DIAGNOSIS OF HEPATIC CAVERNOUS HEMANGIOMA USING TECHNETIUM-99M RED BLOOD CELL IMAGING

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ABSTRACT

Thirty-one patients with various focal hepatic lesions suspected of hepatic cavernous hemangiomas(HCHs) on liver ultrasonography(US) and/or computed tomography(CT) were evaluated by Technetium-99m red blood cell imagings. All patients were studied with blood-flow and sequential planar blood-pool images. Additional single-photon emission CT (SPECT) images were also performed in 19 patients. Twenty-five patients with scinti-graphic characteristic of HCH were diagnosed as HCH, 5 proven by angiography and 20 proven by maintaining a stable clinical course ranging from 6 to 24 months with the absence of any signs and symptoms of a liver malignancy, either primary or metastatic disease. All except 3 patients with a history of hepatitis B or C virus carrier had completely normal liver function tests. Six of 25 hemangioma patients had multiple lesions. Twenty-two cases of HCHs were clearly diagnosed by planar imagings and the other 3 patients needed SPECT imagings for diagnosis of HCHs. The remaining 6 patients, 4 had a final diagnosis as hepatoma proven by angiography and liver biopsy, and the other 2 patients were diagnosed as liver metastases proven by follow-up clinical course and liver US study.

INTRODUCTION

Hepatic cavernous hemangioma(HCH) is the most common benign tumor of the liver. It is the second most common hepatic tumor following hepatic metastases. It is usually an incidental finding during examination of the liver.[1] When they are found, they may make troublesome in the differential diagnosis, especially in patients with known primary malig-nancy outside the liver or high risk for developing hepatic malignancy.

HCH is more common in females and can be occurred in any age group, but it is most frequently found in older patients. Most of these tumors are small, discrete and usually solitary, but multiple lesions are also found in about 10% of cases.[1] Most HCHs are typically less than 3 cm in diameter, however they may grow slowly to large size with increasing age, which are classified as giant hemangiomas when they are larger than 4 cm.[2] The lesions are frequently found in a subcapsular location and more commonly in the right hepatic lobe, especially the posterior segment.[1,3] HCHs are usually asymptomatic, but larger tumors may result in liver enlargement and abdominal discomfort secondary to pressure effect on adjacent organs.[1]

Although HCHs are usually asymptomatic and require no treatment, the differentiation from other hepatic lesions is still important. Several noninvasive imaging techniques such as ultrasono-

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graphy (US),[4-10] computed tomography(CT),[4,8-11] magnetic resonance imaging(MRI)[8-10,12-14] and liver scintigraphy with Technetium-99m labeled red blood cells(Tc-99m RBC)[3,6,7,13-22] have been used for differential diagnosis HCH from other focal hepatic lesions. Among these mo-dalities, blood-flow and sequential planar blood-pool(BP) imagings with/without single-photon emission CT(SPECT) images of the liver with Tc-99m RBC are well recognized as a sensitive and specific procedure for the diagnosis of HCH. Definitive diagnosis of a HCH will eliminate the need for further workup, because most of them require no treatment.[23]

The purpose of this article is to reiterate the usefulness and effectiveness of noninvasive Tc-99m RBC liver imagings for the differential diagnosis of HCH from other focal hepatic lesions.

MATERIALS AND METHODS

Thirty-one patients with various focal hepatic lesions suspected of HCHs on liver US and/or CT images, were referred for further evaluation with Tc-99m RBC imagings. There were 20 women and 11 men, ranging in age from 36 to 68 years (mean, 50.3). Of the 31 patients, 6 had a known primary malignancy in another site and the focal hepatic lesions were found during metastatic workup. The remaining patients had no prior evidence of malignancy, 18 of these presented with right upper abdominal discomfort, 2 were known cases of hepatitis B virus carrier, one was carrier of hepatitis C virus, and the last 4 patients, focal hepatic lesions were found as an incidental finding during examination of the liver.

