Original Article

Diagnosis of Deep Vein Thrombosis Using Platelet Scintigraphy

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Purpose: We reviewed the usefulness of platelet scintigraphy, in which autologous platelets labeled with indium-111-oxine reveal thrombotic activity, for evaluating deep vein thrombosis (DVT).
Materials: During the past 2 years, 39 cases with DVT were enrolled in this study. DVT was definitely diagnosed by color duplex scanning, platelet scintigraphy or both in all cases. For semiquantitative analysis, we estimated the ratio of accumulation in the abnormal region to that in the normal vein on the other side, and defined an abnormal accumulation ratio as over 1.2.
Results: Abnormal accumulation ratio showing active DVT was recognized in 30 cases (77%), and showed a good correlation with clinical symptoms. In addition, in 19 cases with crural DVT, platelet scintigraphy showed abnormal accumulation ratio in 16 cases (84%), while duplex scanning detected thrombi in 13 cases (68%). In cases with an abnormal accumulation ratio, thrombolytic and anticoagulant therapy were very effective for improving clinical symptoms as well inducing regression of the accumulation ratio.
Conclusions: Platelet scintigraphy was very useful for the diagnosis and treatment of DVT and for evaluation of the effect of anticoagulant therapy. Limitations in the definite diagnosis of deep vein thrombosis (DVT) have been apparent for more than three decades.[1)] During the last decade, duplex scanning has reached a high level of accuracy[2-4)] and has been considered the gold standard in the diagnosis of DVT, instead of venography. However, duplex scanning and venography demonstrates only the anatomic alterations associated with venous lesions. In contrast, in platelet scintigraphy, the labeled platelets are incorporated directly into the thrombus and can reveal thrombus activity.[5-7)] We noticed that autologous platelets labeled with indium-111-oxine accumulated on fresh lesions of DVT. This observation suggested two applications of this technique: 1) evaluation of the role of platelets in the pathophysiologic characteristics of DVT; and 2) monitoring the effects of anticoagulant therapy. (Ann Thorac Cardiovasc Surg 2001; 7: 138–42)

Materials and Methods

From January 1996 to December 1997, 39 cases who were clinically diagnosed with DVT were enrolled in this study. They were 12 men and 27 women, ranging in age from 24 to 86 years (mean, 61 years). DVT was definitely diagnosed by color duplex scanning, platelet scintigraphy or both. Color duplex scanning was performed everyday after admission. Platelet scintigraphy was performed immediately after admission and 6 weeks later. Clinical symptoms included phlegmasia alba dolens in 15 cases, pain in 20, and leg swelling in 4. In color duplex scanning using Toshiba model SSA-340A with 7.5 MHz linear transducer, all veins were examined in the transverse and longitudinal views, and four vein segments of common femoral, superficial femoral, poplitial, and all three calf veins were evaluated prospectively. All subjects gave informed consent for the procedures performed

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Received November 16, 2000; accepted for publication February 8, 2001.
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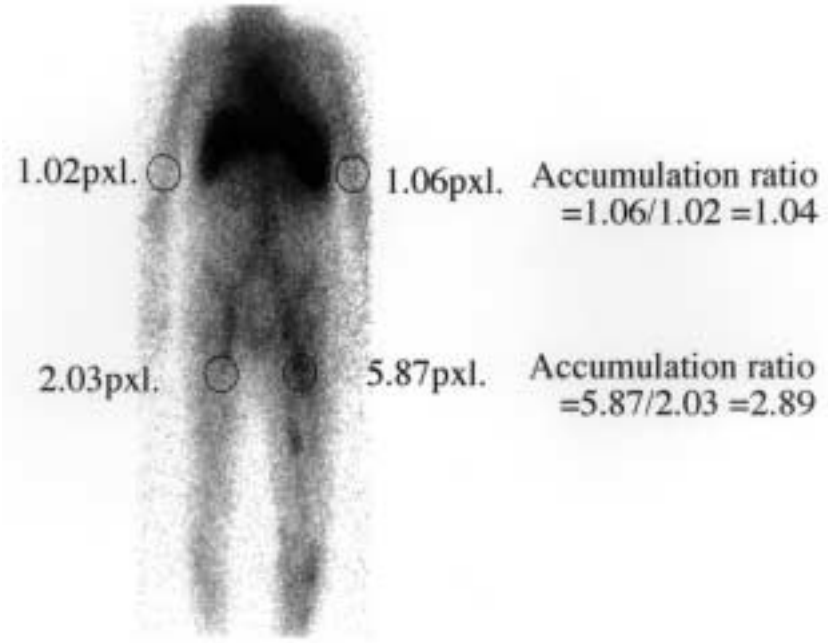

