Indium-111 WBC Imaging—False-Positive in a Simple Fracture

TO THE EDITOR: Indium-111-labeled leukocyte ([^{111}In] WBC) scanning has proven useful in investigation of acute infection (*1–3,7,10*). With increased usage, a number of noninfectious processes including noninfected hematomas (*4*), intramuscular injection sites (*7*), deep venous thrombosis (*6*), noninfectious arthritis (*5,7*), various tumors with skeletal metastatis (*1,8*), and noninfected open fractures (*5*) have been reported to show localized uptake. We recently evaluated a patient in whom intense activity on the indium WBC scanning was present in a simple clavicular fracture.

A 20-yr-old white woman involved in motor vehicle accident sustained a number of injuries including multiple complex pelvic fractures and a simple right clavicular fracture. Three weeks after the injury, an [^{111}In]WBC scan was performed to evaluate a fever of unknown origin and suspected pelvic abscess or osteomyelitis of the pelvis. On the anterior chest image at 24 hr following the infusion of 500 μCi of [^{111}In]WBC, an area of increased activity (Fig. 1) was noted over the right clavicle. The pelvic fracture showed only mild increase in activity. A right subclavian venous catheter had been in place for eight days but had been removed 3 days earlier. It was felt that the activity represented probable osteomyelitis of the clavicle, or possibly an abscess or septic thrombophlebitis. There was no swelling, tenderness, or discoloration to indicate a hematoma. Chest x-ray revealed no signs of osteomyelitis—instead there was a normal healing non-displaced clavicular fracture (Fig. 2). A contrast subclavian venogram was performed which was normal. Percutaneous aspirations of the suspicious area were performed, but only a small volume (<1 cc) of serous fluid could be aspirated. Aerobic and anaerobic cultures were negative. A gallium-67 scan revealed localization in the fracture site consistent with normal healing bone, but there was no soft-tissue uptake. Subsequent radiographs showed normal healing of the fracture.

Indium-111 WBC scanning is now the radionuclide test of choice in the evaluation of suspected acute infection, particularly abscesses (*1,2,7,10*). Sensitivities as high as 100% (*2, 10*) and specificities up to 97% and 98% have been reported (*1,10*). Unfortunately, a variety of noninfective causes of localization of [^{111}In]WBC have been described. These include inflammatory causes such as active rheumatoid arthritis (*7*), bland thrombophlebitis (*6*), localized collections of blood such as bone marrow biopsy sites or bone graph donor sites (*3*), and sites of arterial or venous puncture probably due to surrounding hematomas may show local activity (*1,4*). Deep injection sites, even when noninfected, may show increased activity as well (*7*). Rarely, metastatic tumor deposits from breast cancer, prostate cancer, Hodgkin's disease and muco-

FIGURE 1
Anterior chest image of In-WBC scan shows markedly increased activity in mid-right clavicle. The area of mild increased uptake superior and medial to fracture site probably represents inflammation from previous intravenous line.

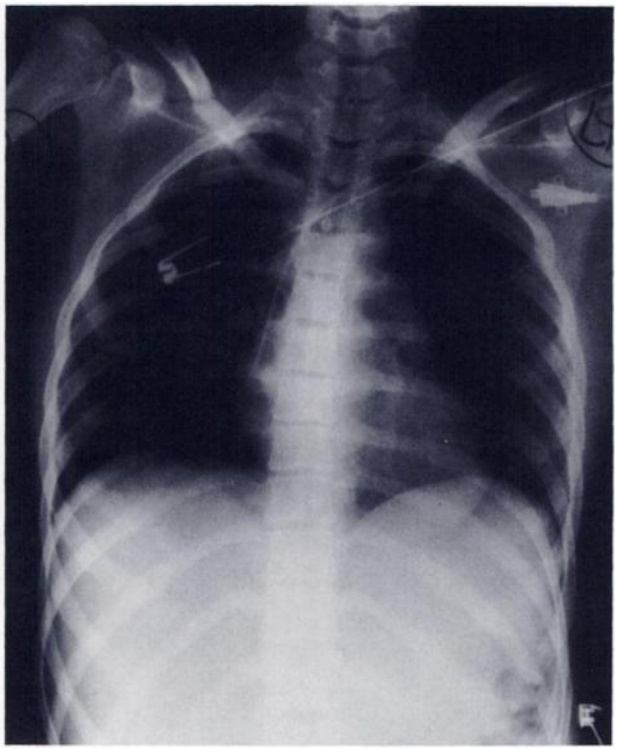

FIGURE 2
Chest x-ray shows healing fracture of right clavicle.