All patients had Tc-99m RBC imagings performed with 20 mCi (740 MBq) of Tc-99m labeled red blood cells using a modified in vivo technique as described by Callahan et al.[24] The patients were positioned under a large-field-of-view gamma camera, equipped with a low-energy all-purpose parallel hole collimator in the projection that best demonstrated the lesion as seen on the US and/or CT imagings. Blood-flow images of the liver were obtained at 2 sec per frame for 1 min after a bolus injection. Then, sequential planar BP imagings were acquired for 1000 Kcounts for each image in the same position at 1, 5, 15, 30 min, 1 hr and 2 hr after injection. Additional projections such as right lateral or oblique views were also obtained in some cases. Additional SPECT imagings were also performed in 19 patients at 30 min after injection, by a rotating single-headed gamma camera (Apex-SP4 Elscint) equipped with a low-energy, all-purpose collimator. SPECT imagings were acquired in 128 x 128 matrix, using a 360 degree rotation with 60 angular projectional images for 25 seconds per frame (continuous-shoot technique). The total time for SPECT imaging was approximately 25 minutes. Computerized reconstructions were processed at 1-2 pixel width per slice in the transaxial, sagittal and coronal planes. Three dimensional imagings were also performed in all patients.

RESULTS

Of the 31 patients with various focal hepatic lesions evaluated with Tc-99m RBC imagings, 25 patients had the scintigraphic characteristic of hemangiomas and were diagnosed as HCH, 4 had a final diganosis as hepatoma and the last 2 patients were diagnosed as liver metastases. Of the 25 hemangioma patients, 5 proven by angiography and 20 proven by maintaining a stable clinical course ranging from 6 to 24 months with no definite signs and symptoms of a liver malignancy, either primary or secondary disease. All except 3 patients with a history of hepatitis B or C virus carrier also had completely normal liver function tests, and had no change in size and appearance of the lesions on follow-up US and/or CT images. Twenty-two hemangioma patients were diagnosed by planar Tc-99m RBC imagings and they all demonstrated definite focal increased BP activity on serial BP imagings, with persistent in uptake upto 2 hr after injection. The remaining 3 patients had negative planar BP images and needed SPECT imagings for the diagnosis of HCHs.

The 4 patients with a final diagnosis as hepatoma were proved by selective angiography and liver biopsy. The last 2 patients with liver metastases were proved by clinical course and follow-up liver imagings with US and liver colloid scan, which revealed increased in size of the previous lesion with multiple new focal lesions seen in the liver. None of

these 6 patients demonstrated definite focal increased BP activity on either delayed planar or SPECT images.

Of the 25 patients with HCHs, 11 had no symptoms, and 14 complained of symptoms attributable to the lesions discovered such as right upper abdominal discomfort and/or pain. All of these patients had liver US studies, 15 had CT examination of the liver and 5 had selective angiography for the final diagnosis.

The 25 patients had a total of 37 hemangiomas. Nineteen patients had solitary HCH and 6 patients had multiple lesions. Of the 6 patients with multiple HCHs, 3 had 2 lesions and the other 3 had 4 lesions. These lesions ranged in size from 1.0-12.0 cm in diameter (average, 3.8 cm), as measured on US and/or CT. Seven of these were smaller than 2 cm, 20 were between 2-4 cm, and 10 were larger than 4 cm. Of these HCHs, 31 lesions were located in the right hepatic lobe and 6 in the left lobe.

Twenty-five of the 37 HCHs (67.6%) were identified on planar Tc-99m RBC imagings and 32 lesions (86.5%) were identified with the adjunctive SPECT images. The sensitivity of Tc-99m RBC imagings was 100%(30 of 30 lesions) for HCHs larger than or equal to 2 cm in diameter, and for lesions less than 2 cm in size, the sensitivity was 28.6% (2 of 7 lesions).

Twenty-five of the 37 hemangiomas were demonstrated on planar imagings as a focal increased BP activity within the liver parenchyma. Seven additional lesions were found on SPECT imagings and these lesions were 1.5-3.5 cm in diameter, average 2.1 cm. Twelve HCHs that could not be demonstrated by planar BP images, were 1.0-3.5 cm in size(mean 1.9 cm), the 3.5 cm lesion was located deep inside the liver parenchyma and adjacent to the inferior vena cava. Five HCHs that could not be identified on SPECT, were 1.0-1.8 cm in size, average 1.2 cm. The smallest HCH identified with SPECT image was 1.5 cm and this lesion was located at subcapsular region of the left hepatic lobe, whereas 2.0 cm was the smallest lesion detected with planar BP imaging.

