The Use of Heparin to Facilitate Bleeding in Technetium-99m RBC Imaging

TO THE EDITOR: Radionuclide imaging using technetium-99m red blood cells ([^{99m}Tc]RBC) and [^{99m}Tc]sulfur colloid ([^{99m}Tc]SC) is an important diagnostic tool for evaluating acute active gastrointestinal (GI) bleeding (*1–4*). In cases of chronic GI blood loss, detection by nuclear medicine methods can often be difficult. There has been one reported case on the pharmacologic use of heparin as a diagnostic aid in nuclear medicine blood loss studies (*5*). We have encountered a case in which the use of heparin helped to localize the site of gastrointestinal blood loss.

A 36-yr-old white woman with a long history of recurrent GI bleeding presented with melena and a hemoglobin (Hg) of 6.6 g per deciliter. The patient required 60 units of packed red blood cells during the 18 mo prior to admission. Multiple extensive workups (including colonoscopies, endoscopies, arteriography, small bowel series, intraoperative endoscopy, radionuclide Meckel's scan and radionuclide blood loss scans) had been performed. A [^{99m}Tc]RBC scan obtained upon admission could not identify the source of bleeding. Because of the risk involved with further transfusions and the possibility of future hemorrhage, it was decided that a provocative study be performed to identify the source of bleeding.

Prior to the examination the patient's prothrombin time (PT) and activated partial thromboplastin time (APTT) values were within normal limits at 13.3 sec (normal 11.4–13.1) and 22 sec (normal 22–31), respectively. Because the patient was clinically stable and had normal coagulation values, the decision to use heparin was made. The patient was given a loading dose of 6,000 units (U) of heparin intravenously (i.v.), followed by 1,000 U i.v. per hour. The patient was closely monitored in the nuclear medicine department. An APTT value obtained 4 hr after the i.v. infusion of heparin was begun was 35 sec.

A radionuclide GI blood loss study was performed using 21.6 mCi (799.2 MBq) of ^{99m}Tc-labeled RBC. Gamma camera images were obtained every 15 min for the first 2 hr and at 3, 4, and 24 hr postdose. The images revealed an early persistent band of increased activity in the upper mid-abdomen (Fig. 1). This activity varied in intensity, but not location. The i.v. infusion of heparin was discontinued after 6 hr once the site of bleeding was confirmed. The patient showed no signs of acute hemorrhage and several follow-up PT and APTT values were within normal limits. In order to better localize the involved region, the patient drank 2.0 mCi (74 MBq) of [^{99m}Tc]SC in water. Sequential gamma camera images were obtained and revealed a segment of proximal jejunum which corresponded to the area of increased activity seen on the labeled RBC blood loss study (Fig. 2). A superior mesenteric angiogram with a subselective jejunal injection was performed. The exam revealed a non-gas filled small bowel segment with prominent staining in the left hemiabdomen. This segment corresponded to the area of increased activity on the blood loss study.

The patient was taken to surgery and 45 cm of proximal jejunum were resected. Pathology reported telangiectatic submucosal vessels with focal areas of hemorrhage. The patient has subsequently remained clinically stable with no episodes of melena.

The pharmacologic use of heparin can be an important diagnostic aid in cases of chronic GI bleeding in which a source cannot be localized by conventional methods. It is important to detect the site of bleeding so that appropriate steps can be performed by the clinician. This may allow the patient to avoid the risk of further transfusions and the possibility of future hemorrhage. The risks and benefits should

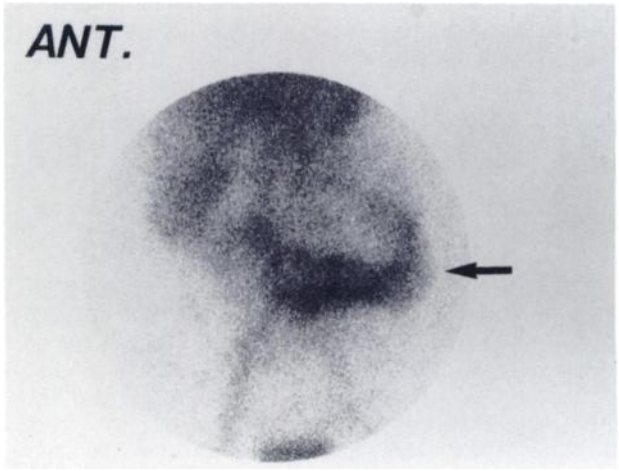

FIGURE 1
Postheparin bleeding scan showing band of increased activity in the upper mid-abdomen 30 min after the administration of [^{99m}Tc]RBC.

