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Small hepatocellular carcinoma visualized with Technetium-99m(Sn)-N-pyridoxyl-5-methyltryptophan

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We report a case of small hepatocellular carcinoma depicted by ^{99m}Tc-PMT scintigraphy. On the X-ray computed tomogram there was no visualization of a SOL in the liver. Ultrasonography showed a hyperechoic mass of less than 2 cm in diameter in the left lateral segment of the liver. In the image obtained at 3 hr after ^{99m}Tc-PMT injection there was an area of markedly increased activity. When the surgery, left lateral segmentectomy of the liver, was performed more than 2 months later, the tumor had enlarged to $2.5 \times 2.0 \times 1.5$ cm in size. ^{99m}Tc-PMT may prove to be useful for scintigraphic localization of small hepatocellular carcinoma.

Key words: ^{99m}Tc-PMT, Small hepatocellular carcinoma, Delayed hepatobiliary image

INTRODUCTION

SINCE INTRODUCED by Shoop in 1969, hepatobiliary agents such as ^{131}I-rose bengal and ^{99m}Tc-pyridoxylidene glutamate have been reported to be sensitive in the detection of hepatoma.[1,2] The cases where liver tumors could be delineated, however, are very rare.[3]

In 1985, the concentration of Tc-99m(Sn)-N-pyridoxyl-5-methyltryptophan (^{99m}Tc-PMT) for detecting hepatocellular carcinomas was reported.[4] However, these masses reported were greater than 4 cm in diameter.

CASE REPORT

A 50-year-old man has been known to have impairment of liver function since 45 years of age. The patient, who had been under a family doctor's care with a diagnosis of chronic hepatitis, was referred to the radiological clinic of this medical center for a complete medical evaluation because of elevation of alpha fetoprotein level. He had no particular complaint. Father died as a result of liver cirrhosis, but no other members of the family or close relatives have or have had hepatitis or jaundice. The quantity of alcohol that he drinks every day is 100 m*l* of whisky and he has been smoking 30–40 cigarettes daily for 30 years.

Laboratory studies disclosed the following values: white blood cell count 4,700; red blood cell count 422×10^4; hemoglobin 15.5 g/d*l*; hematocrit 44.2%; platelet 14.9×10^4/mm^3; serum total protein 7.5 g/d*l*; A/G 0.92; total bilirubin 0.6 mg/d*l*; alkaliphosphatase 211 IU/*l*; GOT 71 IU/*l*; GPT 84 IU/*l*; ZTT 13 U; TTT 1.6 U; γ-globulin 22.4%; Hbs-antigen (−), Hbs-antibody (−); CEA 2.3 ng/m*l*; AFP 1,490 ng/m*l*; and ferritin 475.4 ng/m*l*.

Hepatic sonogram showed a hyperechoic lesion of 1.6×1.3 cm in diameter in S_2 of the left lateral segment (Fig. 1). There was no tumor embolization in the portal vein.

The mass could not be identified by CT; there was an artifact in an area which involved the mass (Fig. 2).

Hepatobiliary scintigraphy with 5 mCi (185 MBq) of ^{99m}Tc-PMT was performed on this patient (Fig. 3). There was good liver concentration of the tracer by the end of the first 10 minutes. At the same time, the intrahepatic bile ducts, gallbladder and duodenum had already begun to accumulate radioactive material. After 60 minutes activity in the liver had de-

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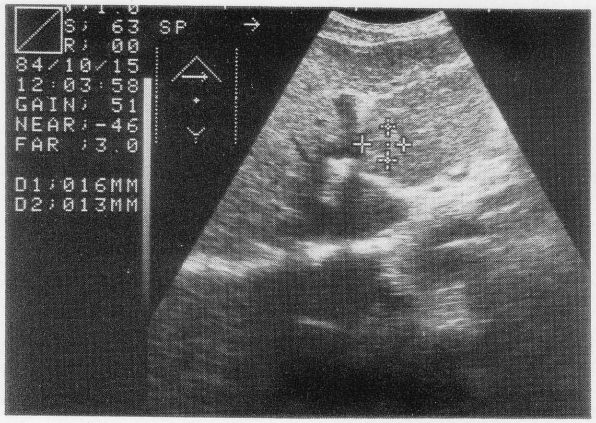


Fig. 1 Hepatic sonogram revealed a hyperchoic lesion in the left lateral segment.

