CASE REPORTS

Concentration of Tc-99m Methylenediphosphonate in Hepatic Metastases from Squamous Cell Carcinoma

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A case is described in which Tc-99m methylene diphosphonate concentrated in a hepatic metastasis from esophageal squamous cell carcinoma. We observed radiopharmaceutical concentration in the hepatic metastases, which was probably related to the presence of necrosis with calcification.

J Nucl Med 20: 303–305, 1979

We report a case in which hepatic metastases from a squamous cell carcinoma concentrated Tc-99m medronate sodium [previously Tc-99m (Sn) methylene diphosphonate]. Previous reports with bone-scanning radiotracers have shown increased concentration in liver metastases in patients with colorectal adenocarcinomas and a cholangiocarcinoma.

CASE REPORT

A 47-year-old emaciated man was admitted to the Durham Veterans Administration Hospital with a history of dysphagia, weight loss, night sweats, constipation, polyuria, nocturia, and ataxia. On physical examination the patient was found to have hepatomegaly and a painful right shoulder. Laboratory data included abnormally low hemoglobin and hematocrit, elevated serum alkaline phosphatase, calcium and uric acid, and a leucocytosis. A rectilinear liver/spleen scan with Tc-99m sulfur colloid demonstrated an enlarged liver with multiple focal areas of decreased tracer concentration, consistent with hepatic mass lesions such as metastases (Fig. 1, A and B). A Tc-99m medronate tomographic* total-body bone study was performed four days later. Abnormal tracer accumulation was noted within the region of the markedly enlarged liver (Fig. 2). Regional anterior and posterior rectilinear scan images (Fig. 1, C and D) revealed abnormal tracer accumulation within the same regions as the hepatic focal defects demonstrated on the earlier liver/spleen scan.

A barium-enema study with air contrast was normal. Proctoscopy was negative except for a guaiac-positive stool. A liver biopsy was performed. An upper G-I series showed a moderate-sized hiatal hernia with large gastric folds and recommended that an endoscopic examination be performed. This was done, and a mass at the gastroesophageal junction was observed and biopsied. As a consequence of the biopsy reports, it was elected to give palliative radiation therapy to the lower esophageal region and the esophago-gastric junction.

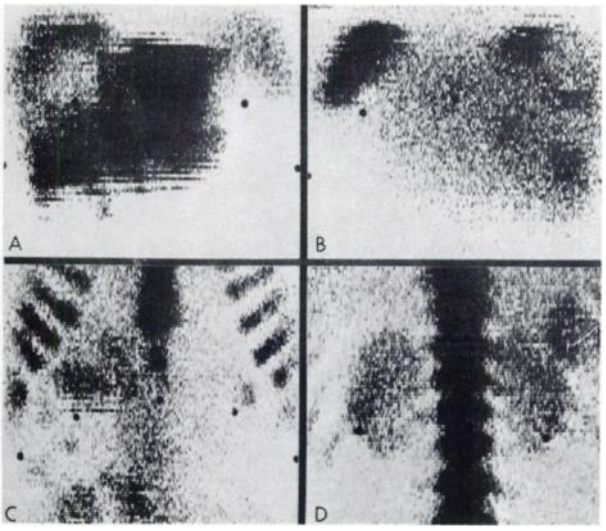

FIG. 1. Anterior and posterior Tc-99m sulfur colloid liver/spleen scans demonstrating focal defects. Anterior and posterior regional images of the Tc-99m medronate bone scan, demonstrating tracer concentration in region of liver metastases.

Received May 2, 1978; revision accepted Oct. 4, 1978.

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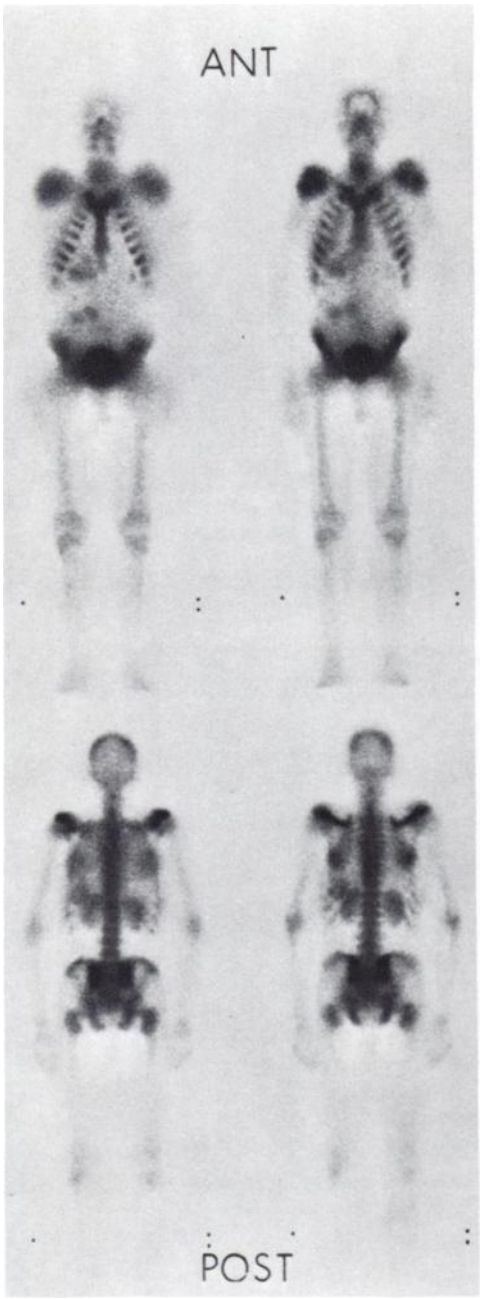

