

## In-111 platelets used in evaluation of emboli and thrombi in patients with cerebrovascular accident

N.Ö. KÜÇÜK,\* G. ARAS,\* E. İBİŞ, A. SOYLU,\* N. TAŞCILAR,\*\*  
N. YÜCEMEN\*\* and N. MUTLUER\*\*

*Departments of \*Nuclear Medicine and \*\*Neurology, Ankara University Medical Faculty, Ankara, Turkey*

Studies with In-111 platelets were conducted to evaluate pulmonary embolus, deep vein thrombus and cardiac thrombus. This study aimed to evaluate active thrombi and possible new emboli in patients with cerebrovascular accident (CVA) in the first 24 hours by using autologous In-111 platelets. Twenty-five patients were included in the study. Carotid artery thrombi observed in 10 patients with this technique were confirmed by Doppler ultrasonography. Intracranial thrombi appearing in 3 cases were verified by X-ray computed tomography (CT). Scintigraphy of 8 patients who showed findings suggesting CVA in CT revealed no abnormal accumulation. This was attributed to the possibility that they were small in size, deep in location and/or were also quite aged. Abnormal accumulations observed in the lungs of 3 patients and in the mediastinum and pelvis in one patient were verified by other radiological methods. In-111 platelet study was found to be useful in patients with CVA to evaluate the active thrombi and possible emboli in the early period before clinical symptoms appeared.

**Key words:** cerebrovascular accident, thrombus, emboli, In-111 platelets

### INTRODUCTION

ACUTE CEREBROVASCULAR ACCIDENT (CVA) is one of the most common neurological illnesses. Causes of CVA are ischemia in 70%, intracerebral hematoma in 20% and subarachnoid hemorrhage in 10% of all cases.<sup>1</sup> The most common cause of ischemic CVA is atherosclerotic changes developed in small or large vessels. Multifocal infarcts are observed in the background. In these patients, acute thrombi increase morbidity and mortality because they may cause subsequent new emboli.<sup>2</sup> Follow up of these newly developed emboli may be very difficult because the general condition of these patients is impaired and their symptoms cannot be evaluated definitely. There is not a routine nuclear medical method to diagnose and monitor active thrombi and subsequent emboli.<sup>3</sup>

Pulmonary emboli,<sup>4,5</sup> deep vein thrombosis<sup>6,7</sup> and car-

diac thrombi<sup>8,9</sup> were evaluated with In-111 platelet studies, and a high rate of success is reported with this method.

The objective of this study is to determine active thrombosis and subsequent emboli with autologous In-111 platelets early in patients with ischemic CVA.

### MATERIALS AND METHOD

A total of 25 patients (10 males and 15 females) who were in follow-up in Ankara University Faculty of Medicine Department of Neurology with a diagnosis of acute ischemic CVA and whose ages were between 55 and 81 (mean  $67 \pm 8$ ) were included in the study. In the first 24 hours after the CVA autologous platelets were labeled with In-111 (Table 1).<sup>10</sup> 4 hr, 24 hr and if necessary later images were taken with GE Starcam 3200 and Starcam 4000i SPECT cameras and a medium energy collimator at 87, 184 and 256 keV peaks at 20% window intervals. Whole body scans were performed with a  $128 \times 512$  matrix and static images were obtained with a  $256 \times 256$  matrix. Cranial tomographies (CT) and Doppler ultrasonography (USG) were performed in addition to the routine tests.

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For reprint contact: N. Özlem Küçük, M.D., Ankara Üniversitesi Tıp Fakültesi, Nükleer Tıp Anabilim Dalı, 06100 Cebeci, Ankara, TÜRKİYE.

