Technetium-99m-Red Blood Cell Scintigraphy in the Localization of Nonenteric Hemorrhage

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Rapid detection and localization of the bleeding site(s) are important factors in successful management of actively bleeding patients. Technetium-99m-red blood cell imaging is a sensitive, noninvasive modality commonly used for localization of gastrointestinal bleeding. Outside the gastrointestinal tract, experience with this technique has been limited. In this report, we present three cases of nonenteric bleeding successfully located using ^{99m}Tc red blood cells. The current literature regarding the scintigraphic localization of nonenteric bleeding is reviewed and discussed.

Key Words: nonenteric hemorrhage; subcutaneous hematoma; intramuscular hematoma; radionuclide scintigraphy; technetium-99m-red blood cell scintigraphy

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Although scintigraphic techniques for the location of bleeding sites have been most widely employed for occult gastrointestinal hemorrhage, they are, in principle, equally applicable to bleeding at any other site. By making use of ^{99m}Tc-labeled red blood cells (RBCs) which persist within the intravascular compartment for up to 24 hr, slow or intermittent bleeding may be demonstrated when contrast radiographic studies are unsuccessful or inappropriate. We present three cases of soft tissue and/or intramuscular hemorrhage in which ^{99m}Tc-RBC scintigraphy proved efficacious.

METHODS AND CASE REPORTS

Patient One

A 61-yr-old female with a history of rheumatic heart disease and mitral valve replacement presented with confusion following several falls. Physical examination disclosed severe congestive cardiac failure. A large ecchymosis (15 × 15 cm) was present on her right thigh and buttock. Smaller ecchymoses were also noted on the trunk. Medications on admission included Warfarin, Digoxin, Lasix, Slow K, Amiloride and Nortryptiline. Hemoglobin was 10.6 gm/dl, hematocrit 31.2%, white blood cell count 5.2 × 10^9/liter and platelets 152 × 10^9/liter. Anticoagulation was converted to heparin. Over the next several days her hematocrit dropped progressively, while the right thigh became increasingly swollen and tense. Radionuclide imaging with ^{99m}Tc-red blood cells (using a modified in vitro method) was undertaken to detect active bleeding in the thigh or elsewhere. Scintigraphy 1 hr postinjection showed a large cold defect on the lateral aspect of the right mid-thigh, consistent with hematoma having accumulated prior to tracer injection. Images obtained 24 hr later showed tracer activity within this region, compatible with subsequent active bleeding (Fig. 1). Angiographic embolization therapy was scheduled, but the patient died after a sudden respiratory arrest. At necropsy a large hematoma containing old and fresh blood was found in the right thigh.

Patient Two

A 92-yr-old female with a history of adenocarcinoma of the colon and Parkinson's disease was admitted for suspected bleeding into the right upper extremity associated with swelling and pain, but no history of prior trauma. Plain radiographs were negative for fracture. On admission, swelling and ecchymoses were noted over the right arm and smaller lesions were noted over the lower extremities. A 6-cm abdominal aortic aneurysm, as well as smaller aneurysms of the iliac arteries, was present. Laboratory investigations revealed a hematocrit of 22.7%, white blood cell count of 5.1 × 10^9/liter, platelet count of 122 × 10^9/liter, prothrombin time of 14.6 sec (reference range 11.3–13.2 sec.) and partial thromboplastin time of 24.7 sec (20.9–28.2 sec). Serum fibrinogen was depressed at 125 mg/dl (189–350 mg/dl). Scintigraphy with ^{99m}Tc-labeled red blood cells was undertaken (using modified in vitro method) and revealed a focus of abnormal tracer activity in the mid-portion of the right upper arm consistent with active hemorrhage (Fig. 2). Due to the patient's poor general condition, conservative management was instituted. She was transfused with packed red blood cells, and a pressure bandage was applied to the right arm. The ecchymosis spread into the right breast and down the right flank but the bleeding stopped after several days and she was discharged with a hematocrit of 29.2%.