Fig. 1. Estimation of accumulation ratio.
For semiquantitative analysis, we estimate the accumulation ratio of abnormal legion to normal lesion of In-111-oxine-platelet scintigraphy.

in this study.

Platelet scintigraphy

Autologous platelets were obtained from 40 ml of blood and were labeled under aseptic conditions in a laminar flow hood as described by Thakur et al.[8] Autologous platelets labeled with indium-111-oxine were administered intravenously at doses of 0.25-1.19 mCi. Scintigraphic imagings of the whole body were obtained 48-72 hours after tracer administration.

For semiquantitative analysis, we estimated the ratio of accumulation in the abnormal region to that in the normal vein on the other side (Fig. 1), and defined an abnormal accumulation ratio as over 1.2, based on the following observations. In the upper extremities with no thrombotic lesion, all of the accumulation ratios in comparison to bilateral ones were under 1.2 in all cases (1.06 ± 0.05, $p<0.0001$). We ascertained that the vein was normal by physical examinations and duplex scanning.

Treatment

Prior to the evidence of platelet scintigraphic images, all cases initially underwent oral anticoagulant therapy using warfarin sodium and aspirin. In 15 cases with phlegmasia alba dolens in which the thrombus was definitely detected by duplex scanning, heparin sodium at 100 units/kg/day and urokinase at 24×104 units/day were administered intravenously. Heparin was continued for four days, and urokinase was reduced by half every two days and stopped one week after. In 9 cases with accumulation ratios of below 1.2 in platelet scintigram, who were definitely diagnosed with DVT by duplex scanning, the anticoagulant therapy was reduced and discontinued within three months in light cases. Another obesity case underwent the anticoagulant therapy for twelve months. In contrast, in cases with abnormal accumulation ratios of over 1.2, the oral anticoagulant therapy has been continued under the control of international ratio (INR) of over 2.0. The follow-up period is 3-24 months (mean, 11 months).

Statistical analysis

For comparisons between three groups, we used analysis of variance, including post hoc comparisons with the Fisher's PLSD. Values are expressed as the mean+standard deviation. Statistical significance was defined as $p<0.05$.

Results

Platelet scintigraphy vs. duplex scanning

All of 39 cases were diagnosed as having DVT by duplex scanning, platelet scintigraphy or both. The scinti-

Table 1. Comparisms of planet scintigraphy and duplex scanning for diagnosis of DVT

	Duplex scanning		
	abnormal	normal	total
Platelet scintigraphy			
abnormal	23	7	30
normal	9	0	9
Total	32	7	39

Table 2. Comparisms of platelet scintigraphy and duplex scanning of diagnosis of crural DVT

