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Scintigraphic prediction of therapeutic outcomes of splenectomy in patients with thrombocytopenia

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In patients with thrombocytopenia, platelet scintigraphy has been used to locate the site of platelet sequestration and destruction and to determine whether splenectomy will be of benefit. However, its efficacy in predicting the outcome of splenectomy is controversial. We assessed the feasibility of platelet scintigraphy in this regard. ***Methods:*** Platelet scintigraphy was performed in five patients (2 women, 3 men, mean age 48 years) before splenectomy. Four patients were diagnosed with idiopathic thrombocytopenic purpura and one with hypersplenism due to portal hypertension caused by intrahepatic chemotherapy against metastatic liver tumors of rectal cancer. Platelets labeled with 37 MBq of In-111 oxine or 1110 MBq of Tc-99m HMPAO were intravenously injected. Anterior images were obtained with a gamma camera 3–5 and 23–29 hours post-injection in five patients. Additional images were obtained 48 hours post-injection in three patients. For the analysis, a spleen/liver ratio (S/L ratio) was calculated using mean counts in regions of interest defined on the spleen and the liver. Serum platelet counts were measured before and after the operation; in three patients, splenectomy effectively resolved the thrombocytopenia (Group A), while it was ineffective in two patients (Group B). ***Results:*** The S/L ratios were apparently higher in Group A than in Group B; in Group A, the ratios were 6.05, 6.97 and 3.16 at 3–5 hours, 12.67, 7.48 and 3.46 at 23–29 hours and 17.66 and 8.12 at 48 hours, whereas, in Group B, they were 0.67 and 0.66 at 3–5 hours, 0.52 and 0.54 at 24 hours, and 0.42 at 48 hours. ***Conclusion:*** The results of this study indicate that platelet scintigraphy is of value in predicting the therapeutic efficacy of splenectomy in patients with thrombocytopenia.

Key words: platelet scintigraphy, idiopathic thrombocytopenic purpura, splenectomy

INTRODUCTION

PLATELET SCINTIGRAPHY has been used to locate the site of platelet sequestration and destruction. It has long been used to predict the outcome of splenectomy in patients with idiopathic thrombocytopenic purpura (ITP).[1–8] Splenectomy is the most effective treatment for ITP especially medically intractable ITP.[9,10] Such patients are, however, a heterogeneous population and they include a significant subset.[4] Splenectomy does not resolve thrombocytopenia in approximately 20 to 30% of them.[10,11] These facts require pre-operative prediction to avoid the physical burden imposed by unsuccessful surgical treatment. The lack of useful clinical predictors of response to splenectomy has been reported.[12,13] As to scintigraphy, there were also many controversies concerning its efficacy. We assessed the feasibility of scintigraphy retrospectively in patients representing with thrombocytopenia who underwent splenectomy.

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SUBJECTS AND METHODS

Subjects

Platelet scintigraphy was performed in five patients before splenectomy. Four patients were diagnosed with ITP

Table 1

No.	age	sex	diagnosis	platelet count (cells/mm^3)		S/L ratio			outcome
				pre-operation	post-operation	3–5 hr	23–29 hr	48 hr	
1	54	F	ITP, DM	20000	170000	6.05	12.67	17.66	effective
2	46	M	ITP	4000	300000	3.16	3.46	not done	effective
3	58	M	Portal HT	34000	220000	6.97	7.48	8.12	effective
4	59	M	ITP	38000	35000	0.67	0.52	0.42	ineffective
5	23	F	ITP	26000	40000	0.66	0.54	not done	ineffective

ITP: idiopathic thrombocytopenic purpura, DM: diabetes mellitus, HT: hypertension

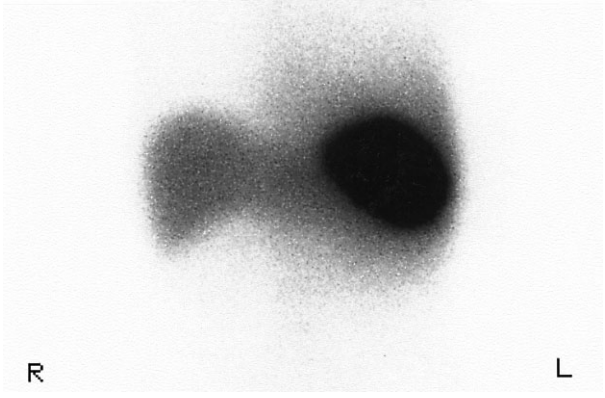

Fig. 1 Anterior image 48 hours post-injection in a 54-year-old woman with idiopathic thrombocytopenic purpura and diabetes mellitus. She was a responder to splenectomy. The spleen/liver uptake ratio was 17.66.