FIG. 2. Selected images from tomographic Tc-99m medronate total-body bone study.

The biopsy specimens included a liver biopsy and the tumor seen by esophagoscopy. Both specimens were fixed in neutral buffered formalin and were stained with hematoxylin and eosin. Additional sections were stained by von Kossa's silver nitrate method for the demonstration of calcium (*). Both specimens showed carcinoma of the moderately well-differentiated squamous type. No calcium was seen in the esophageal biopsy except in the wall of a blood vessel. In the liver biopsy, deposits of calcium were seen in areas of tumor that had undergone necrosis. Comparison with adjacent sections stained with hematoxylin and eosin showed an amorphous basophilic granular material in the areas corresponding to the positive calcium staining and consistent with the appearance of calcium in the H & E section.

DISCUSSION

Guiberteau et al. recently reported hepatic metastases, demonstrated by liver/spleen imaging with Tc-99m sulfur colloid, in three patients with colon carcinoma and one patient with cholangiocarcinoma. Subsequent radionuclide bone imaging revealed the hepatic metastases to concentrate Tc-99m (Sn) diphosphonate significantly (*2*). Balachandran reported similar findings in a patient with color carcinoma (*3*). Ghaed and Marsden reported that a biopsy-proven adenocarcinoma metastatic to the liver concentrated Tc-99m (Sn) diphosphonate (*2*). The origin of the metastases was believed to be from an undisclosed carcinoma of the gastrointestinal tract. Chaudhuri et al. reported accumulation of Sr-87m citrate within intraphepatic defects seen on a Tc-99m sulfur colloid liver/spleen study in a patient with colon carcinoma and proven hepatic metastases (*5*). An In-113m transferrin "blood-pool" scan revealed " . . . little or no activity in the metastatic lesion," and the authors felt that this ruled out increased tumor vascularity as a possible explanation for their finding. There was no radiographic evidence of calcification within the lesions. In another article, Chaudhuri et al. report concentration of Tc-99m (Sn) polyphosphate and Sr-87m citrate within an abdominal-wall metastasis secondary to a primary adenocarcinoma of the rectum (*6*).

Stevens and Clark report accumulation of Tc-99m pyrophosphate in biopsy proven hepatic metastases secondary to colon adenocarcinoma (*7*). The liver metastases demonstrated collagen but no gross or microscopic calcification. Garcia et al. found seven colon carcinoma patients in whom F-18, Tc-99m diphosphonate, or Tc-99m pyrophosphate was concentrated in hepatic metastases (*8*). Radiographic evidence for calcification was identified in only two of the seven patients.

Schultz et al. have described increased concentration of Tc-99m (Sn) polyphosphate within both breasts of a patient with proven infiltrating mucoid adenocarcinoma of the rectum (*9*). Biopsy of the right breast revealed neoplastic cells like those of the primary tumor.

In addition to both benign and malignant bone abnormalities, increased tracer concentration of the various Tc-99m phosphate complexes has been reported to occur with varying degrees of predictability in a number of pathologic states, including several soft-tissue neoplasms, myocardial infarctions, cerebral infarctions, myocardiopathies, unstable angina pectoris, arteriosclerotic heart disease, malignant pleural effusions, metastatic calcification in soft tissue secondary to hypercalcemia, dermatomyositis, etc.

The mechanism for deposition of a Tc-99m phosphate complex in bone has been ascribed to chemabsorption onto the calcium of hydroxyapatite. Enzymes (e.g., alkaline phosphatase) have been implicated as factors in this bone deposition because of their presence at sites of active calcification. Blood flow, a primary factor in the bone accumulation of tracer, is apparently increased (*10*). Mechanisms similar to those in bone probably exist with soft-tissue calcification. Rather than the crystal surface of bone, it has been suggested that Tc-99m (Sn) pyrophosphate may have a greater affinity for immature collagen (*10*).