	Duplex scanning		
	abnormal	normal	total
Platelet scintigraphy			
abnormal	10	6	16
normal	3	0	3
Total	13	6	19

graphic imagings revealed abnormal accumulation ratios of over 1.2 in 30 cases (77%), while duplex scanning detected venous thrombi in 32 cases (82%). Duplex scanning detected thrombi which scintigraphy could not image in 9 cases, while scintigraphy imaged DVT which duplex scanning could not detect in 7 cases (Table 1). There was not a statistically significant correlation between the results of the two methods (Yates corrected χ^2=1.25, p=0.26). In contrast, in 19 cases with crural DVT, scintigraphic imaging showed abnormal accumulation in 16 cases (84%), while duplex scanning detected thrombi in 13 cases (68%). Scintigraphy imaged crural DVT which duplex scanning could not detect in 6 cases, while duplex scanning detected thrombi which scintigraphy could not image in 3 cases (Table 2). Duplex scanning was superior to scintigraphy for detecting thrombi above the knee, and scintigraphy was better for detecting thrombi below the knee. However, there was not a statistically significant correlation between the results of the two methods (Yates corrected χ^2=0.41, p=0.52).

Scintigraphy and clinical symptoms

Fifteen cases with phlegmasia alba dolens had significantly higher accumulation ratios (1.68±1.56) than those with swelling (1.22±0.78, p=0.002) and with pain (1.36±0.82, p=0.003). However, no significant difference was seen between those with swelling and pain. Clinical symptoms of DVT showed a good correlation with the accumulation ratio of platelet scintigram. (Fig. 2)

Posttreatment course

Nine cases with accumulation ratios of under 1.2 had no deterioration of clinical symptoms under the initial oral anticoagulant therapy, nor recurrence after discontinuation of it. In 30 cases with abnormal accumulation, thrombolytic and anticoagulant therapy remarkably improved the clinical symptoms and scintigraphic imaging which was performed six weeks later, showed remarkable regression of the accumulation ratio (Fig. 3). However, in 3 cases, in which the accumulation ratio remained over 1.2, pain due to DVT recurred during anticoagulant therapy, and required more intensive anticoagulant therapy for improvement of symptoms. These three cases have been followed now under INR of above 2.0 with no symptoms.

Discussion

Platelet scintigraphy offers potentially greater specificity for the detection of active DVT, because labeled platelets are incorporated directly into the thrombus and can detect thrombus activity.[9,10] Such activity generally shows a close correlation with clinical symptoms in acute DVT cases. Therefore, accumulation of platelets in this method appears to correlate well with the degree of clinical symp-

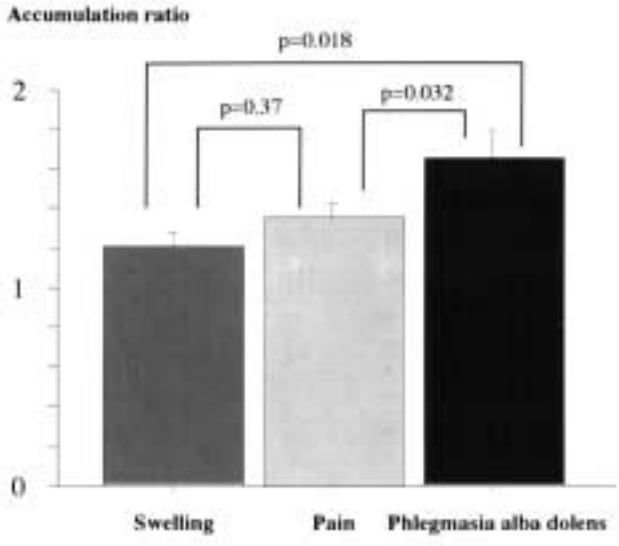

Fig. 2. Relationships between clinical symptoms and accumulation ratio.
The phlegmasia alba dolens group showed a significantly higher accumulation ratio (1.68±1.56) than swelling (1.22±0.78, p=0.002) and pain groups (1.36±0.82, p=0.003). Clinical symptoms due to DVT showed a good correlation with the accumulation ratio.