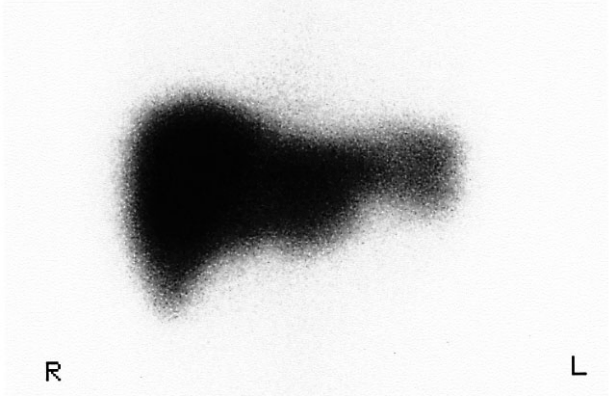

Fig. 2 Anterior image 48 hours post-injection in a 59-year-old man with idiopathic thrombocytopenic purpura. He was a non-responder to splenectomy. The spleen/liver uptake ratio was 0.42.

and one with hypersplenism due to portal hypertension caused by intrahepatic chemotherapy against metastatic liver tumors of rectal cancer (Table 1). Serum platelet counts were measured before and after the operation; in patients 1, 2 and 3, splenectomy effectively resolved the thrombocytopenia, but was ineffective in patients 4 and 5.

Labeling of platelets

Homologous platelets were labelled with 37 MBq of indium-111 oxine (In-111 oxine) in patients 1, 3, 4 and 5. In patient 2, platelets were labeled with 1110 MBq of technetium-99m-hexamethyl propyleneamine oxime (Tc-99m HMPAO). Protocol of labeling was as follows; Platelet-rich plasma (PRP) was obtained from platelets for transfusion by centrifugation at 600 g for 15 min, and PRP was transferred to polystyrene tubes. After acidifying to pH 6.2–6.5 with acid-citrate-dextrose, platelets were sedimented by centrifuging at 800 g for 15 min, resuspended in physiological saline, incubated for 20 min with In-111 oxine or Tc-99m HMPAO at 37°C, washed once with platelet-poor plasma and finally resuspended in platelet-poor plasma.

Imaging and analysis

Anterior images were obtained with a rectangular gamma camera (GCA-901A, Toshiba Co., Tokyo, Japan) equipped with a medium-energy collimator for In-111 oxine or a low-energy, high-resolution collimator for Tc-99m HMPAO, interfaced to a computer (GMS 550-U, Toshiba Co., Tokyo, Japan) 3–5 and 23–29 hours post-injection in five patients. Additional images were obtained 48 hour post-injection in three patients. For the analysis, the spleen/liver ratio (S/L ratio) was calculated using mean counts in regions of interest defined on the spleen and the liver. Regions of interest were defined on the spleen and the liver respectively, both circular and same size, where the activity seemed to be maximum visually.

RESULTS

The S/L ratios were apparently higher in the operation-effective three patients than in the ineffective two patients and there was no overlap between these two groups (Table 1). Images in a responder and a non-responder are shown in Figures 1 and 2, respectively.

DISCUSSION

Many investigations have assessed the efficacy of predicting the outcome of splenectomy by means of platelet scintigraphy. This remains controversial. Some found no

significant differences in sequestration patterns before splenectomy.[1,3,4] Others indicated that the sequestration site is a good predictive element[6] with failure of splenectomy associated with a marked elevation in liver destruction.[5,7]

These discordant results are partly due to the labeling technique and to the different methods used for monitoring platelet sequestration. Chromium-51 labeling, which was developed more than 40 years ago, was used by Ries et al.,[1] and Fenaux et al.[3] However, its labeling efficiency is typically less than 15%. Furthermore, energy of its gamma emission is not suitable for imaging with a gamma camera. Recently, In-111 is mainly used as a radiolabel because its sufficient quantity of external counting enables kinetic evaluation even in cases with severe thrombocytopenia with no radiobiological risk.[6]

Various analytical methods have been reported; some of them simply used mean or total splenic counts,[6,7] while others used S/L ratio based on a geometric mean count,[4,14–16] or % organ activity.[2,5] Difference in the analytical methods used are one factor according for the different conclusions reached. Heterogeneous populations with a significant subset might be another cause of discrepant results.

Our study demonstrated that scintigraphy is of value in predicting the therapeutic efficacy despite the limited number of subjects. The S/L ratios, calculated simply from mean counts, were distinguishable between responders and non-responders even from the early phases of imaging without an any overlap. Our study also included a patient with hypersplenism due to portal hypertension, which is rare in previous reports. However, the subject number in the current investigation is limited, with different conclusions possibly reached if the study population had been bigger.

Splenectomy benefited patients with high S/L ratios; high S/L ratios would indicate significant platelet sequestration in the spleen and active platelet destruction there, namely so-called hypersplenism, which is difficult to treat with medication.[15]

Platelet labeling with In-111 is a well established technique. In-111 is stable tracer that shows almost no excretion in the urine or feces after intravenous injection. Tc-99m HMPAO has been also evaluated as a platelet label; however, the short physical half life limits the observation time. Furthermore, considerable Tc-99m radioactivity is released from platelets *in vivo* as compared with an In-111 label.[17] In addition, the labeling efficiency with Tc-99m HMPAO is significantly lower than that with In-111.[18] These facts support the use of In-111 as a radiolabel for platelet scintigraphy.

