Original Article

Correlation of splenectomy with portal vein thrombosis in β-thalassemia major

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Abstract

Objective: To evaluate the correlation of portal vein thrombosis and splenectomy in β-thalassemia major patients visiting Babol Medical University, Iran.

Methods: This cohort study was done from 1997 to 2008. In our study, major β-thalassemic patients visiting for transfusion at least once a month at Amirkola Children's Hospital were selected. Portal vein thrombosis was diagnosed through Doppler ultrasound in symptomatic patients. Cases were 160 β-thalassemia major patients who underwent splenectomy and 160 remaining thalassemic patients without splenectomy were controls. Statistical comparison with Fisher exact test was performed.

Results: Five cases had suffered from portal vein thrombosis (P=0.03). Majority patients with portal vein thrombosis had their symptoms after first month of the operation.

Conclusion: Correlation of splenectomy with portal vein thrombosis is statistically significant among β-thalassemic children from Iran.

Keywords: Splenectomy, Portal vein thrombosis, β-thalassemia major (JPMA 61:760; 2011).

Introduction

The alpha and beta thalassaemias are the most common inherited single-gene disorders in the world with the highest prevalence in areas where malaria was or still is endemic. The burden of this disorder in many regions is of such a magnitude that it represents a major public health concern. For example in Iran, it is estimated that about 8,000 pregnancies are at risk each year.[1] Some kinds of thalassemia are blood transfusion dependent. Without blood transfusion, these patients will not survive more than two decades. Homeostasis maintains the integrity of a closed, high-pressure circulatory system after vascular damage with regulatory mechanisms of homeostasis. When pathologic processes overwhelm the regulatory mechanisms of homeostasis, excessive quantities of thrombin form that initiate thrombosis.[2] In some conditions, vein thrombosis occurred more than usual. In pathologic process, platelet aggregation, thrombin formation and large thrombosis overcome the natural regulatory of anti-coagulation and clot splitting system.[3]

Vein thrombosis may occur more frequently under certain circumstances such as increased blood coagulation disorders, splenectomy, abdominal infections, pancreatitis, huge spleen at the time of splenectomy, umbilical vein catheterization, schistosomiasis, CVP-line, OCP user, pancreatectomy and malignancy.[4,5] A few studies showed that thalassemia per se is susceptible to vein thrombosis too. They show thrombosis of portal vein and other abdominal vessels in thalassemia with or without splenectomy.[6-9] And the others believe splenectomy is the cause of vein thrombosis even in non-thalassemic patients.[10,11] Anyway this important complication may initially be asymptomatic and symptoms will appear gradually when thrombosis progresses. Venous pressure will be high in the adjacent thrombotic branches and causes abdominal vessels blood flow disturbances and pain in it.Symptoms of increased portal vein pressure such as gastrointestinal bleeding, stomach pain appear. Intestinal infarction and abdominal pain due to simultaneous involvement splenic artery and vessels occur.[12] For diagnosis of this serious complication, many methods such as CT scan, angiography, ultrasound and color Doppler are used. Thrombosis is defined as an echogenic foci in the vessel, collateral of portal vein, dilation behind part of thrombotic region and cavernous formation in color Doppler sonography.[13,14] Incidence of these complications in thalassemia vary in different centers. Some centers have reported it as a case report.[15] Some had reported 3.3% to 6.6%.[16,17] Some centers recommend to screen that patients who referred for blood transfusion because of thrombotic risks.[18]

Some showed that many factors, such as V-Leiden, prothrombin 20201-A, thrombocytosis are responsible for portal vein thrombosis.[19] With early diagnosis and treatment with thrombolytic agents in acute portal vein

thrombosis,this can even open the portal system.[20] We aimed to evaluate the correlation of thrombosis and splenectomy in β-thalassemia major patients. We studied this phenomenon in a Cohort study. If there were significant correlations between splenectomy and PVT, this procedure should be done judiciously.

Methods

Our study was a cohort study, conducted from 1997 to 2008. β-thalassemia major patients who were referred to Amirkola Children's Hospital at the Babol Medical University in Iran for regular transfusion were included. Among these patients, 160 β-thalassemia major patients were splenectomised (case) and 160 β-thalassemia major patients were not splenectomised (control). The estimated number of study subjects for a group was calculated by the formula; $n=(z\ 1-\alpha/2+ z\ 1-\beta)^2\ (p1q^1+p^2q^2) / d^2$ (α error=5%, power=80%, p1=6%, p^2=0.5%). Among these; any patients with history of schistosomiasis, umbilical vein catheters, abdominal infection, OCP user,hypercholesterolemia were excluded from the study. In our study, no patients met these conditions. Also no patient voluntered for laparoscopy. They were followed and assessed with colour Doppler sonography only if they were symptomatic.Statistical comparison with Fisher exact test was performed.

