Hepatic Angiosarcoma: Mimicking of Angioma on Three-Phase Technetium-99m Red Blood Cell Scintigraphy

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A [^{99m}Tc]RBC study in a 63-yr-old man showed intrahepatic lesions which initially had less activity than surrounding liver tissue. When viewed 3 hr later, these had "reversed" and the lesions revealed increased uptake of the radiolabeled red cells. Some extrahepatic areas showed the same pattern (these were in the mesentery of the small bowel). The lesions proved to be angiosarcomas. Hence, the behavior of labeled red cells in these angiosarcomas mimicked that in benign hemangiomas.

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The three-phase technetium-99m red cell ([^{99m}Tc] RBC) imaging technique has been reported as highly specific for identifying benign intrahepatic hemangiomas; the imaging pattern has not been described in any other lesion (*1–3*). We describe a case with an imaging study identical to that of intrahepatic hemangiomas, but which was due to a malignant tumor.

CASE REPORT

A 63-yr-old white male was admitted to the hospital as a result of a 35-lb weight loss over several months, and severe left lower quadrant pain of 1 wk duration. Physical examination revealed a palpable liver and a tender mass in the left lower quadrant of the abdomen. Initial diagnostic studies included an ultrasound examination which revealed a diffusely nonhomogeneous liver with multiple echogenic lesions. A nonenhanced computed tomogram of the abdomen showed multiple well-defined areas of decreased attenuation in the liver. Both examinations were nonspecific but were believed to be most likely due to metastatic disease. Two liver biopsies were performed; the second was under ultrasonic guidance, but both were nondiagnostic. The patient developed intra-abdominal bleeding, requiring transfusions.

The past history was remarkable in that 45 yr previously, the patient was found to have an "inoperable lymphoma in the left lower quadrant of the abdomen" and was treated with ~1,500 rad external radiation to the region. During a cholecystectomy performed 10 yr prior to the current admission, careful exploration of the abdomen revealed only thickening of the left retroperitoneum. There was no evidence of tumor at that time and the liver was noted to be normal.

An exploratory laparotomy was performed 3 wk after admission; it revealed multiple intrahepatic masses as well as multiple smaller nodular lesions involving most of the small bowel mesentery. Biopsies of the small bowel mesentery revealed findings consistent with hemangiomas, and biopsy of the liver was negative except for "mild chronic inflammation."

In order to evaluate the extent of the disease in the lower abdomen and to further define the nature of the lesions in the liver, a three-phase ^{99m}Tc tagged red blood cell study was performed.

The patient was first injected with stannous pyrophosphate intravenously, and then [^{99m}Tc]pertechnetate was added to RBC in vitro. The initial phase (Fig. 1, left) did not show any intrahepatic abnormality. The early blood-pool images had moderately decreased uptake of labeled RBC in the upper and lower portions of the liver (Fig. 1, center). Delayed blood-pool images obtained 3 hr later (Fig. 1, right) showed intense uptake in multiple focal lesions throughout the liver as well as in the large irregular area in the left lower quadrant. The liver findings were consistent with multiple hemangiomas, and similar lesions were suspected in the lower abdomen.

One month later the patient was readmitted complaining of severe abdominal pain and weakness. Intra-abdominal bleeding was suspected and an emergency angiogram was performed. This revealed an enlarged liver and "multiple small areas of contrast puddling" which persisted late into the venous phase. A second large abnormal area appeared to involve the mesentery of the distal jejunum and proximal ileum.

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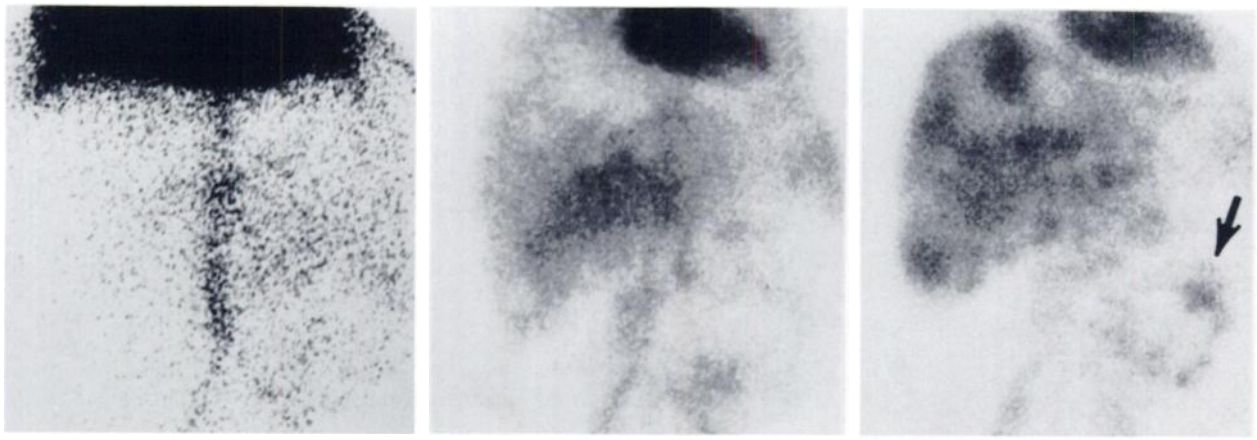

