Localization of Tc-99m-Pyrophosphate in the Liver
Due to Massive Liver Necrosis: Case Report

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Technetium-99m-pyrophosphate (PP3) has recently gained popularity as an agent for imaging necrosis of myocardial tissue. A case showing concentration of Tc-99m PP3 in a liver undergoing massive necrosis is presented. Possible mechanisms are discussed.


Myocardial scintigraphy with Tc-99m Pyrophosphate (Tc-99m PP3) has been shown to be a sensitive indicator of acute myocardial infarction (1,2). Other cardiac anomalies including ventricular aneurysm and cardiomyopathy will also concentrate Tc-99m PP3 (3–5). Bone seeking radionuclides will concentrate in various soft tissue lesions such as carcinoma of the breast, lung, or ovary (6,7). Technetium-99m-labeled phosphates will concentrate in carcinoma metastatic to the liver or in reticuloendothelial cells if colloid is formed (7,8), but there is no reported case of localization in the liver due to parenchymal liver disease.

Some authors postulate that the phosphate localizes within the mitochondria of damaged cells in a complex with hydroxyapatite (9,10). Others have suggested that Tc-99m PP3 binds to soluble protein resulting from denatured macromolecules rather than in the damaged mitochondria (11).

Concentration of Tc-99m PP3 in almost any tissue undergoing cellular infarction could be predicted. The following is the first report of increased radiotracer deposition in severely damaged liver tissue.

CASE REPORT

A 52-year-old retired glass blower with known hypertension and well compensated congestive heart failure, was admitted to the hospital with a 1 month history of progressive nausea, vomiting, coughing, fever, and chills. During the previous month he was hospitalized briefly for presumed digitalis intoxication, and his digoxin and furosemide were discontinued. Examination revealed a moderately dyspneic male with a normal temperature, blood pressure of 170/113 mm Hg and heart rate of 112/min. There was cervical vein distension, diminished breath sounds, bilateral basal rates, and a regular cardiac rhythm. Mild tenderness was elicited over the slightly enlarged liver. There was a trace of pitting pretibial edema.

Chest roentgenogram showed cardiomegal, vascular congestion, B lines of Kerley, and small bilateral pleural effusions. Serum bilirubin was 0.9 mg %, alkaline phosphatate 14 U, urea nitrogen 20.8 mg %, glutamic oxalacetic transaminase (SGOT) 58 U, lactic dehydrogenase (LDH) 280 U, creatine phosphokinase (CPK) 112 U, and hydroxybutyrate dehydrogenase (HBD) 445 U. Hepatitis associated antigen was negative on two separate occasions. Electrocardiograms showed left ventricular hypertrophy and left atrial enlargement but no evidence of old or new myocardial infarction.

Since the patient responded poorly to therapy and the cause of his refractory decompensation was uncertain, Tc-99m PP3 myocardial scintigram was performed on the third hospital day. An intense concentration of radiotracer was observed in the liver but none in the heart. Repeat serum enzymes on the same day showed a marked increase: glutamic pyruvic transaminase (SGPT) was 4,630 U; SGOT

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6,270 U; LDH 11,720 U; CPK 1,240 U; and HBD 11,650 U.

The Tc-99m PP₃ scintigram repeated the next day again showed an intense hepatic concentration of radionuclide (Fig. 1).

Over the next 2 weeks, he was treated with parenteral antibiotics for a right lower lobe infiltrate. After completing his course of antibiotics, he developed a low grade fever but multiple blood cultures showed no growth. His condition continued to deteriorate, he developed bradycardia, became obtunded, azotemic, and died.

Autopsy revealed severe massive central lobular necrosis of the liver (Fig. 2).

**DISCUSSION**

Technetium-labeled phosphates localize in organs with cellular injury and necrosis. Although the mechanism is uncertain, the association of influx of labeled phosphates with necrosis is well established (7,11).

In this case, the hepatic uptake of the radiopharmaceutical appears to be due to the necrosis rather than a chemical alteration of the agent. Injection of radiotracer from the same vial into other patients yielded a normal biodistribution with no concentration in the liver. The pyrophosphate was returned to the commercial supplier for their analysis and was found to be of proper chemical purity and constitution. The ability to reproduce the finding the following day is further evidence that the finding was due to the liver pathology rather than a technical or chemical artifact. The lack of concentration of tracer in the spleen mitigates against an in vivo colloid formation. Excluding the liver activity, the remainder of the biodistribution was typically that of pyrophosphate.

The precise mechanisms involved in cell injury and death of various tissues from many causes is not well understood. The alterations in cellular metabolism under hypoxic conditions, however, have been fairly well described and provide insight into a possible mechanism for the uptake of bone seeking radiopharmaceuticals in soft tissue lesions. Although not accounting for all the effects of hypoxia on the cell, it has been shown that the major effect is on mitochondrial respiration (12). The integrity of the cell membrane becomes weakened as energy stores are depleted; sodium diffuses into the cell and potassium diffuses out (12). Calcium also diffuses into the cell and attaches to the mitochondria as has been
shown in myocardial ischemia (10,13,14) and carbon tetrachloride poisoning (15).

Localization of bone seeking radiopharmaceuticals in soft tissue may be due to calcium accumulation on mitochondria after disruption of the cell membrane. The bone agent enters the cell and is either deposited with calcium on the mitochondria or attaches to calcium already deposited by replacing other anions (16).

The concentration of a technetium-labeled phosphate in the liver in this case was a marker of necrosis in that organ. The extent of necrosis in this case proved to be lethal, however, lesser degrees of injury or cellular death might also result in liver concentration. With this in mind patients are now being studied who demonstrate liver damage from alcohol, hepatitis, hepatotoxicity, and passive congestion to determine if this phenomenon may have potential diagnostic and predictive benefit.

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REFERENCES


SNM GREATER NEW YORK CHAPTER
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The 3rd Annual Scientific Meeting of the Greater New York Chapter of the Society of Nuclear Medicine will be held Friday through Sunday, November 11—13, 1977, at the New York Hilton at Sixth Avenue and 53rd Street in New York City.

In addition to selected scientific papers and commercial exhibits, the meeting will feature survey papers, teaching sessions, and workshops conducted by invited faculty. There will be a Business Meeting on November 12 at 4:00 p.m.

Submitted papers should be sent no later than Sept. 15, 1977, to:

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