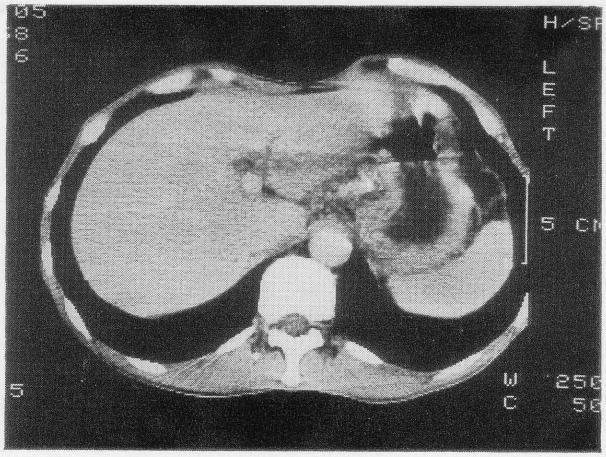


Fig. 2 No mass was depicted in the liver by thoracic CT.

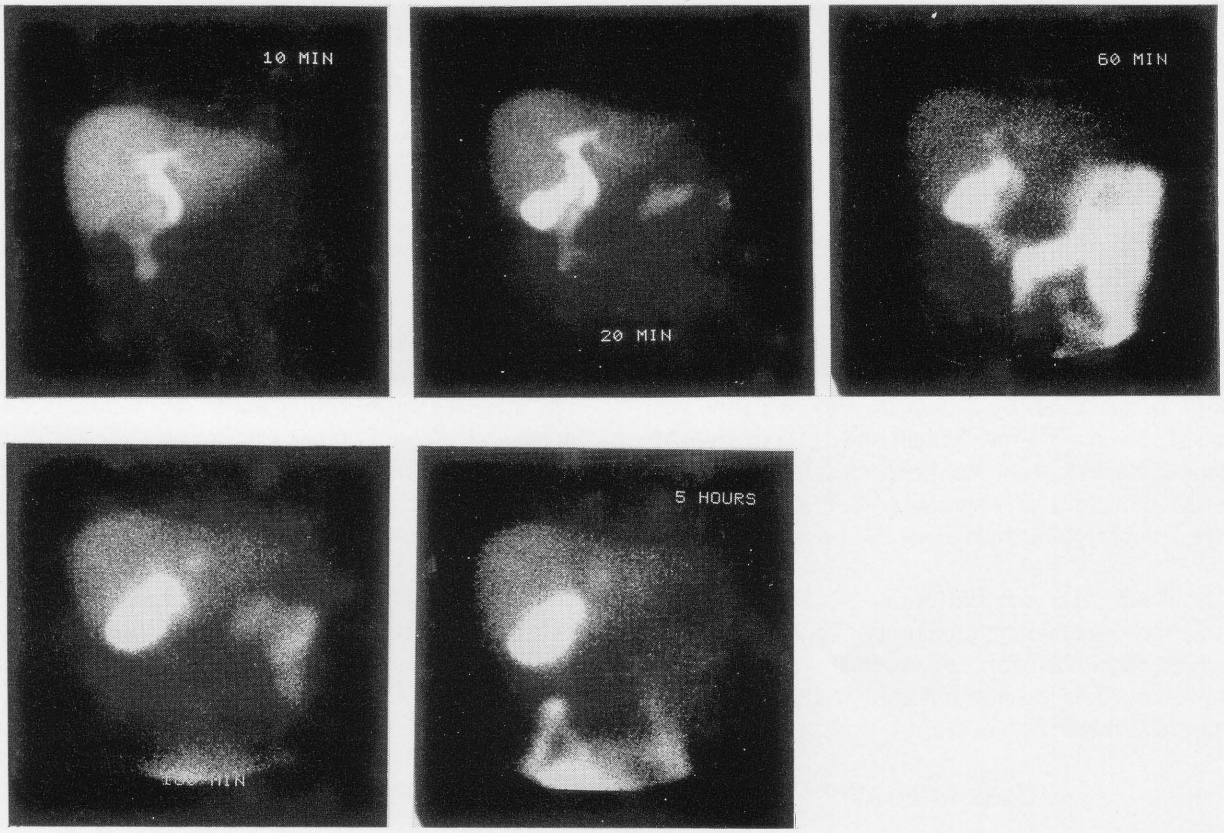
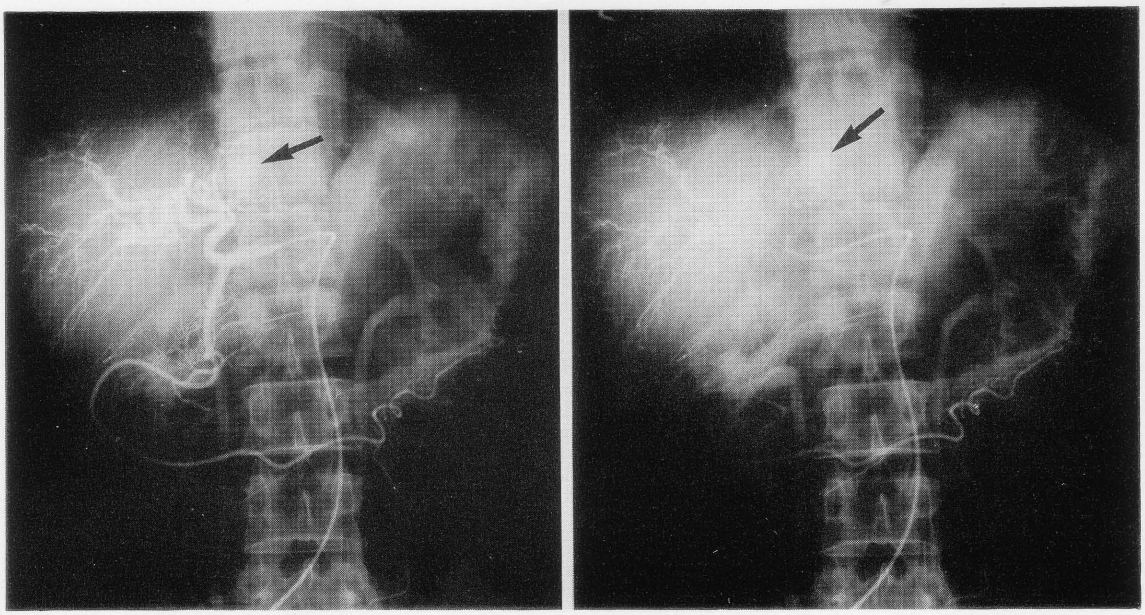