As to another aspect of methodology, there is a choice as to whether autologous platelets or homologous ones should be used to locate the site of platelet sequestration and destruction. We prefer to use homologous platelets because the number of labeled platelets is guaranteed, and the burden on and inconvenience to patients is somewhat reduced.[3,14–16] On the other hand, labeling with autologous platelets has an advantage in eliminating the risks of unknown infection and occurrence of alloantibodies. Labeling to autologous platelets should be considered first if a sufficient number of platelets is likely to be labeled.

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REFERENCES

1. Ries CA. Platelet kinetics in autoimmune thrombocytopenia: Relation between splenic platelet sequestration and response to splenectomy. *Ann Intern Med* 1977; 86: 194–195.
2. Heyns A duP, Lotter MG, Badenhorst PN, Kock F, Pieters H, Herbst C, et al. Kinetics and site of destruction of In-111-oxine-labeled platelets in idiopathic thrombocytopenic purpura: A quantitative study. *Am J Hematol* 1982; 12: 167–177.
3. Fenaux P, Caulier MT, Hirschauer MC, Beuscart R, Goudemand J, Bauters F. Reevaluation of prognostic factors for splenectomy in chronic idiopathic thrombocytopenic purpura (ITP): A report on 181 cases. *Eur J Haematol* 1989; 42: 259–264.
4. Siegel RS, Rae JL, Barth S, Coleman RE, Reba RC, Kurlander R, et al. Platelet survival and turnover: Important factors in predicting response to splenectomy in immune thrombocytopenic purpura. *Am J Hematol* 1989; 30: 206–212.
5. Stratton JR, Ballem PJ, Gernsheimer T, Cerqueira M, Slichter SJ. Platelet destruction in autoimmune thrombocytopenic purpura: Kinetics and clearance of indium-111-labeled autologous platelets. *J Nucl Med* 1989; 30: 629–637.
6. Najean Y, Dufour V, Rain JD, Toubert ME. The site of platelet destruction in thrombocytopenic purpura as a predictive index of the efficacy of splenectomy. *Br J Haematol* 1991; 79: 271–276.
7. Lamy T, Moisan A, Dauriac C, Ghandour C, Morice P, Le Prise PY. Splenectomy in idiopathic thrombocytopenic purpura: Its correlation with the sequestration of autologous indium-111-labeled platelets. *J Nucl Med* 1993; 33: 182–186.
8. Uchida Y, Minoshima S, Miyazaki M, Kuyama J, Kitahara H, Ito H. Normalized spleen/liver ratios on In-111-labeled platelet scintigraphy to predict the outcome of partial splenic embolization in patients with idiopathic thrombocytopenic purpura. *Nucl Med Commun* 2000; 21: 441–447.
9. Stasi R, Stipa E, Masi M, Cecconi M, Scimo MT, Oliva F, et al. Long-term observation of 208 adults with chronic idiopathic thrombocytopenic purpura. *Am J Med* 1995; 98: 436–442.
10. Berchtold P, McMillan R. Therapy of chronic idiopathic

thrombocytopenic purpura in adults. *Blood* 1989; 74: 2309–2317.
11. Pizzuto J, Ambriz R. Therapeutic experience on 934 adults with idiopathic thrombocytopenic purpura: Multicentric trial of the cooperative Latin American group on hemostasis and thrombosis. *Blood* 1984; 64: 1179–1183.
12. Julia A, Araguas C, Rossello J, Bueno J, Domenech P, Olona M, et al. Lack of useful clinical predictors of response to splenectomy in patients with chronic idiopathic thrombocytopenic purpura. *Br J Haematol* 1990; 76: 250–255.
13. Fabris F, Zanatta N, Casonato A, Randi ML, Luzzatto G, Girolami A. Response to splenectomy in idiopathic thrombocytopenic purpura: Prognostic value of the clinical and laboratory evaluation. *Acta Haemat* 1989; 81: 28–33.
14. Castle VP, Shulkin BL, Coates G, Andrew M. The use of indium-111 oxine platelet scintigraphy and survival studies in pediatric patients with thrombocytopenia. *J Nucl Med* 1989; 30: 1819–1824.
15. Oriuchi N, Korkmaz M, Kim EE, Delpassand ES, Wong F, Wallace S, et al. Role of indium-111 labelled platelet scintigraphy in the management of thrombocytopenic patients with malignant neoplasms. *Eur J Nucl Med* 1998; 25: 247–252.
16. Hammersmith SM, Jacobson AF, Mankoff DA. Scintigraphy with indium-111-labeled homologous (donor) platelets in the platelet transfusion refractory bone marrow transplant patient. *J Nucl Med* 1997; 38: 1135–1138.
17. Becker W, Borst U, Krahe T, Borner W. Tc-99m-HMPAO labelled human platelets: *in vitro* and *in vivo* results. *Eur J Nucl Med* 1989; 15: 296–301.
18. Dewanjee MK, Robinson RP, Hellman RL, Ganz WI, Serafini AN, Sfakianakis GN. Technetium-99m-labeled platelets: comparison of labeling with a new lipid-soluble Sn(II)-mercaptopyridine-*N*-oxide and ^{99m}Tc-HMPAO. *Int J Rad Appl Instrum B* 1991; 18: 461–468.