Case Report: Bone Marrow Visualization with Tc-99m Disofenin

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Technetium-99m-N-substituted iminodiacetic acid derivatives are currently being investigated in nuclear medicine for possible use in the evaluation of hepatobiliary diseases. Disofenin (diisopropyl iminodiacetic acid) is the derivative most highly regarded at present. We report a case in which, although Tc-99m disofenin was prepared according to the manufacturer's directions, an altered biodistribution pattern was noted on images.

The patient was an 82-year-old woman admitted with a history of coronary artery disease and myocardial infarction in 1967, as well as a diagnosis of cholelithiasis in 1962. She had not had a cholecystectomy or any subsequent gallbladder symptomatology.

Technetium-99m disofenin was prepared using 43 mCi of sodium pertechnetate in 1.8-ml volume from a Squibb generator. Kits of all IDA derivatives are stored at room temperature and following preparation, the pharmaceuticals have a 6 12-hr expiration time. At 20-min postpreparation, a dose of 5.0 mCi in 0.2 ml was administered to the patient after informed consent was obtained. Radionuclide hepatobiliary imaging demonstrated gallbladder filling, thus excluding cystic duct obstruction and acute cholecystitis. The intriguing feature of the study was visualization of the vertebrae and bony pelvis, not unlike that seen on liver scans in cirrhotic patients (Fig. 1A and B). The patient had not had any previous radionuclide scans.

Radiochromatography to determine radiochemical purity was not performed before patient injection because the lot had produced clinically acceptable images. Because there had been no evidence of free pertechnetate on the other images, we did not determine the percent of free pertechnetate. Subsequently, radiochromatography was performed using Gelman ITLC-SG, saline, and the Squibb Q.C. Analyzer® to determine the amount of hydrolyzed-reduced technetium in the preparation (*1*). The chromatography results obtained approximately 1 hr after radiopharmaceutical preparation indicated approximately 80% hydrolyzed-reduced technetium-99m. The biodistribution of the radiopharmaceutical seen in the hepatobiliary system and lack of stomach activity implied that the remainder of the radiopharmaceutical was composed of Tc-99m disofenin with no significant amount of free pertechnetate.

Discussion

This case appears to be one in which the radiopharmaceutical was unstable, and a reduced-hydrolyzed colloid was formed. To our knowledge this phenomenon has not previously been reported with technetium-labeled iminodiacetic acid derivatives; for example, Wistow has reported that no colloid formation had been observed with the newer hepatobiliary agents (*2*).

Organ distribution of reduced technetium was studied by Koester et al. (*3*) at three pH levels. Similar biodistribution patterns for the reduced technetium were seen at pH 1, 3, and 6. Approximately 30–40% of the dose was unaccounted for and conceivably was localized in the bone marrow. Lin (*4*) states that colloid formation may depend on pH, hydrolysis time, relative abundance of ligands present, and their relative strength as donors.

Determination of particle size in our preparation would have necessitated the use of an electron microscope or various pore size filters. Technologies such as these were not immediately available and, therefore, particle size determination was felt to be impractical.

It is recognized that such colloidal particles may be phagocytized by the reticuloendothelial (RE) system. Abnormal liver uptake has been reported with bone scanning agents when abnormal colloid formation has occurred (*5*). This same mechanism, phagocytosis of colloid particles, is utilized in sulfur colloid liver scan-