Fig. 3 Serial hepatobiliary scintigraphy. A: 10 min, B: 20 min, C: 1 hr, D: 3 hr, E: 5 hr after intravenous administration of ^{99m}Tc-N-pyridoxy–5-methyltryptophan. A hot area was seen in the left lateral segment of the liver on 1 hr (C), 3 hr (D) and 5 hr (E) images.

creased, but there was an area of slight concentration in the left lateral segment. After 3 and 5 hours there was a hot area of marked concentration of activity in the region which corresponds to the hyperechoic lesion by ultrasonogram in the S_2 of the left lateral segment of the liver.

The arterial phase of a hepatic angiogram indicated tumor vessels arising from the lateral branches of the left hepatic artery supplying this small, vascular tumor, and demonstrated characteristic intrahepatic arterial tortuosity due to fibrosis in a contracted cirrhotic liver, especially in the right lobe (Fig. 4-a). Venous phase of the angiogram showed a small tumor stain of 2 cmϕ in diameter (Fig. 4-b).

At two months after celiac angiography a subsegmentectomy in the lateral segment of the left lobe of the liver was performed on this patient. There was an encapsulated mass of $2.5 \times 2.0 \times 1.5$ cm in



A B

Fig. 4 Arterial phase (A) of hepatic angiography showed tumor vessels arising from the lateral branches of the left hepatic artery. Venous phase of the angiography (B) revealed a small tumor stain in the left lateral segment of the liver.

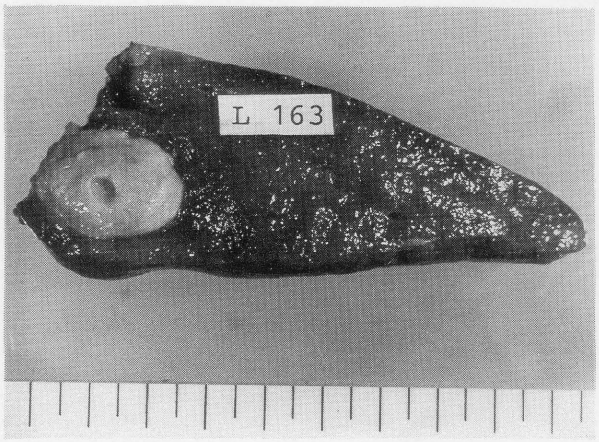


Fig. 5 Specimen of the tumor showed an encapsulated mass.