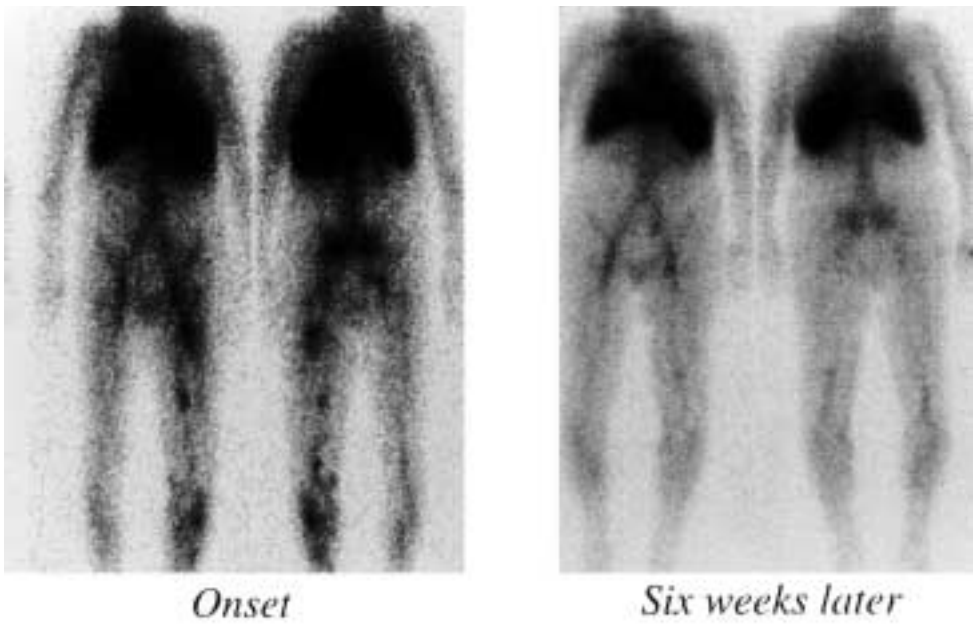

Fig. 3. A case presentation with abnormal accumulation ratio.
The case had severe phlegmasia alba dolens with high abnormal accumulation ratio of 3.0. The intensive thrombolytic and anticoagulant therapy remarkably improved the clinical symptoms, and scintigraphy performed six weeks later showed complete disappearance of abnormal accumulations.

toms. In this study, the ratio of accumulation in the abnormal region to that in the normal vein on the other side was used as an estimate in this semiquantitative analysis, and an abnormal accumulation ratio was defined as the value of over 1.2. Clinical symptoms of DVT showed a good correlation with abnormal accumulation ratios.

Some previous papers insisted that the sensitivity of duplex scanning for symptomatic DVT patients were over 90%.[9,12,13] However, we indicated that the sensitivity of duplex scanning was 82%, because it can not detect such small thrombi. Platelet scintigraphy can reveal thrombus activity, although it does not detect an inactive (chronic) thrombus.[5-7] The adherence and aggregation of platelets at DVT lesions or other vascular lesions are pathophysiological processes that depend primarily on the loss of integrity of the vascular endothelial lining. On acute phase of DVT, platelet scintigraphy can detect the adherence and aggregation of platelets even in the small thrombi. Therefore platelet scintigraphy can evaluate the activity of DVT that other methods such as venography and duplex scanning can not. Our results indicated no marked differences in diagnostic sensitivity of DVT between duplex scanning and platelet scintigraphy. However, platelet scintigraphy proved to be superior to duplex scanning in its ability to diagnose crural DVT, in which an early diagnosis is very difficult because of the unclear symptoms and the small thrombi.[11-13] Thus, platelet scintigraphy can prevent the proximal progression of crural DVT leading to the serious sequlae such as pulmonary embolism.

Though oral anticoagulant therapy is given routinely to patients who have had clinical episodes of DVT, DVT often recurred or worsened in spite of good anticoagulant control. The optimal duration and quantity of anticoagulant therapy remain controversial.[14-20] Platelet scintigraphy is very useful for evaluation of the effects of anticoagulant therapy, and its accumulation ratio can provide determination whether the further anticoagulant therapy is mandatory or not. Thus, platelet scintigraphy can also be very useful in evaluating the effect of anticoagulant therapy, despite some drawbacks such as it being expensive, troublesome, and emitting radiation.

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