**Table 1** Flow sheet diagram illustrating the labeling of platelets with indium-oxine

### I. COMPLEX FORMATION

- a. 0.5–1.0 mCi In-111 chloride  
+  
50 µg oxine in 50 µl absolute ethanol  
+  
4 ml ACD : saline (1 : 7 V/V)
- b. Adjust to pH 6.5

### II. CITRATED PLASMA

- a. 18 ml/ whole blood  
+  
2 ml 3.8% sodium citrate
- b. Centrifuge at  $180 \times g$  for 15 min
- c. Withdraw supernatant
- d. Centrifuge at  $1800 \times g$  for 7 min
- e. Withdraw and save supernatant

### III. CELL SEPARATION AND LABELING

50 ml/ whole blood ACD (6 : 1 V/V)

1

Platelet-rich plasma

2

Platelet Button

3

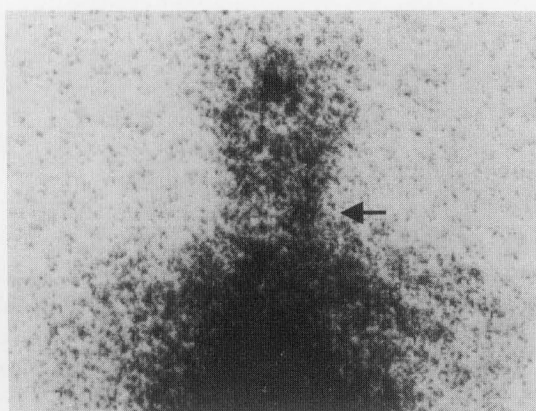
Labeled Platelets

4

Labeled Platelet Injectate

PPP: Platelet poor-plasma

- a. Centrifuge at  $180 \times g$  for 15 min
- b. Remove supernatant
- c. Discard red cells and white cells
- a. Centrifuge at  $1800 \times g$  for 7 min
- b. Withdraw and save PPP
- c. Wash with 4 ml ACD: saline to remove contaminating plasma
- d. Centrifuge at  $1800 \times g$  for 7 min
- e. Discard wash solution
- a. Add In-111 oxine complex from step 1b
- b. Incubate 20 min at room temperature
- c. Centrifuge at  $1800 \times g$  for 7 min
- d. Withdraw supernatant
- a. Wash with 4 ml PPP from step 2b to remove loosely bound In-111
- b. Centrifuge at  $1800 \times g$  for 7 min
- c. Withdraw supernatant
- d. Resuspend in 4 ml citrated plasma from step IIe



**Fig. 1** Left carotid uptake in a patient who had thrombosis in left carotid artery.

### RESULTS

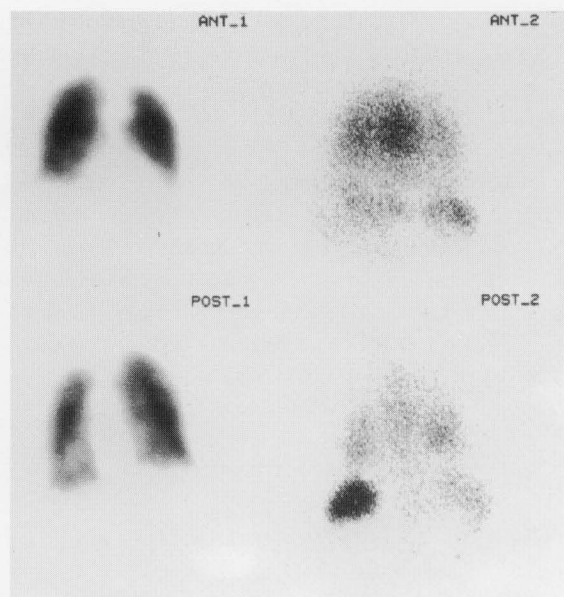
This study was conducted to show thrombi and emboli in the acute phase in patients who had been diagnosed with CVA. Pathological activity accumulation in the carotid artery was detected in 10 patients as thrombi by Doppler USG (Fig. 1). Intracranial abnormal uptake in 3 cases was revealed as thrombi by X-ray CT. No abnormal activity was found in 8 cases other than in physiological accumulation areas. But findings consistent with CVA were present in their CT scans. SPECT images revealed the same results but no additional information was obtained. Multiple pulmonary uptake was present in 3 cases and shown to be pulmonary emboli with Tc-99m MAA lung perfusion scintigrams (Figs. 2, 3). One of these patients showed activity accumulation in the right iliac region (Fig. 4), which was confirmed by Doppler USG. Transesophageal Doppler echography verified the presence of an active thrombus in a patient with mediastinal pathological activity. The results of In-111 platelet scintigraphy revealed active thrombi and/or emboli in 17 out of a total of 25 CVA cases.