An explanation for the localization of tracer bone-seeking in hepatic metastases from colorectal adenocarcinoma has been proposed by Papavasiliou (*10*). Primary mucinous colonic adenocarcinoma is known to develop both microscopic and radiographically discernible calcification within liver metastases, and this may be an explanation for its concentration when calcification is present. Papavasiliou also alludes to the deposition of calcium in necrotic regions (*10*). Such deposition of calcium salts (dystrophic calcification) is a well-known phenomenon, although the exact pathogenesis is unclear (*11*). Dystrophic calcification is commonly seen in anoxic areas of both benign and

malignant tumors of various cell types. It may be even more common than is generally appreciated, since the amorphous vasophilia seen in necrotic areas with the usual H & E staining may be attributed to "nuclear debris" and there is seldom an indication to pursue the matter further with the von Kossa technique for the specific identification of calcium.

Two reports, however, state that biopsy section did not show microscopic evidence of calcification (*3, 7*). The authors do not state whether staining specifically for calcification was performed. The presence of collagen in an apparently noncalcified hepatic metastases was considered a possible factor in accumulation of the radiopharmaceutical (*7*). Garcia et al. note that bone-seeking radiopharmaceuticals have been reported to concentrate in nonosseous metastases (*8*). In our case calcification within necrosis was established. The possible existence of necrosis with histologically poorly defined calcifcation in the previous reports might be a factor affecting the concentration of these radiopharmaceuticals. This would presume blood perfusion to the region or regions in question.

CONCLUSION

A case is described in which hepatic metastases from an esophageal squamous cell carcinoma concentrated TC-99m medronate. Although concentration of T-99m phosphate complexes in hepatic metastases has previously been reported only in patients with primary gastrointestinal adenocarcinomas, the nonspecificity of this bone-scan finding in terms of histology is demonstrated by this case.

FOOTNOTE

*Pho Con, Searle Corp.

REFERENCES

1. LUNA LG, ed.: *Manual of Histologic Staining Methods of the Armed Forces Institute of Pathology*, 3rd ed. New York, McGraw-Hill, 1968, pp 176–177
2. GUIBERTEAU MJ. POTSAID MS, MCKUSICK KA: Accumulation of ^{99m}Tc-diphosphonate in four patients with hepatic neoplasm: Case reports. *J Nucl Med* 17: 1060–1061, 1976
3. BALACHANDRAN S: Localization of ^{99}Tc-Sn-pyrophosphate in liver metastases from carcinoma of colon. *Clinical Nucl Med* 1: 165, 1976
4. GHAED N, MARSDEN RJ: Accumulation of ^{99m}Tc-diphosphonate in hepatic neoplasm. *Radiology* 126: 192, 1978
5. CHAUDHURI TK, CHAUDHURI TK, Go RT, et al: Uptake of ^{87m}Sr by liver metastasis from carcinoma of colon. *J. Nucl Med* 14: 293–294, 1973
6. CHAUDHURI TK, CHAUDHURI TK, CHRISTIE JH: Tumor uptake of ^{99m}Tc-polyphosphate: Its similarity with ^{87m}Sr-citrate and dissimilarity with ^{67}Ga-citrate. *J. Nucl Med* 15:458–459, 1974
7. STEVENS JS, CLARK EE: Liver metastasis of colon adenocarcinoma demonstrated on ^{99m}Tc-pyrophosphate bone scan. *Clin Nucl Med* 2: 270–271, 1977
8. GARCIA AC, YEH SD, BENUA RS: Accumulation of bone-seeking radionuclides in liver metastasis from colon carcinoma. *Clin Nucl Med* 2: 265–269, 1977
9. SCHULTZ MM, MORALES JO, FISHBEIN PG, et al: Bilateral breast uptake of ^{99m}Tc polyphosphate in a patient with metastatic adenocarcinoma. *Radiology* 118: 377–378, 1976
10. PAPAVASILIOU C: Cancer of the colon visualized by strontium scintigraphy. *J Nucl Med* 15: 824, 1974
11. ROBBINS SL: *Pathologic Basis of Disease*. Philadelphia, WB Saunders Co., 1974, pp 51–52
12. JONES AG, FRANCIS MD, DAVIS MA: Bone scanning: Radionuclidic reaction mechanisms. *Semin Nucl Med* 6: 3–18, 1976

Skull Scintigraphy in Infantile Hypophosphatasia

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The authors describe the advantage of skull scintigraphy in evaluating the abnormal growth pattern of the cranial sutures in infantile hypophosphatasia.

J Nucl Med 20: 305–306, 1979

Recognition of hypophosphatasia as a distinct clinical entity began in 1948 with Rathbun's description (*1*). His report included the biochemical, clinical, radiographic, and autopsy observations. Since the original description, additional information has been recorded (*2-4*).

Received Aug. 21, 1978; revision accepted Oct. 26, 1978.

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Hypophosphatasia rarely occurs. The disorder is: a) genetically conditioned: b) one parent has an abnormally low serum alkaline phosphatase value even in the absence of clear-cut skeletal aberrations: c) the affected child and parent show increased urinary excretion of phosphoethanolamine; and d) hypophosphatasia should be regarded as a disorder of endogenous metabolism (*5*).

Craniosynostosis is a major complication in infantile hypophosphatasia (*6*); besides being a cosmetic abnormality, it may lead to mental retardation if not corrected early.