S- β -thalassemia in whom functional hyposplenism was shown by scanning (Table 2). More pronounced platelet elevation in patients with thalassemia after adrenalin infusion would be related to their splenomegaly in accordance to the findings of Aster (13) and Branchög et al (14). Higher platelet counts in children and adult patients with Hb SS disease were reported by Schwartz (6) and Freedman and Karpatkin (17). Marked thrombocytosis was also present in two of our patients with Hb S- β -thalassemia without palpable spleen.

In conclusion, the splenic function in patients with β -thalassemia by 99m Tc-sulfur colloid phagocytosis and platelet elevation after adrenalin infusion is normal. But by phagocytosis, it is found decreased in at least 30% of the patients with Hb-S- β -thalassemia.

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