Patient Three

A 49-yr-old white male with a history of alcoholism and hepatic cirrhosis was hospitalized for severe anemia, right back and flank pain. Two weeks prior to admission, he had fallen down a flight of stairs. On physical examination, he manifested ascites, jaundice, muscle wasting and spider angiomas. A large ecchymosis was noted over the right scapula extending to the lateral chest wall. Admission hematocrit was 12.5%; platelet count was 220 × 10^9/liter. The prothrombin time was 19.4 sec (11.3–13.2 sec); par-

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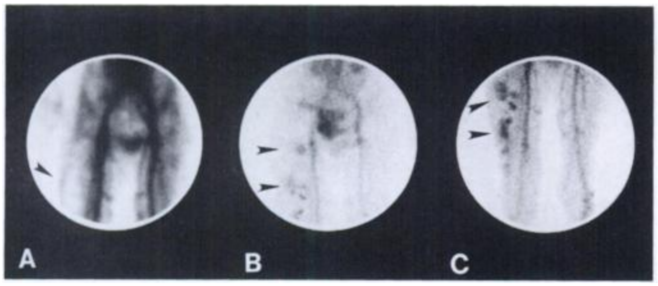

FIGURE 1. Anterior pelvis and proximal lower extremities scintigram after red-cell labeling with ^{99m}Tc. (A) Image at 60 min shows a large cold defect in the lateral aspect of the mid-right thigh (arrow) consistent with hematoma. At 24 hr, (B) and (C), multiple foci of increased uptake are identified within large hematoma compatible with active bleeding.

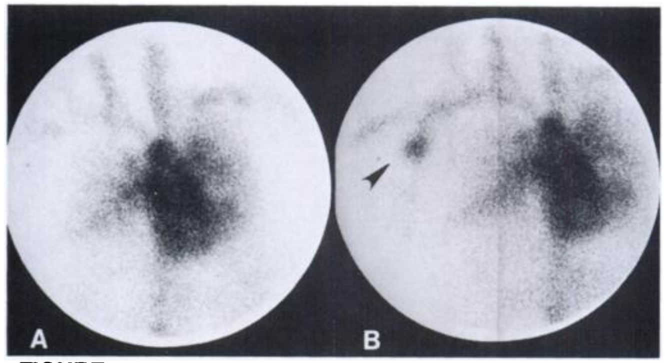

FIGURE 3. Anterior scintigram of chest after red-cell labeling with ^{99m}Tc. (A) At 5 min postinjection, there is normal blood-pool activity. (B) At 60 min, there is abnormal collection of tracer in the right chest (arrow) at the site of bleeding.

tial thromboplastin time was 53.1 sec (20.9–28.2 mg/dl). A computed tomographic scan of the chest demonstrated marked asymmetric enlargement, with evidence of hemorrhage in the right paraspinous muscles extending to the lower chest and into the abdominal wall.

The patient was transfused with packed red blood cells and fresh frozen plasma, which increased the hematocrit to 32%. A further episode of symptomatic anemia (hematocrit 24.5%) and extension of the dorsal hematoma led to ^{99m}Tc-RBC scintigraphy (using in vitro cell labeling method) to locate sites of active bleeding. This revealed several foci of RBC activity in the right posterolateral chest wall (Fig. 3, 4). Selective lateral thoracic and subscapularis arteriograms showed lateral displacement by a large hematoma in the right lateral chest wall without active bleeding. The right subscapularis and a branch of the right lateral thoracic artery were embolized.

DISCUSSION

The use of radioactive tracers for the evaluation of bleeding began in the late 1970's when Alavi et al. first demonstrated active gastrointestinal bleeding lesions using ^{99m}Tc-sulfur colloid (^{99m}Tc-SC) (*1,2*). The use of ^{99m}Tc-red blood cells (^{99m}Tc-RBC) has now largely replaced ^{99m}Tc-SC. Normally, activity is seen within the vasculature and organ blood pools, resulting in higher background radioactivity. Extravasation of red cells results in a focal "hot spot." The half life of ^{99m}Tc and its retention in red blood cells in the circulation permits imaging for up to 24-hr postinjection. This is an advantage over ^{99m}Tc-SC given that most bleeding occurs intermittently (*3,4*). Labeling of RBC may be done in vitro (Case Three), in vivo, or by a combined in vivo/vitro technique (Cases One, Two) (*5,6*).