Of the 32 HCHs found on Tc-99m RBC images, 14 revealed normal perfusion, 15 had focal decreased perfusion, and 3 had some areas of increased perfusion during the blood-flow studies. However, all hemangiomas demonstrated definite focal increased BP activity on delayed planar and/or SPECT imagings, with persistent in uptake upto 2 hrs after injection, which were characteristic of hemangiomas. In our study, only hemangiomas revealed evidence of focal increased BP activity on either delayed planar BP or SPECT images.

DISCUSSION

Most of HCHs are asymptomatic and usually found as an incidental finding during examination of the liver.[1] It is important to differentiate HCH from other focal hepatic lesions, in order to avoid inadvertent needle biopsy of a hemangioma, which can result in an extensive bleeding. Noninvasive diagnosis of HCH can be made easily using sequential Tc-99m RBC imaging, which is reported to be highly sensitive and specific in distinguishing HCH from other focal hepatic lesions.[3,17-19,25]

HCHs, particularly if they are larger than 2 cm in diameter, can be visualized with high accuracy by Tc-99m RBC imaging.[7,25] Like in our study, all HCHs equal to or larger than 2 cm in size were identified on the Tc-99m RBC images.

Front et al[18] had described the characteristic scintigraphic findings of HCH on Tc-99m RBC imaging as a perfusion/BP mismatch, which revealed decreased blood-flow activity on dynamic images and increased BP activity on delayed imagings. This perfusion/ BP mismatch is the key to the scintigraphic diagnosis of HCH, which is observed only in the HCH and has not been reported in any other type of focal hepatic lesions,[16-18] except for a rare case of hepatic angiosarcoma.[26] The perfusion/BP mismatch is highly specific for HCH and usually can be used to diagnose most hemangiomas 3 cm or larger on planar BP imagings.[17] However, in smaller lesions, they usually reveal normal perfusion during the blood-flow imagings with typically focal increased activity on delayed BP images. In our series, only 15 HCHs demonstrated this characteristic of perfusion/BP mismatch and all of them were equal to or larger than 3.5 cm in size (range 3.5-12.0 cm, mean 6.2 cm).

Pathologically, HCH consists of various sized blood-filled vascular spaces lined by a single layer of flat endothelial cells, which are separated by fibrous septae.[1] Therefore, sluggish blood-flow through these large vascular spaces produces a pattern of perfusion/ BP mismatch on Tc-99m RBC imaging, which reveals hypoperfusion on dynamic images with gradually increasing BP activity on sequential delayed imagings.[22] Since Tc-99m labeled RBC is an excellent intravascular marker, it can directly fill-in the vascular spaces of HCH and permit the typical scintigraphic finding of HCH.

While some hypervascular hepatic tumors such as hepatomas, hepatic adenomas, focal nodular hyperplasia or metastatic disease may reveal increased BP activity on delayed imagings like HCH, these lesions would be expected to demonstrate increased activity on early blood flow images. Thus, HCH and these tumors can be differentiated on the basis of the flow pattern during the dynamic imagings. HCHs usually demonstrate normal or hypoperfusion, whereas hepatomas and other hypervascular lesions typically reveal increased perfusion during the early dynamic images.[8,16,25]

Despite its highly sensitive for diagnosis of HCH, planar Tc-99m RBC imaging usually fails to detect HCH equal to or smaller than 2 cm in size and/ or deep-seated lesion within the liver parenchyma.[3,25] Therefore, SPECT image plays an important role as an adjunctive imaging, in order to enhance the image contrast and increase the sensitivity for detection of small or deep-seated lesions that beyonds the resolution of the planar imaging. Many reports have documented that additional SPECT image has significantly increased the sensitivity and specificity of the Tc-99m RBC imaging in the detection of small or deep-seated HCHs, due to improve the image contrast.[16,20,25,27,28] The use of SPECT imagings help to demonstrate the lesions equal to or smaller than 2 cm in size or deep-seated lesions , especially lesions adjacent to normal vascular structures, which can not be detected on conventional planar BP images. However, detection of HCH on SPECT imaging is primarily dependent on the size and location of the lesion. Therefore, the limitations of SPECT imaging for identifying small HCH are also described, particularly for lesions less than or equal to 1 cm in size or lesions located near major vascular structures, due to the limits of the resolution of conventional gamma camera.[20,25,27] However, higher resolution multi-headed SPECT system has shown to improve the performance for identifying as small as 0.5 cm HCH, as demonstrated by Ziessman et al.[29]