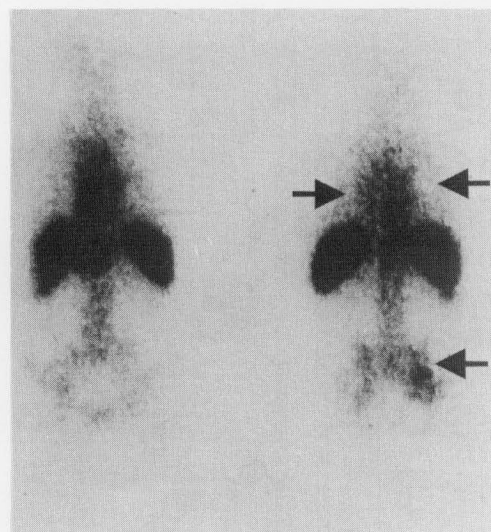
**Fig. 2** Thoracic diffuse uptake in a patient who had multiple pulmonary embolism (anterior and posterior whole body images).

### DISCUSSION

Autologous platelets labeled with In-111 are used<sup>11,12</sup> in order to diagnose various thromboembolic diseases such as deep vein thrombosis<sup>6</sup> cardiac thrombus<sup>8,13</sup> and pulmonary embolism<sup>4,14</sup> and its sensitivity has been reported to be quite high.<sup>15</sup> After the first report of Thakur et al.<sup>5</sup> in 1976 on imaging thrombi, Fax et al.,<sup>8</sup> Clark et al.<sup>4</sup> and Verheugt et al.<sup>9</sup> used In-111 platelets in possible pulmonary emboli cases and in coronary artery thrombi with high success rates. Ezekowitz et al.<sup>6</sup> concluded that the results of In-111 platelet scintigraphy were in good agreement with those of contrast venography in patients who had undergone orthopedic operations, specificity being 97% and sensitivity 92%. CVA risk increases substantially after 40 years of age and generally takes a fatal course. A major cause of CVA is ischemic events, and subsequent new emboli caused by active thrombi increase mortality and morbidity.<sup>2</sup> In this study, thrombi and emboli are evaluated in patients with acute CVA by using In-111 labeled autologous platelets. The results correlated well with those of other radiological techniques. The reasons for no abnormal activity in these patients were



**Fig. 3** Thoracic diffuse uptake of In-111 and Tc-99m MAA perfusion scintigraphy in a patient who had multiple pulmonary embolism. Ant 1: Anterior Tc-99m MAA images, Ant 2: Anterior In-111 platelet images, Post 1: Posterior Tc-99m MAA images, Post 2: Posterior In-111 platelet images



**Fig. 4** Thoracic and pelvic uptake in a patient who had multiple pulmonary embolism (anterior and posterior whole body images).

thought to be the size of thrombi which might be relatively small compared to the limits of scintigraphic resolution and/or deep localization. The general condition of the patients are usually quite bad in the early phase of CVA and this limits the use of In-111 platelet scintigraphy for such cases, but detection of active thrombi and emboli is crucial for these patients in diagnosis and treatment planning. Although CT is a valuable method routinely used in

the diagnosis of CVA, the rates of morbidity and mortality are closely related to newly forming emboli and active thrombi<sup>1,2</sup> which are not clearly demonstrated by CT or any other technique. Another advantage in using In-111 platelets is that whole body scanning is performed which may demonstrate pulmonary emboli and peripheral thrombi in addition to cerebrovascular thrombi. This may help in planning therapy and subsequent prognosis. Because of the limited number of patients we have studied with SPECT, no additional information was obtained.

In conclusion, In-111 platelets may be useful in establishing the presence of active thrombi and subsequent emboli early in patients with ischemic acute CVA.

## ACKNOWLEDGMENTS

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