Although radionuclide studies are well established for location of gastrointestinal bleeding, their use for detection of bleeding sites outside the gastrointestinal tract has not been widely employed. Nevertheless, there are reports of successful identification of bleeding sites almost everywhere in the body. Bateman et al. successfully utilized ^{99m}Tc-RBC scintigraphy to detect occult pericardial hemorrhage early after open heart surgery, and subsequently, in work with dogs, found this technique to be 100% sensi-

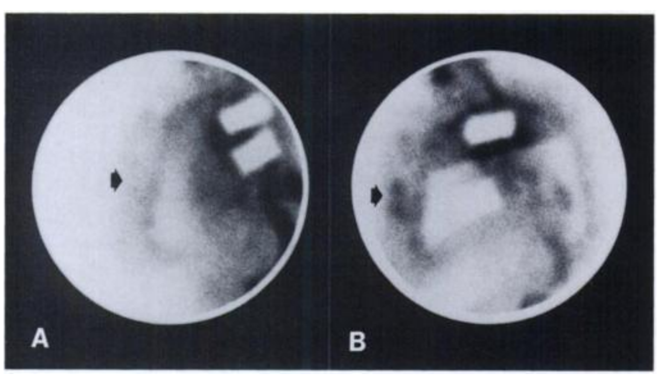

FIGURE 2. Anterior right-upper extremity scintigram after RBC labeling with ^{99m}Tc. (A) Five minutes postinjection, normal blood-pool activity is identified. At approximately 1 hr postinjection (B) a focus of accumulating activity was noted in the mid-portion of the right-upper arm (arrow) consistent with hemorrhage. Lead shields are placed over the chest.

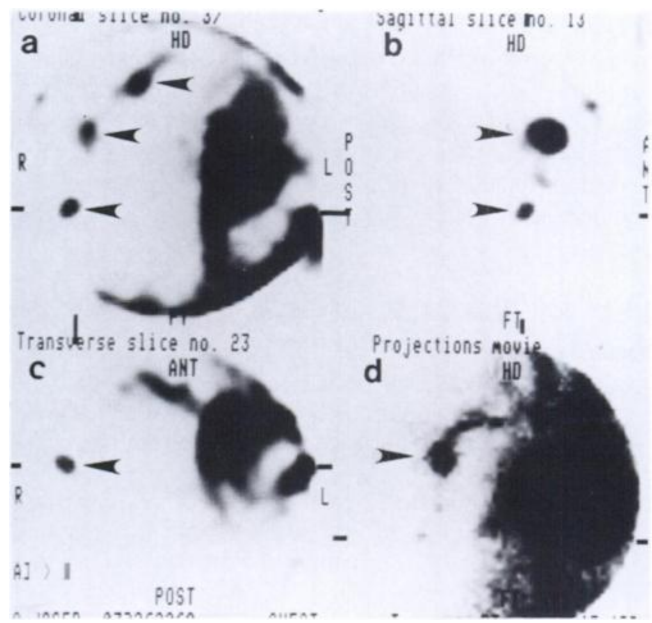

FIGURE 4. SPECT images (a: coronal, b: sagittal, c: transverse, d: projection) identify several foci of increased activity in the right lateral chest wall (arrows), consistent with active bleeding.

