Thrombosis After Splenectomy in Patients with Thalassemia

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ABSTRACT

Thrombosis is one of the most important complications after splenectomy and requires fast diagnosis, effective therapy and good follow-up. The aim of this study is to investigate the effects of thrombocytosis and natural inhibitors on thrombosis after splenectomy. We detected thrombosis in the portal vein system in 7 of the 30 splenectomized patients (23.3%) by Doppler Colour Flow Imaging. There was no statistical increase of thrombocyte count in patients with or without thrombosis. Natural inhibitor levels in all patients were lower than controls ($p< 0.001$), but there was not any statistical difference between the patients with and without thrombosis.

Key Words: Thalassemia, Splenectomy, Thrombosis, Thrombocytosis, Natural inhibitors.

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INTRODUCTION

Thromboembolic complications have been reported in thalassemic patients in association with known risk factors such as diabetes, complex cardiopulmonary abnormalities, hypothyroidism, liver function anomalies and postsplenectomy thrombosis[1]. Portal thrombosis and other thromboembolic complications in patients with ß-thalassemia have been detected by doppler colour flow imaging (DCFI) which is a noninvasive technique used at the clinical evaluation of hemodynamic changes in splenectomy[2]. Thrombosis is one of the most important complications after splenectomy and requires fast diagnosis, effective therapy and good follow-up[3]. The aim of this study is to investigate thrombosis after splenectomy by DCFI and the effects of thrombocytosis and natural inhibitors on thrombosis.

MATERIALS and METHODS

A total 30 patients (15 female, 15 male) with thalassemia major (n: 16), thalassemia intermedia (n: 11) and S-ß thalassemia (n: 3) were included in this study. The mean age of patients and their splenectomy time were 17.8 ± 9.3 and 15.1 ± 9.2 years respectively (Tab-

le 1). Thrombosis was investigated by the DCFI method before and after splenectomy. Measurements of portal vein and splenic vein diameter were performed in a fasting state and in the supine and left lateral position in order to determine the diameter variations during respiration. The presence of thrombus gives low

Table 1. The features of the splenectomized patients

No	Age (years)	Sex	Diagnosis	Risk factors	Splenectomy (years)	Doppler USG
1	9	M	TM	Hepatitis	5	-
2	18	F	TM	-	10	-
3	69	F	TI	-	65	-
4	34	M	TI	Hepatitis	30	THRM
5	9	M	TM	-	5	-
6	33	F	S+ß	-	29	-
7	16	F	TM	-	12	-
8	23	F	TI	Cardiac	20	-
9	32	M	TI	Cardiac	29	THRM
10	9	F	TM	-	6	-
11	25	F	TI	Diabetes	22	-
12	9	M	TM	-	6	-
13	25	F	TI	Hepatitis	25	-
14	37	F	TI	-	34	THRM
15	14	F	S+ß	Hepatitis	11	-
16	13	M	TI	-	9	-
17	17	M	TM	Cardiac	14	THRM
18	12	M	TM	-	9	-
19	26	M	TI	Hepatitis	24	-
20	13	M	TM	-	11	-
21	15	M	TM	Cardiac	13	-
22	19	F	TM	Cardiac	17	-
23	13	F	TM	Hepatitis	11	THRM
24	14	M	S+ß	-	12	-
25	7	M	TM	-	5	THRM
26	32	M	TI	-	30	-
27	6	F	TM	-	4	-
28	26	F	TI	Hepatitis	25	-
29	6	F	TM	Hepatitis	6	-
30	5	F	TM	Hepatitis	5	THRM
Mean ±	17.8 ±				15.1 ±	
SD	9.3				9.2	

M: Male, F: Female, TM: Thalassemia major, TI: Thalassemia intermedia, S+ß: Sickle cell + beta-thalassemia,
THRM: Thrombosis.

echo. Platelets were counted by electronic counters (Coulter MaxM) in the first 7 days of splenectomy, then three times per week. Protein C antigen, total Protein S and AT-III levels were assayed with commercial elisa kits (Thrombonostika Protein C-Organon Teknika), (Thrombonostika Protein S-Organon Teknika) and (Chromostrate™ Antithrombin III assay-Organon Teknika). Student's t test was used for statistical analysis.

RESULTS

7 (4 TM, 3 TI) out of 30 patients (23.3%) were determined to have thrombosis in their portal vein system. There were 9 hepatitis, 5 cardiac and 1 diabetic problem as risk factors in our splenectomized patients. 3 out of 7 patients with thrombosis had hepatitis, and 2 had cardiac problems.

The mean platelet count of patients was 226.7 ± 122.5 (range: 64-498) x 10^9/L in the preoperative period. The postoperative period platelet counts were as follows; 526.7 ± 357.8 (range: 193-1318) x 10^9/L on the 3rd day, 611.8 ± 333.5 (range: 273-1291) x 10^6/L on the 7th day, 672 ± 305.2 (range: 142-1177) x 10^9/L on the 15th day (Table 2). There was a statistical increase of thrombocyte count ($p< 0.001$) after in patients splenectomy, but there was no difference between patients with and without thrombosis.