epidermoid carcinoma have shown increased local activity thought to be due to local marrow hyperplasia (*1,8*). There is one reported study which revealed mild to moderate [^{111}In] WBC uptake in some noninfected closed fractures (*11*). However there are no reported cases of uptake of the magnitude we describe. A mechanism for this phenomenon has not been reported. Proposed explanations include persistent inflammation around fracture site or less likely in our patient hemorrhage (since there was no evidence of thrombus in this case). Since many patients with severe trauma develop fever, radiologists should be aware of the possibility that there may be increased activity present in simple fracture sites, and thus avoid costly unnecessary tests.

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Radiochemical Purity of [^{99m}Tc]HM-PAO

TO THE EDITOR: Technetium-99m d,l-hexamethyl propyleneamine oxime ([^{99m}Tc]HM-PAO) is an exciting new radiopharmaceutical which permits SPECT imaging of regional cerebral perfusion with the convenience of a technetium kit. It was approved for general use in Canada in November, 1986 (Ceretec, Amersham Canada, Ltd.)

Addition of pertechnetate to a freeze-dried HM-PAO kit produces a mixture of radiochemical species which changes with time. In addition to the desired lipophilic [^{99m}Tc]HM-PAO complex, there are free pertechnetate, reduced-hydrolyzed technetium, and an unidentified secondary complex which is less lipophilic than [^{99m}Tc]HM-PAO (*1*). The relative amounts of these components are influenced by the "quality" of pertechnetate used in preparation (time since elution and amount of carrier ^{99}Tc) and the time after reconstitution of the kit. It is recommended that the pertechnetate be eluted <4 hr previously from a generator with no more than 24 hr of in-growth and that the radiopharmaceutical be injected within 30 min of reconstitution (*1,2*). These constraints emphasize the importance of determining the radiochemical purity of [^{99m}Tc]HM-PAO. Furthermore, determination of the amount of lipophilic [^{99m}Tc]HM-PAO present will be required for mathematical modelling of HM-PAO kinetics and quantification of regional cerebral perfusion.

Neirinckx and others (*1*) present a chromatographic procedure which uses paper and instant thin-layer strips in three solvent systems to determine the amounts of the three impurities and then the amount of the desired complex by difference. This seemingly complex procedure results in many users neglecting quality control completely. It consumes much of the 30-min shelf-life of the radiopharmaceutical. In addition, we have obtained anomalous results ~15% of the time.

We would like to propose the following simpler, more rapid procedure for routine quality control of [^{99m}Tc]HM-PAO. Several drops of the radiopharmaceutical are added to a test tube which contains 3 ml ethyl acetate and 3 ml saline. The tube is capped, mixed on a vortex mixer for 1 min, then allowed to stand for 1 min to let the phases separate. The top layer (ethyl acetate) is transferred by pipet to another tube and the activities in each layer are measured in a dose calibrator. The fraction present as lipophilic [^{99m}Tc]HM-PAO is calculated as the activity in the top layer divided by the total activity in the two layers. The lipophilic [^{99m}Tc]HM-PAO is extracted into ethyl acetate while free pertechnetate, reduced-hydrolyzed technetium, and the secondary complex remain in the aqueous layer.

Comparison of the results of the extraction and three-system chromatographic methods produced a regression line with a slope of 1.02, an intercept of 3.2%, and a correlation coefficient of 0.985 ($p < 0.001$) for 24 measurements. The coefficient of variation was 1.2% for the extraction method and 3.2% for the chromatographic method. Ethyl acetate was selected because it is easier to handle than diethyl ether and phase separation is more rapid than with octanol. Chloroform produced equivalent results.

A similar approach to direct quantification of the lipophilic complex has been suggested by the Missouri group (*3*) who used paper chromatography with diethyl ether as solvent, but this is not as rapid as the extraction method. An alternative to solvent extraction might be the use of an extraction cartridge (C-18 SEP-PAK, Waters Associates), which would be even more rapid but also more expensive.

In conclusion, we suggest that the radiochemical purity of [^{99m}Tc]HM-PAO be routinely checked with an extraction procedure which requires <5 min to complete, can be per-