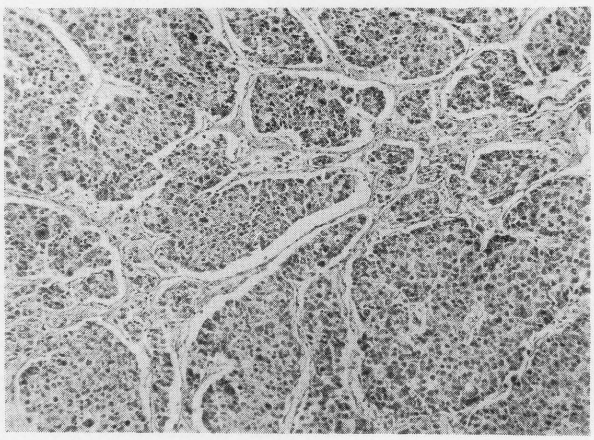


Fig. 6 Photomicrograph revealed hepatocellular carcinoma of grade II by Edmondson's classification.

size (Fig. 5). In macroscopic appearance, the tumor showed a nodular type accompanied by cirrhosis. Microscopically, the tumor showed trabecular pattern and grade II by Edmondson's classification (Fig. 6).

DISCUSSION

As a radionuclide examination for the diagnosis of hepatocellular carcinoma, space occupying lesion is detected by liver scintigram, showing the reticuloendothelial system with a ^{99m}Tc labeled colloidal agent, and accumulation of ^{67}Ga-citrate into a tumor is studied by image. However, for the detection of small hepatocellular carcinoma, even if SPECT apparatus is used, these examination methods do not seem to be superior to a sonographic examination or X-ray CT.

In the 1960s, when hepatobiliary scintiscanning was performed with ^{131}I-rose bengal using a scintiscanner, Shoop[1] reported the accumulation of ^{131}I-rose bengal in hepatocellular carcinoma. One of the authors, Isamu Narabayashi, studied the rate of accumulation of this hepatobiliary radiopharmaceutical into a liver tumor in a few patients with hepatocellular carcinoma in Kobe University Hospital at that time, but found no uptake in all cases. In the

latter half of 1970s, when several types of ^{99m}Tc labeled hepatobiliary agents were developed in place of iodine-131, Narabayashi carefully studied the existence of accumulation of ^{99m}Tc-pyridoxylidene isoleucine into a hepatocellular carcinoma at Kawasaki Medical School Hospital, but no case showed the accumulation into a hepatocellular carcinoma, probably because of the shortness of interval for imaging after intravenous administration. Although several cases have been reported using ^{99m}Tc labeled biliary agents,[2,3,5] these agents were not always useful for the diagnosis of hepatocellular carcinoma. Canon et al reported the uptake of ^{99m}Tc-PIPIDA by metastatic lesions from hepatoma,[6] and Yasunaga et al showed the uptake of ^{99m}Tc-HIDA by extrahepatic foci of hepatoma.[7]

Thereafter, ^{99m}Tc-PMT was developed, and Hasegawa et al, reported that it accumulated markedly in a hepatocellular carcinoma[8] and its metastatic site.[9] This time, we have experienced a case of markedly positive delineation, which was negative in X-ray CT, but showed a small liver cancer of less than 2 cm in diameter by sonographic examination. It underwent imaging with ^{99m}Tc-PMT, which started to accumulate in the tumor from one hour after intravenous administration, and peaked after 3 hours. When an operation was performed 2 months after the initial examination, the excised tumor was slightly more than 2 cm in diameter, but it could be confirmed that the small hepatocellular carcinoma, measuring less than 2 cm in diameter by sonography at the time of imaging diagnosis, was indicated as positive by imaging with ^{99m}Tc-PMT.

The mechanism of accumulation in a hepatocellular carcinoma is not quite clear. In this case, however, since bile pigments are seen histologically in the cancer cells, it is not considered that biliary excretion was hindered by compression of the bile canalicules by the mass. Probably ^{99m}Tc-PMT was taken up into the tumor cells through competition with serum bilirubin.

For positive delineation of a hepatocellular carcinoma it is necessary that imaging is performed more than 3 hours after intravenous administration of ^{99m}Tc-PMT. It goes without saying that patients with severe liver dysfunction should be tested much later by scintigraphy because of delayed excretion of radioactivity from liver parenchyma.

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