The mean protein C level was 0.55 ± 0.17 (range: 0.35-0.87) IU/mL, protein S level was 43.2 ± 8.4% (range: 29-52), and AT-III level was 86.3 ± 28.1% (range: 62-160). Natural inhibitor levels of all patients were lower than the control ($p< 0.001$), but there was no statistical difference between patients with and without thrombosis (Table 3).

DISCUSSION

Splenectomy is indicated in thalassemic patients when they develop hypersplenism and yearly transfusion requirements exceed 200 mL packed cells per kilogram body weight[4]. Total splenectomy, partial splenectomy, laparoscopic splenectomy and partial dearterialization of spleen are procedures used in thalassemia[5-7]. Indication of splenectomy in our patients was due to hypersplenism in thalassemia intermedia and increased transfusion in both thalassemia major and S + ß-thalassemia.

Thrombosis has been reported in splenic or portal vein system after splenectomy in 26.7% patients with thalassemia major and hemolytic diseases[8]. We detected thrombosis in the portal vein system in 7 (23.3%) of 30 patients with thalassemia.

It has been reported that thrombotic events after splenectomy in thalassemic patients have many causes such as: Increasing platelet number, heterogeneity, spontaneous platelet aggregation, protein C and protein S deficiency with correlated liver damage, low heparin cofactor-II levels, and increasing platelet factor-3 activity[9-13]. Another mechanism may be the presence

Table 2. Platelet count in patients with thalassemia

	Preoperative Platelet x 10^9/L	Postoperative 3rd day Platelet x 10^9/L	Postoperative 7th day Platelet x 10^9/L	Postoperative 15th day Platelet x 10^9/L
All patients (n: 30)				
Mean ± SD	226.7 ± 122.5	526.7 ± 357.8	611.8 ± 333.5	672.0 ± 305.2
Range	64-498	193-1318	273-1291	142-1177
Patients with thrombosis (n: 7)				
Mean ± SD	258.4 ± 168.9	596.8 ± 483.2	672.2 ± 244.7	763.8 ± 190.6
Range	83-344	193-1318	310-1291	215-1177
Patients without thrombosis (n: 23)				
Mean ± SD	216.2 ± 110.1	502.7 ± 323.5	591.6 ± 367.4	629.8 ± 326.6
Range	64-498	213-853	273-1225	142-1092

Table 3. Protein C, protein S and AT-III levels in patients with thalassemia

	Protein C (IU/mL)	Protein S (%)	AT-III (%)	p
All patients (n: 30)				< 0.001
Mean ± SD	0.55 ± 0.17	43.2 ± 8.4	86.3 ± 28.1	
Range	0.35-0.87	29-52	62-160	
Patients with thrombosis (n: 7)				< 0.001
Mean ± SD	0.50 ± 0.15	44.4 ± 12.8	85.8 ± 22.3	
Range	0.35-0.66	29-49	62-92	
Patients without thrombosis (n: 23)				< 0.001
Mean ± SD	0.57 ± 0.18	42.8 ± 7.3	86.5 ± 30.4	
Range	0.38-0.87	36-52	64-160	
Control (n: 20)				
Mean ± SD	0.92 ± 0.30	70.6 ± 19.3	129.2 ± 18.9	
Range	0.72-1.32	62-132	90-160	

of lupus anticoagulants[14]. The number of platelets in our patients increased after splenectomy but there was no statistical increase of thrombocyte count in patients with and without thrombosis. Kemahl› et al reported that hypercoagulobility in thalassemic patients was not only due to a marked decrease in protein C and protein S activity but also increased level of D-Dimer and fibrinopeptide A and lupus anticoagulants. They noted that threre was no difference between splenectomized and nonsplenectomized patients with regard protein C antigen, protein S activity and antigen AT-III and FPA levels[15]. Shirahata et al[11]. Reported that protein C and S were significantly lower in splenectomized patients. In our study, protein C, protein S and AT-III levels were lower in all patients than in the control (p< 0.001) but there was no statistical difference between the splenectomized patients with and without thrombosis.

Recently, a new cause of thrombosis, common genetic variants (FV1691 G-A, FV 4070 G-A, PT 20210 G-A) were reported in chronic hemolytic disease patients with post-splenectomy thrombotic events[16]. Molecular genetic investigation of FV Leiden was performed with a polymerase chain reaction in 8 splenectomized patients but there was no detected mutation.

In conclusion, there are a lot of factors play a role on producing thrombosis in thalassemic patients when splenectomized. Thrombocytosis and low natural inhibitors are only a predisposing condition for thromboembolic events. The patients with known risk factors should be followed up by DCFI during the pre and postsplenectomy period. It may be prevented with prophylactic therapy.

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