Results

A total of 320 thalassemic patients were enrolled in the study. Of these, 160 were splenectomised (case) and 160 thalassemic were not splenectomised and were taken as controls. All of splenectomised patients were operated by open surgery. The splenectomised patients (case) were 16 to 45 years old with 69 females and 9 males. The non-splenectomised patients (control) were 15 to 45 years age with 85 females and 75 males. There were no significant differences in these groups. Among these 320 patients , only five patients in the case group and no one in control group suffered from portal vein thrombosis (P =0.03) (Table-1). Thrombotic patients presented with severe abdominal pain. Four patients came to our clinic in the first month after operation. One patient suffered from portal vein thrombosis 3 years after splenectomy. The youngest patient was 18 years old and the oldest patient was 33 years old. Although two groups of study partially matched the age and sex, only one male was identified with portal vein thrombosis. All of portal vein thrombosis was diagnosed by color Doppler ultrasound (Table-2).

Table-1: Correlation of splenectomy with portal vein thrombosis in major β-thalassemia.

	No.of patient	PVT	P
Case	160	5	
Control	160	0	0.03

Discussion

The results of this study show that splenectomy in β-thalassemia major is the cause of portal vein thrombosis. Among the 160 cases of splenectomised major β-thalassemic patients, 5 (3.12%) suffered from portal vein thrombosis but none of nonsplenectomised patients developed portal vein thrombosis (P=0.03). In our study the incidence of portal vein thrombosis was slightly more than some other studies.[18] Patients in our study had gross splenomegaly and all of them were operated by open surgical technique. All the patients presenting to the clinic were assessed by colour Doppler ultrasound. All complained of abdominal pain. None had gastro intestinal bleeding portal hypertension or cirrhosis. It was unlike the Belli study conducted in 1989.[5] Non-splenectomised patients did not experience portal vein thrombosis, which proves that β-thalassemic patients are not inherently prone to this complication. Four patients with portal vein thrombosis came to our clinic within the first month of splenectomy similar to the study by Skarsgard E, et al in Toronto, Ontario, Canada.[21] One patient came to our clinic three years after splenectomy. Similar to the experience of Zandiyeh in Ahvaz-Iran,[15] who reported a case of portal vein thrombosis that occurred two years after splenectomy. We believe that color Doppler ultrasound method is an investigation with acurate results. Other investigators have reported similar experience.[22,23] This method is preferred over the other methods because of the cost and easy diagnosis. In our study, no patients voluntered for laparoscopy. That was the reason it was not possible to compare these two different technical surgeries. Thrombosis is a complication that can be fatal. We

Table-2: The frequency of Portal vein thrombosis in ?-thalassemia major whom underwent splenectomy.

	Age	Sex	Symptoms at presentation	Diagnosis	Duration after operation	Treatment
Portal Vein Thrombosis						
1-	20	F	Abdominal. Pain	color Doppler ultrasound	21 Days	Anticoag.
2-	28	M	Abdominal. Pain	color Doppler ultrasound	17 Days	Anticoag.
3-	33	F	Abdominal. Pain	color Doppler ultrasound	25 Days	Anticoag.
4-	18	F	Abdominal. Pain	color Doppler ultrasound	3 Years	Anticoag.
5-	20	F	Abdominal. Pain	color Doppler ultrasound	30 Days	Anticoag.

administer anti-coagulants for four months which has shown good results.

Conclusion

Splenectomy in patients with β-Thaliasemia should be performed when strongly indicated. If splenectomy has to be performed anticoagutant prophlaxis should be instituted Doppler ultrasonography provides accurate results for diagnosing portal vein thrombosis.