False negative and false positive studies on Tc-99m RBC imagings may also be encountered. False negative study may be found in cases of HCH with extensive thrombosis and/or fibrosis[16,17] and false positive study may be found in case of hepatic angiosarcoma, which is extremely rare in contrast to HCH.[26]

In our study, only HCHs revealed definite focal increased BP activity more than normal liver parenchyma on delayed BP imagings, with persistent up to 2 hr after injection. In 2 patients with metastatic disease and 4 cases with hepatoma showed focal increased perfusion during the blood-flow images with isoactive or slightly decreased BP activity on delayed images. Thus, isoactive or hypoactive lesions on delayed BP imagings are unlikely to be HCH and indicate a need for further investigations.[19]

Selective angiography is well accepted as the most sensitive and specific method for diagnosis of HCH, but its technically invasive, expensive and several complications make the procedure unsuitable for a routine investigation in these patients. Therefore, angiography should be reserved only for patients who can not be confidently diagnosed by other noninvasive diagnostic methods, including Tc-99m RBC imaging.[9]

Although US is very sensitive for detecting small HCH, its appearance of HCH is variable and nonspecific, especially in large lesions. HCH may appear as hyperechoic, mixed-echoic or hypoechoic lesion within the liver parenchyma.[4-10] Thus, this modality does not permit a definitive diagnosis of HCH.[8,9]

CT and MRI demonstrate superior sensitivity in the detection of lesions smaller than 2 cm, especially the deep-seated lesion adjacent to normal vascular structures. Although Tc-99m RBC imaging with SPECT has a lower sensitivity for small lesions less than 2 cm, as compared with the US, CT or MRI,

its specificity and positive predictive value for diagnosing HCH are reported to be very high and approach 100% in many series.[16,19,25]

As compared with dynamic CT, MRI or selective angiography, Tc-99m RBC imagings with either planar or SPECT image is noninvasive, economical, low-risk, easily performed and relatively specific method for diagnosing HCH. Therefore, Tc-99m RBC imaging of the liver has recently been recommended as a procedure of choice for the differential diagnosis of HCH from other focal hepatic lesions. Because of its high sensitivity and high specificity, focal hepatic lesions that demonstrate the classic scintigraphic findings of HCH on Tc-99m RBC imagings,usually require no further diagnostic workup.[14,19,25]

In conclusion, Tc-99m RBC imaging is highly recommended as a further noninvasive investigation of choice to confirm the suspected diagnosis of HCHs found on US and/or CT images, especially in patients with a history of known primary malignancy or high-risk for developing hepatocellular carcinoma. Furthermore, additional SPECT imagings should be routinely performed as an adjunctive method in the evaluation of suspected hemangioma patients. We also consider that Tc-99m RBC imaging of the liver is probably the best noninvasive imaging modality available for confirming the suspected diagnosis of HCH found on other noninvasive diagnostic images.