FIGURE 1
Images from [^{99m}Tc]RBC study. Left: Dynamic sequence. Center: Early blood-pool image demonstrates areas of decreased uptake. Right: Delayed study at 3 hr shows increased uptake in these same areas ("filling in"). Extrahepatic site in small bowel and mesentery is indicated by arrow on delayed image

Contrast puddling was also noted in parts of the bowel wall. These findings were felt to be due to extensive hemangiomatous involvement; no bleeding point was identified. Despite multiple transfusions, bleeding continued requiring a second laparotomy. Multiple bleeding points in the mesentery of the small bowel were found and bleeding was controlled after a segment of small bowel and adjacent mesentery was removed. The pathology report of the specimen described numerous small vascular channels lined by endothelial cells which merged into areas of neoplastic appearing cells, the appearance of which was consistent with angiosarcoma.

Ten days later, uncontrollable bleeding recurred and a third laparotomy was performed. This time however, examination of the liver revealed numerous bleeding points which could not be controlled and the patient expired in the intensive care unit shortly after surgery was completed. A subsequent autopsy confirmed the presence of extensive angiosarcoma of the liver, mesentery, and small bowel.

DISCUSSION

Angiosarcomas are malignant neoplasms of vascular origin. They occur at all ages and may be found virtually anywhere in the body, especially in the skin, liver, spleen, lungs, and bones (*4–6*). Grossly, the tumors may grow quite large with frequent central necrosis and hemorrhage, and poorly defined margins (*4,7*). All degrees of differentiation are seen microscopically. They may invade locally or disseminate through blood or lymphatic pathways (*4*).

Hepatic angiosarcomas (HAS) are rare (*6,8*), but are nevertheless the most common sarcomas of the liver. There are ~10 to 20 new cases of HAS per year in the United States (*9*) with the majority occurring in males between 50 and 60 yr of age. They tend to produce multiple hemorrhagic nodular masses within the liver (*6*). Metastases may be found in the lungs, portal and mesenteric lymph nodes, spleen, abdominal viscera or other organs (*6,10*). Hepatic angiosarcomas have been associated with chronic exposure to thorotrast, vinyl chloride, arsenicals and radium; they have also been associated with idiopathic hemochromatosis (*8–12*). Some authors consider malignant transition of benign cavernous hemangiomas of the liver as a possible cause (*10*). The clinical presentation of HAS is nonspecific; abdominal pain, weakness, and weight loss are the most common complaints (*8,9*). The prognosis is poor and few patients survive longer than two years (*8,9*). Angiosarcomas of the small bowel are quite rare malignant tumors; Wood (*5*) has stated that the rarity of these lesions suggests that most small bowel angiosarcomas probably represent metastases. They may be quite aggressive and are frequently intramural in location with mucosal extension and ulceration possible. Such occurrences may result in a clinical presentation of gastrointestinal hemorrhage, a feature shared with benign hemangiomas of the small bowel (*13*).

Because of their vascular nature, percutaneous biopsy of hepatic angiosarcomas and cavernous hemangiomas may result in severe bleeding or even exsanguination (*7,14*). A reliable method of differentiating these tumors from other liver pathology is necessary. Selective hepatic angiography has been considered the "gold standard" and the characteristics of cavernous hemangiomas and angiosarcomas have been well described by several authors (*11,15*). Less invasive diagnostic methods have been sought. Ultrasound has been found to be too nonspecific. Computed tomography appears to be quite reliable (*16–20*). Recently, magnetic resonance imaging (MRI) achieved 90% sensitivity and 92% specificity in detecting cavernous angiomas (*21*).

Three-phase [^{99m}Tc]RBC scintigraphy has been shown to be of value in the diagnosis of hepatic cavernous hemangiomas (*1,22,23*). The initial phase is variable with either normal, increased, or decreased flow to

the lesions possible. Early blood-pool imaging most frequently shows some degree of filling of either a portion or the entire lesion. In the delayed images, however, most hemangiomas have shown significantly increased uptake within the lesion. A perfusion blood-pool mismatch (the initial phase shows decreased red cell concentration, with slow increase in activity which is not complete for some time), has been reported only in cavernous hemangiomas with a specificity of 100% (*6,23*). Three-phase [^{99m}Tc]RBC scintigraphy was performed on our patient following the i.v. administration of stannous pyrophosphate, and then in vitro labeling with 25 mCi of [^{99m}Tc]pertechnetate. The initial dynamic phase demonstrated no hepatic "hot spots." There was a relatively decreased blood-pool image in the superior and inferior portions of the liver. Faintly increased activity was noted in the left lower quadrant. The delayed images (3 hr later) demonstrated multiple areas of considerably increased activity in the upper and lower hepatic poles as well as in the left lower quadrant of the abdomen.