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References

1. Control of hereditary disorders: Map of global distribution of haemoglobin disorders.Report of WHO Scientific meeting (1996).
2. Gerotziafas GT. Risk factors for venous thromboembolism in children. Int Angiol 2004; 23: 195-205.
3. Setiabudy R, Wahidiyat PA, Setiawan L. Platelet aggregation and activation in thalassemia major patients in Indonesia. Clin Appl Thromb Hemost 2008; 14: 346-51.
4. Lee SE, Jang JY, Lee KU, Kim SW. Clinical comparison of distal pancreatectomy with or without splenectomy. J Korean Med Sci 2008; 23: 1011-4.
5. Belli L, Romani F, Riolo F, Rondinara G, Aseni P, Di-Stefano M, et al. Thrombosis of portal vein in absence of hepatic disease. Surg Gynecol Obstet 1989; 169: 46-9.
6. Panigrahi I, Agarwal S. Thromboembolic complications in beta-thalassemia: Beyond the horizon. Thromb Res 2007; 120: 783-9.
7. Targarona EM. Portal vein thrombosis after laparoscopic splenectomy: the size of the risk. Surg Innov 2008; 15: 266-70.
8. Stamou KM, Toutouzas KG, Kekis PB, Nakos S, Gafou A, Manouras A, et al. Prospective study of the incidence and risk factors of postsplenectomy thrombosis of the portal, mesenteric, and splenic veins. Arch Surg 2006; 141: 663-9.
9. Cadili A, de-Gara C. Complications of Splenectomy. Am J Med 2008; 121: 371-5.
10. Maalouf M, Papasavas P, Goitein D, Caushaj PF, Gagne D. Portal vein thrombosis after laparoscopic splenectomy for systemic mastocytosis: a case report and review of the literature. Surg Laparosc Endosc Percutan Tech 2008; 18: 219-21.
11. Cappellini MD, Grespi E, Cassinerio E, Bignamini D, Fiorelli G. Coagulation and splenectomy: an overview. Ann N Y Acad Sci 2005; 1054: 317-24.
12. Amitrano L, Guardascione MA, Brancaccio V, Margaglione M, Iannaccone L, Manguso F, et al. Risk factors and clinical presentation of portal vein thrombosis in patients with liver cirrhosis. J Hepatol 2004; 40: 736-41.
13. Honar-Bakhsh A, Seyed-Maleki MM. Application of ultrasound in portal hypertension. J Iran Univ Med Sci 1994; 3: 184-92.
14. Pivovarov GN, Kuranova ND. [Thrombosis of the portal vein.] Lik Sprava 2007; 71-2.
15. Zandian K, Naderi A, Jazayeri SS. A case report of 2 years post-splenectomy chronic vein thrombosis in Beta-Thalassemia major. Sci Med J Ahwaz Univ Med Sci 2006; 48: 451-46.
16. Abdi R, Kosarian SA. Ultrasonographic evaluation of portal vein thrombosis (P.V.T) in patients of beta Thalassemia major in Sari in the year 1995-96.
17. Krauth MT, Lechner K, Neugebauer EAM, Pabinger I. The postoperative splenic/portal vein thrombosis after splenectomy and its prevention - an unresolved issue. Haematologica 2008; 93: 1227-32.
18. Canatam D, Zorlu M, Bayk N, Erturk C, Darak A, Oguz N, et al. Thrombosis After Splenectomy in Patients with Thalassemia. Turk J Haematol 2001; 18: 259-63.
19. Walker ID. Congenital thrombophilia. UK Baillieres Clin Obstet Gynaecol 1997; 11: 431-45.
20. Al-Hawsawi ZM, Haouimi AS, Hassan RA, Tarawah AM. Portal vein thrombosis after splenectomy for beta-thalassemia major. Saudi Med J 2004; 25: 225-8.
21. Skarsgard E, Doski J, Jaksic T, Wesson D, Shandling B, Ein S, et al. Thrombosis of the portal venous system after splenectomy for pediatric hematologic disease. J Pediatr Surg 1993; 28: 1109-12.
22. Van-Gansbeke D, Avni EF, Delcour C, Engelholm L, Struyven J. Sonographic features of portal vein thrombosis. Am J Roentgenol 1985; 144: 749-52.
23. Wermke W. [Sonography in prehepatic portal vein occlusion.] Dtsch Med Wochenschr 1987; 112: 90-5.
24. Soyer T, Ciftci AO, Tanyel FC, Senocak ME, Büyükpamukçu N. Portal vein thrombosis after splenectomy in pediatric hematologic disease: risk factors, clinical features, and outcome. J Pediatr Surg 2006; 41: 1899-902.
25. Amitrano L, Guardascione MA, Brancaccio V, Iannaccone L, Ames PR, Balzano A. Portal and mesenteric venous thrombosis in cirrhotic patients. Gastroenterology 2002; 123: 1409-10.