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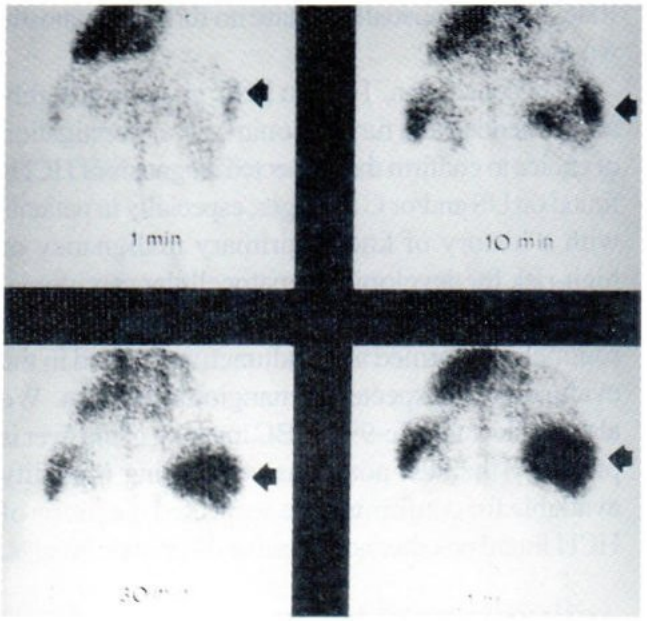
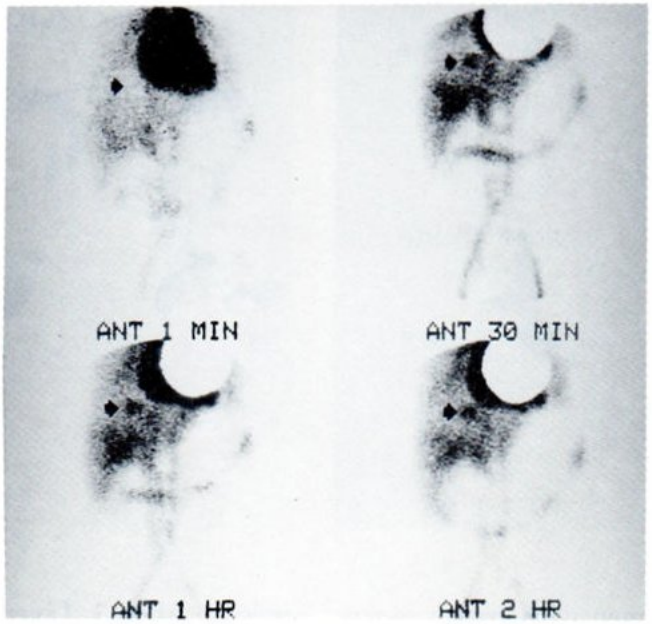
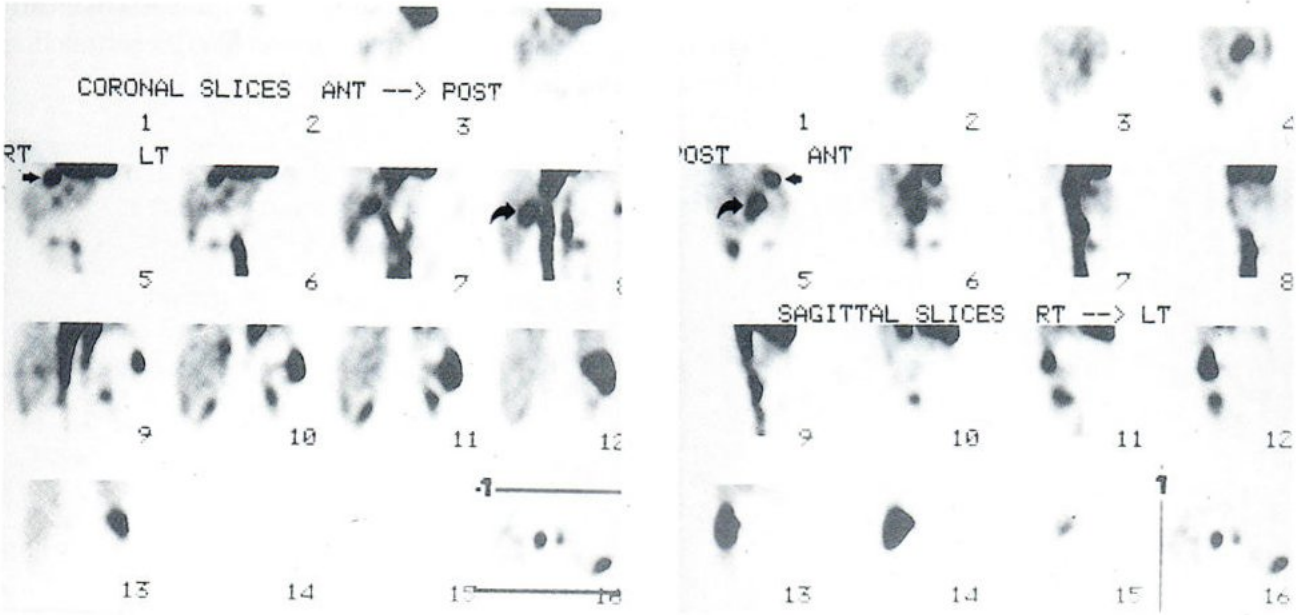