TABLE 1
Scintigraphic Detection of Nonenteric Bleeding

Site of hemorrhage	No. of cases	Findings	Agent	Reference
Abdomen and intraperitoneal (nongastrointestinal)	1	Bleeding into pancreatic pseudocyst in head of pancreas	^{99m}Tc RBC	Ellison et al. (*32*) 1987
	1	Mesenteric hemorrhage in a hemophilic patient after a self inflected injury	^{99m}Tc-RBC	Orzel et al. (*9*) 1986
	1	Photopenic defect in upper portion of the spleen with abnormal intraperitoneal activity due to splenic fracture and free intraperitoneal bleeding	^{99m}Tc-SC	Amster et al. (*26*) 1983
	1	Extra-hepatic activity secondary to mesenteric bleeding after blunt trauma	^{99m}Tc-SC	Nagle et al. (*27*) 1984
	1	Extravasation of radiotracer within the large hematoma in the left anterolateral abdominal wall in a patient with chronic anticoagulant therapy	^{99m}Tc-RBC	Bunker et al. (*29*) 1983
	1	Intraperitoneal bleeding into Morrison's pouch from a hepatocellular carcinoma	^{99m}Tc-RBC	Czarnecki (*30*) 1986
Liver	1	Activity in the gallbladder caused by bleeding varices in a patient with haemocromatosis	^{99m}Tc-Albumin	Miskowiak et al. (*28*) 1979
Lung	1	Diffuse lung uptake in a patient with pulmonary hemorrhage and idiopathic pulmonary hemosiderosis	^{99m}Tc-RBC	Miller et al. (*12*) 1979
	1	Tracer collection in the RUL due to necrotizing hemorrhagic pneumonia	^{99m}Tc-RBC	Winzelberg et al. (*13*) 1981
	1	Activity right upper chest in the area of bronchogenic carcinoma	^{99m}Tc-SC	Winzelberg et al. (*14*) 1981
	1	Activity right hemithorax consistent with intrapulmonary bleeding in the area of oat cell carcinoma	^{99m}Tc-SC	Sanchez et al. (*15*) 1984
Intrathoracic	1	Spontaneous hemothorax in a patient with chronic oral anticoagulant therapy	^{99m}Tc-SC	Taillefer et al. (*20*) 1981
	1	Activity left pleural space from a bleeding intercostal artery after trauma	^{99m}Tc-SC	Winzelberg et al. (*14*) 1981
Heart/pericardium	12	Increased blood-pool activity outside the cardiac chambers, some of the cases presented abnormal activity in the right hemithorax secondary to pericardial hemorrhage	^{99m}Tc-RBC	Bateman et al. (*7*) 1984
	5	"Halo" of abnormal radioactivity surrounding the ventricles in pericardial hemorrhage	^{99m}Tc-RBC	Bateman et al. (*7*) 1984
	1	Collection of labeled RBC into intrathoracic hemorrhage from the anastomotic site of a coronary artery bypass graft	^{99m}Tc-RBC	Orzel et al. (*31*) 1986
Joints	4	Increased vascularity in actively bleeding joints; persistent but less marked increased activity in chronic hemarthroses	^{99m}Tc-RBC	Green et al. (*11*) 1981
Extremities	1	Hematoma right thigh in a patient with hemophilia	^{99m}Tc-RBC	Green et al. (*11*) 1981
	1	Hematoma and active bleeding in the left thigh and both lower legs after trauma	^{99m}Tc-RBC	Shah et al. (*24*) 1979
	1	Increased accumulation in the upper third of the right thigh after right femoral artery angiography	^{99m}Tc-RBC	Gips et al. (*22*) 1986
Buttocks	1	Bilateral hemorrhage into gluteal muscles in paraplegic on anticoagulation	^{99m}Tc-RBC	Rosenbaum et al. (*10*) 1986