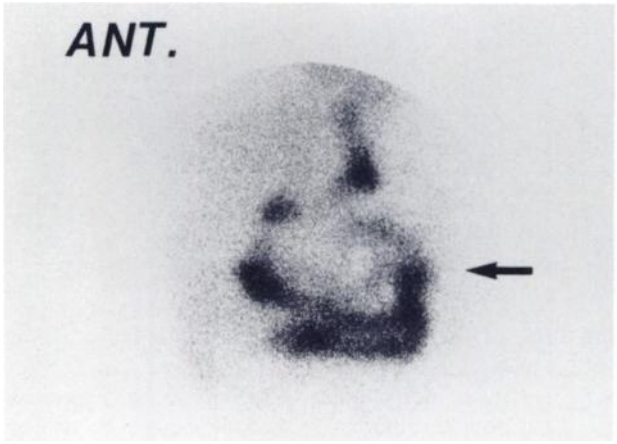

FIGURE 2
Gastric emptying study performed with 2.0 mCi [^{99m}Tc]SC in water showing a segment of proximal jejunum corresponding to the area of increased activity on the blood loss study.

be carefully discussed with the patient and clinician. Close monitoring of the patient is essential, as well as having protamine sulfate (heparin antagonist) and blood available if needed.

The decision to use protamine sulfate is based on the presence of moderate to severe uncontrollable bleeding in a patient receiving heparin. The coagulation studies should be correlated with the clinical condition of the patient and protamine sulfate should not be administered solely on the basis of abnormal laboratory values. Because our patient showed no signs of hemorrhage while receiving the heparin infusion, the administration of protamine sulfate was not necessary. We do not recommend the routine use of protamine sulfate due to its side effects which include bradycardia and hypotension and the fact that heparin is cleared rapidly from the circulation.

If necessary, protamine sulfate should be administered by slow i.v. injection in doses not to exceed 50 mg in any 10 min period. The dose of protamine sulfate is calculated by determining the total dose of heparin administered during the previous 3 to 4 hr with each mg of protamine sulfate neutralizing 90–100 USP units of heparin.

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Uptake of Technetium-99m Diphosphonate by Metastatic Large Cell Carcinoma of the Lung

TO THE EDITOR: Although uptake of technetium-99m (^{99m}Tc) phosphate bone-scanning agents by noncalcified hepatic metastases of a number of primary malignancies has previously been described (*1–3*), we believe this to be the first reported case associated with large cell carcinoma of the lung.

A 50-yr-old female presented with a 2-mo history of cough and weight loss. Significant findings on physical examination included decreased breath sounds in the right upper chest and a slightly tender 14 cm liver. Chest roentgenogram revealed a right upper lobe mass with lobar atelectasis. Bronchoscopy and biopsy yielded a diagnosis of undifferentiated large cell carcinoma.

Neurologic signs prompted computed tomography of the brain which demonstrated a solitary posterior fossa mass. This was resected and shown to be metastatic large cell carcinoma.

At this time the patient underwent radiotherapy of the right upper lobe mass. Seven months after diagnosis the patient developed a submental soft tissue mass. Biopsy showed metastatic disease. Liver function studies revealed elevation of all liver enzymes, with normal serum bilirubin, calcium and phosphate.

Technetium-99m methylene diphosphonate ([^{99m}Tc]MDP) bone scan was performed (Fig. 1A,B). This revealed a large ovoid mass with a rim of radiotracer uptake and a prominent photopenic center. The mass occupied most of the right lobe of the liver, with inferior displacement of the right kidney. Asymmetric uptake of phosphonate was noted between the medial aspect of the ischia, but was not felt to represent metastatic disease. Uptake in the remainder of the skeleton was unremarkable. The bone scan was compared with other scans performed from the same aliquot. All showed normal biodistribution of activity.

Subsequent computed tomography of the abdomen (Fig. 1C) confirmed a 15-cm diameter lesion in the right lobe of the liver, with an inhomogeneous low attenuation center surrounded by an enhancing rim. An inhomogeneous mass was also seen in the right adrenal gland, representing metastatic disease.

The patient is currently receiving palliative care.

Localization of ^{99m}Tc-phosphate compounds within hepatic metastases from colonic adenocarcinoma (*2,3*), oat cell carcinoma of the lung, breast carcinoma, malignant melanoma, and squamous cell carcinoma of the esophagus has previously been described (*2*). In addition, focal uptake by cholangiocarcinoma (*3*) has been described.

This case of uptake within metastatic large cell carcinoma of lung has several interesting features. Uptake of radiotracer appeared to be isolated to the radiographically enhancing rim. Lyons et al. (*4*) described a case of [^{99m}Tc]pyrophosphate localization in a liver due to massive necrosis. In this case the exclusion of radiopharmaceutical from the central necrotic portion is most likely due to nonperfusion. Localization within the ischemic transition zone between viable tumor and frankly necrotic tissue is postulated.

No uptake of radiotracer could be demonstrated in the right adrenal or submental metastases, suggesting that tracer localization may be more dependent on ischemia than on tumor histology. The precise point of accumulation of phosphonate may be within mitochondrial calcium accumulations, which occur following cell membrane disruption (*5*). Phosphate binding in areas of high phophatase enzyme concentration (*6*) and ion exchange between intracellular calcium phosphate and phosphate bone-scanning agents (*7*) have been postulated as possible mechanisms of uptake.

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