Fig.1 A 36-year-old man in whom the US shows a large 8 x 10 cm mixed hyperechoic lesion at the posterior of right hepatic lobe. Tc-99m RBC blood-flow study shows decreased perfusion to the lesion. Serial planar BP imagings on the posterior view demonstrate peripheral enhancement with subsequent central enhancement and complete fill-in of BP activity (arrows) at 1 hr after injection, which is typical for a large HCH.

BP = Blood Pool

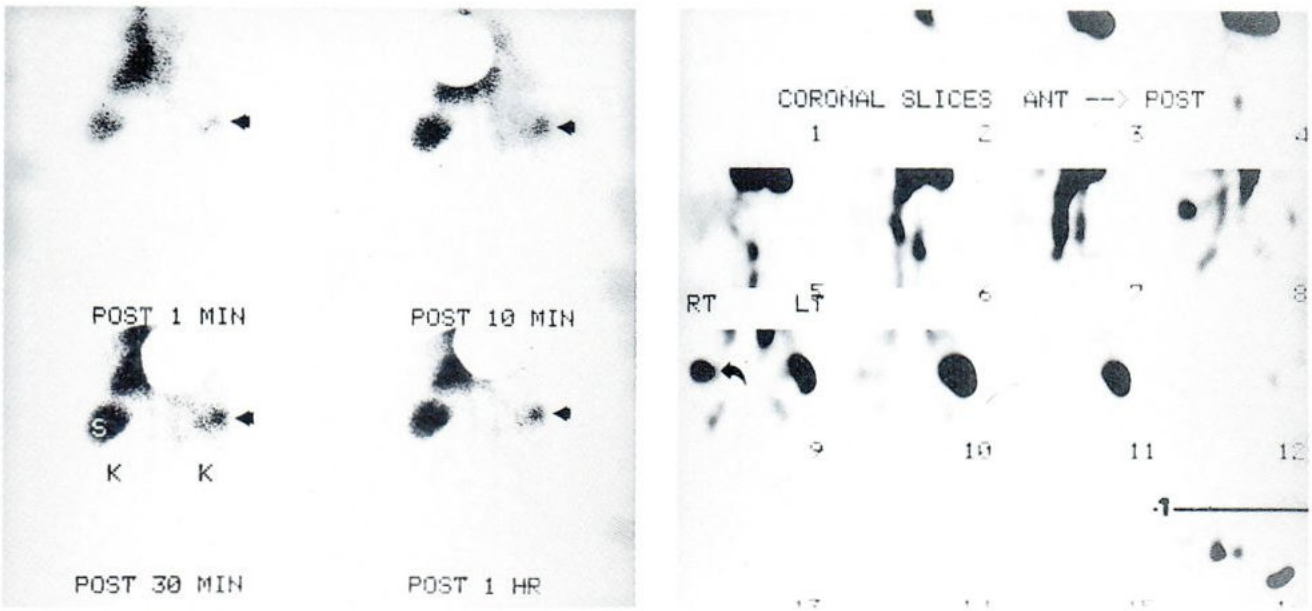


A



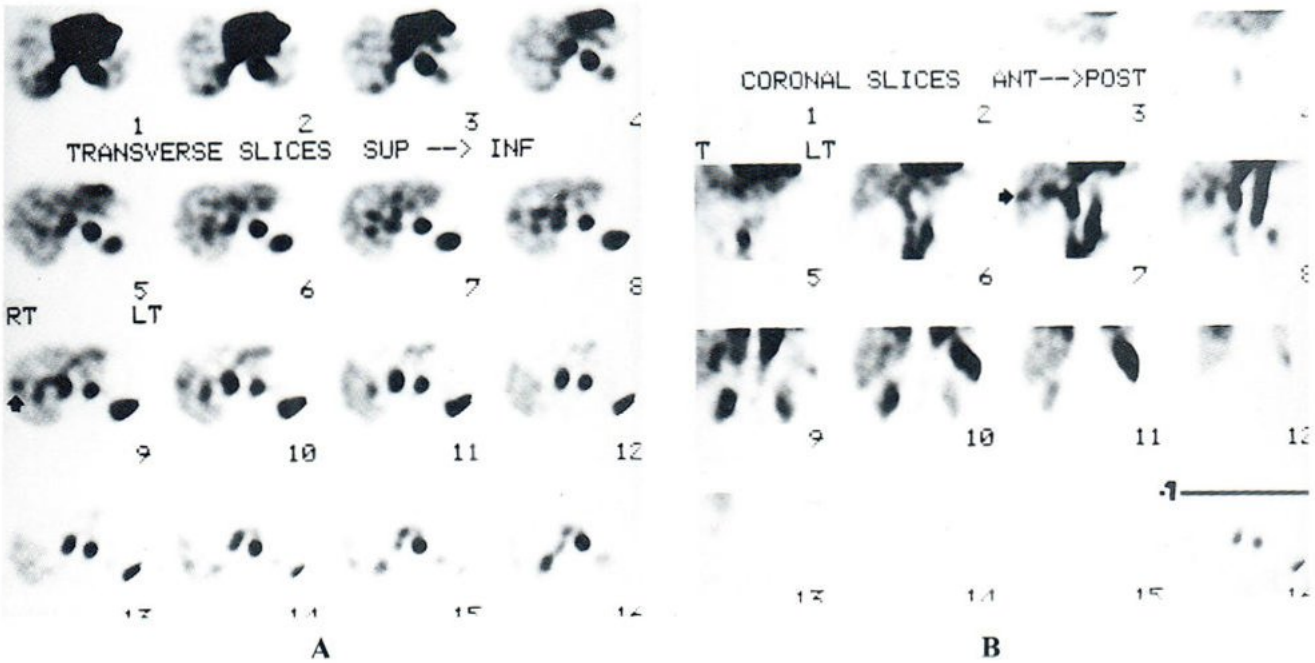
B C

Fig.2 Multiple HCHs in a 54-year-old man with right upper quadrant discomfort. LiverUS shows two hyperechoic lesions, one is 3 x 3 cm at dome of right hepatic lobe and another is 3 x 3.5 cm adjacent to IVC. Serial planar BP images**(A)** are positive only in the lesion at dome of right lobe(arrows). Coronal**(B)** and sagittal **(C)** SPECT images clearly demonstrate these two HCHs, which reveal discrete areas of intensely increased BP activity corresponding to the US findings.(Straight arrow shows lesion at dome of right lobe and curve arrow shows another lesion deepseated within the liver parenchyma adjacent to IVC.)



A B

Fig.3 A 52-year-old woman with known ovarian carcinoma stage 3. Liver US shows a 2.6 x 2.7 cm hyperechoic lesion at right hepatic lobe. Tc-99m RBC blood-flow images reveal normal perfusion to the lesion. Serial BP images**(A)** show gradually increased BP activity within the right hepatic lesion (arrows), which is persisted up to 2 hr after injection. Coronal SPECT images**(B)** clearly demonstrate a focal increased BPactivity within the lesion (arrow) much greater than the surrounding liver paren chyma, compatible with a hemangioma. (S = spleen, K = kidney)



A B

Fig.4 A 51-year-old woman with a history of hepatitis B virus carrier, in whom the US shows a 2 cm hyperechoic lesion at anterior segment of right hepatic lobe. Blood-flow and serial planar Tc-99m RBC images do not show any abnormality. Transverse**(A)** and coronal**(B)** SPECT images clearly demonstrate a focal increased BP activity within the right hepatic lesion(arrow), consistent with a small hemangioma.