This case represents an intrahepatic angiosarcoma detected by three-phase [^{99m}Tc]RBC scintigraphy. It is also a case of a "perfusion-blood pool mismatch" in a lesion other than a benign hemangioma. Due to histologic similarities between benign hemangiomas and malignant angiosarcomas, it is not surprising that these highly vascularized tumors show similar findings in the labeled red cell study. Hence, this noninvasive method cannot be considered to be completely specific for benign hemangiomas.

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REFERENCES

1. Engel MA, Marks DS, Sandler MA, et al: Differentiation of focal intrahepatic lesions with ^{99m}Tc-red blood cell imaging. *Radiology* 146:777–782, 1983
2. Font D, Israel O, Groshar D, et al: Technetium-99m labeled red blood cell imaging. *Semin Nucl Med* 14:226–250, 1984
3. Moinuddin M, Allison JR, Montgomery JH, et al: Scintigraphic diagnosis of hepatic hemangioma: Its role in the management of hepatic mass lesions. *Am J Roentgenol* 145:223–228, 1985
4. Robbins SL: *Pathologic Basis of Disease*, Philadelphia, W.B. Saunders, 1974, pp 628–634
5. Wood DA: *Atlas of Tumor Pathology*, Tumors of the Intestines, Section VI, fasicle 22, Washington, DC, Armed Forces Institute of Pathology, 1967, pp. 19–20
6. Edmondson HS: *Atlas of Tumor Pathology*, Tumors of the Liver and Intrahepatic Bile Ducts, Section VII, fascicle 25, Washington, DC, Armed Forces Institute of Pathology, 1958, pp 139–141
7. Lee TG, Lawrence AG: Angiosarcoma of the liver. Ill. *Med J* 145:324–325, 1974
8. Locker GY, Doroshow JH, Zwelling LA, et al: The clinical features of hepatic angiosarcoma: A report of four cases and a review of the English literature. *Medicine* 58:45–64, 1979
9. Goodman ZD, Kamal KG: Non-parenchymal and metastatic malignant tumors of the liver. In *Bockus Gastroenterology*, Berk JE, ed. Philadelphia, W.B. Saunders, 1985, pp 3377–3387
10. Sugahara K, Shirakura T, Kawano N, et al: Primary malignant hemangioendothelioma of the liver. *Am J Gastroenterol* 62:240–244, 1974
11. Whelan JG, Creech JL, Tamburro CA: Angiographic and radionuclide characteristics of hepatic angiosarcoma found in vinyl chloride workers. *Radiology* 118:549–557, 1976
12. Silpanata P, Illescas F, Sheldon H: Clinical observations, multiple malignant neoplasms forty years after angiography with Thorotrast. *Can Med Assoc J* 128:289–292, 1983
13. DiVita VT, Hellman S, Rosenberg SA: *Cancer, Principles and Practice of Oncology*, Philadelphia, J.P. Lippincott, 1982, pp 633–634
14. Karpas CM, Pavon EE: Fatal hemorrhage following needle biopsy of hepatic hemangioendothelioma. *NY State J Med* 71:770–772, 1971
15. Freeny PC: Angiography of hepatic neoplasms. *Semin Roentgenol* 18:114–122, 1983
16. Freeny PC, Vimont TR, Barnet DC: Cavernous hemangioma of the liver: Ultrasonography, arteriography, and computed tomography. *Radiology* 132:143–148, 1979
17. Wiener SN, Parulekan SG: Scintigraphy and ultrasonography of hepatic hemangioma. *Radiology* 132:149–153, 1979
18. Itai Y, Furo S, Araki AT, et al: Computed tomography of cavernous hemangiomas of the liver. *Radiology* 137:149–155, 1980
19. Mahony B, Jeffrey RB, Federle MP: Spontaneous rupture of hepatic and splenic angiosarcoma demonstrated by CT. *Am J Roentgenol* 138:965–966, 1982
20. Vasile N, Larde D, Zafrani ES, et al: Hepatic angiosarcoma—Case report. *J Comput Assist Tomogr* 7:899–901, 1983
21. Stark DD, Felder RC, Wittenberg J, et al: Magnetic resonance imaging of cavernous hemangiomas of the liver: Tissue-specific characterization. *Am J Roentgenol* 145:213–222, 1985
22. Font D, Hardoff R, Israel O: Perfusion vascularity mismatch in liver hemangiomas. *Clin Nucl Med* 3:212–213, 1978
23. Rabinowitz SA, McKusick KA, Strauss WH: ^{99m}Tc red blood cell scintigraphy in evaluating focal liver lesions. *Am J Roentgenol* 143:63–68, 1984