TABLE 1
Continued

Site of hemorrhage	No. of cases	Findings	Agent	Reference
Breast	1	Traumatic hemorrhage into left breast	^{99m}Tc-RBC	Kahn et al. (*25*) 1987
Retroperitoneal	1	Increased activity right peritoneal hematoma with active bleeding	^{99m}Tc-RBC	Hardoff et al. (*18*) 1991
Pelvis	1	Right rectus sheath hematoma	^{99m}Tc-RBC	Moreno et al. (*21*) 1989
Thyroid	3	Early prompt accumulation on dynamic flow studies in sites of hemorrhage into follicular adenoma of the thyroid	^{99m}Tc-TcO_4	Kim et al. (*19*) 1983
Vascular structures	1	Early abnormal activity in the pelvic region simultaneously with iliac artery visualization in a patient with ruptured aneurysm of the abdominal aorta	^{99m}Tc-TcO_4	Bunko et al. (*23*) 1978

RUL = right upper lobe; TcO_4 = pertechnetate.

tive and 90% specific when the volume of loculated blood was 30 cc or more (*7,8*). The use of ^{99m}Tc-labeled RBC has also been proposed as the method of choice in determining the activity of internal bleeding in patients with hemophilia and other disorders of coagulation, or in those receiving long-term anticoagulation therapy, where invasive techniques could be dangerous (*9,10*). In hemophilic arthropathy, analysis of quantitative blood pool scintigrams has been used to evaluate hemorrhagic joint effusion in conditions such as active versus chronic hemarthrosis, preoperatively and postoperatively in patients undergoing synovectomy or placement of a prosthetic device (*11*). There has also been a growing use of the scintigraphic technique for the detection of pulmonary hemorrhage, especially in patients with massive hemoptysis where the use of fiberoptic bronchoscopy may be limited by large quantities of blood in the trachea. Bronchial artery angiography can then be employed more selectively, thus reducing its inherent risks (*12–15*). Actively bleeding lesions have also been identified in breast, intramuscular structures, retroperitoneum and many other sites, although the majority are single case reports (Table 1).

The advantages of the scintigraphic technique are: high sensitivity for slow and/or intermittent hemorrhage, high specificity, ease and rapidity of performance, noninvasiveness, avoidance of iodinated contrast media and the ability to repeatedly screen large regions (the entire body, if necessary) for active bleeding (*5,6*). In unstable patients, this approach can guide selective angiography when therapeutic embolization is considered.

Computed tomography, ultrasound and conventional radiographic studies are important in the anatomic identification of soft-tissue masses and fluid collections. Nevertheless, their ability to determine the presence of active hemorrhage is limited (*10*). The widely accepted method for the localization of bleeding is contrast angiography (CA). In the gastrointestinal tract, for example, when the bleeding rate exceeds 1 ml/min, CA will detect gastrointestinal bleeding in 65% of patients (*6*). This procedure is invasive, technically challenging, expensive and can be falsely negative if there is slow or intermittent bleeding (*16*). There have been no large scale studies directly comparing CA with scintigraphy in detecting bleeding outside the gastrointestinal tract.

The technique used for the evaluation of nonenteric bleeding is similar to that for gastrointestinal bleeding, with imaging directed to the region(s) of concern. Unlike angiography, scintigraphy is well suited to whole body imaging for the detection of multiple and/or occult bleeding sites. SPECT images may be helpful when anatomic localization is difficult on planar views (e.g., active bleeding in the region of the heart). Attention to the pattern and intensity of activity over time is necessary in order to avoid false-negative or false-positive studies. Potential pitfalls in image interpretation are vascular anomalies (e.g., aneurysm, hemangiomas, varicosities and vascular grafts). In the pelvis, activity in the left ovarian vein, uterine blush (during menstruation) or penile activity, can be misinterpreted as active bleeding (*17*).

A bleeding episode can be managed more safely if the clinician is able to assess whether or not bleeding is continuing. We have presented three cases where active bleeding was detected scintigraphically in the right thigh, right upper extremity and right paraspinal muscle. In the third case, scintigraphy succeeded in demonstrating acute bleeding when contrast angiography failed. We believe that ^{99m}Tc-RBC scintigraphy should be more widely employed as a complementary, noninvasive method for detection of active extra-gastrointestinal bleeding. In addition, it may have a role to guide other invasive, diagnostic and/or therapeutic procedures.

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