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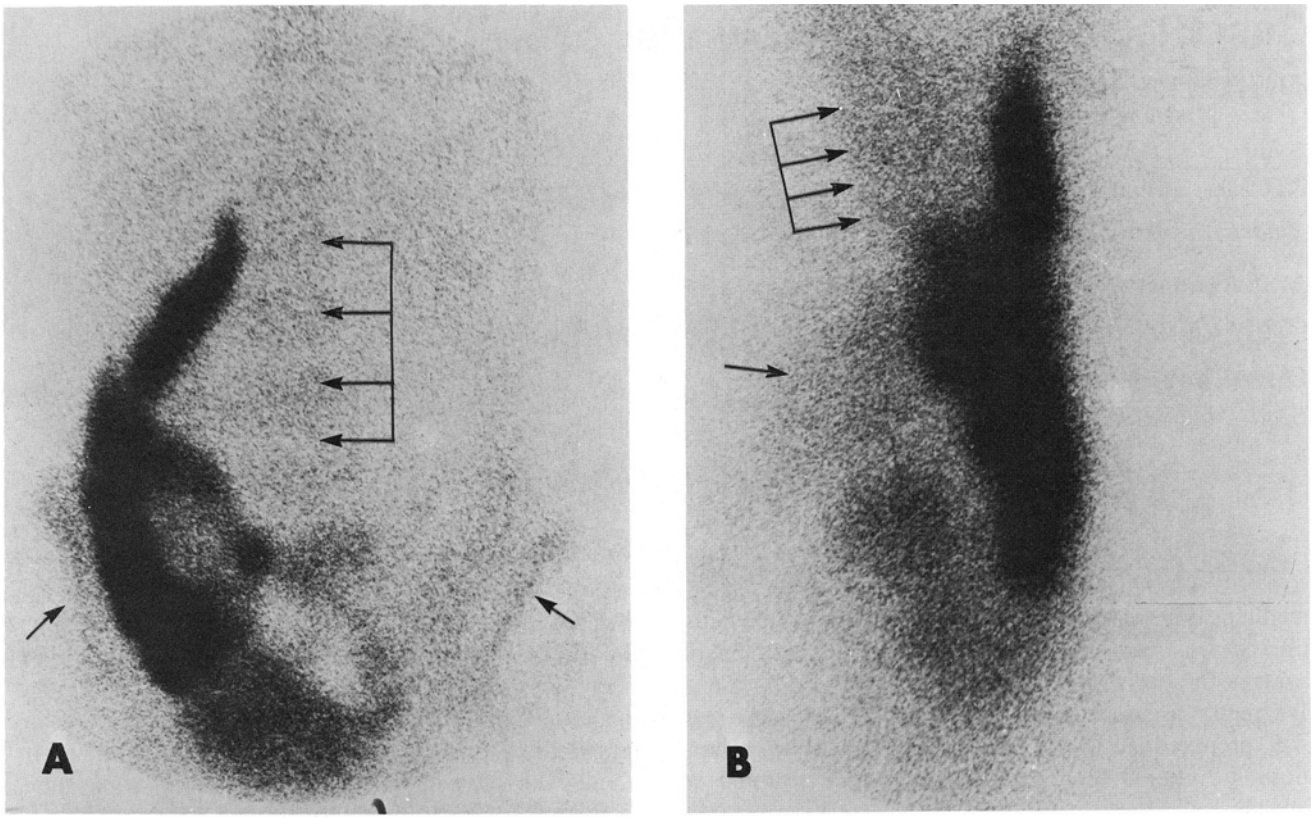

FIG. 1. Abdominal images in anterior (A) and lateral (B) projections demonstrating activity in intestine on the right side of the abdomen and activity in bone marrow of spine (multiple arrows) and pelvic bone (single arrow).

ning. Whether the liver, spleen, or marrow RE system predominates, the phagocytosis appears to depend upon several factors—including particle size, dosage, and method of preparation. There is reportedly a "preference" of the marrow RE system for the smaller colloid particles (*6*). Heyman et al. (*7*) have evaluated radiocolloids for bone marrow imaging in primates; they found that antimony colloid and mini-microaggregated albumin, having particle sizes significantly smaller than other agents, demonstrate three times more localization in the bone marrow. Kloiber et al. (*8*) compared Tc-99m sulfur colloid and an albumin colloid with a known smaller particle size in 15 patients. The albumin colloid demonstrated increased activity in the bone marrow as measured by bone marrow/background ratios and shorter imaging times.

In our case phagocytosis seemed to occur almost exclusively in the marrow RE cells, presumably due to the small particle size of the atypical, reduced-hydrolyzed technetium colloid particles.

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