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Nontumorous decrease in Tc-99m GSA accumulation

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Nontumorous decrease in ^{99m}Tc-GSA accumulation has not been well covered in the literature. Understanding of this phenomenon is, however, essential for accurate evaluation of regional hepatic function. Scintigrams (transaxial SPECT) of 269 patients who underwent ^{99m}Tc-GSA liver scintigraphy were reviewed for the presence of nontumorous decreases in ^{99m}Tc-GSA accumulation. Nontumorous decreases in ^{99m}Tc-GSA accumulation were seen in 32 of 269 patients (12%). In 16 of the 32 patients (6%), nontumorous decreases in ^{99m}Tc-GSA accumulation corresponded to regional decrease in portal venous flow. The causes of such decrease in portal venous flow were portal thrombus of hepatocellular carcinomas in eight patients, portal venous stenosis or occlusion by hilar cholangiocarcinomas in five patients, inter alia. In eight patients (3%), the regions with decreased ^{99m}Tc-GSA accumulation correlated with massive hepatic necrosis in fulminant hepatitis, scar in hepatitis, or confluent fibrosis in cirrhotic liver. In two patients (0.7%) with hilar cholangiocarcinomas, the possible causes of lobar decrease in ^{99m}Tc-GSA accumulation were thought to be lobar decrease in portal venous flow, lobar biliary stasis, or both. In four patients (1.5%), the exact causes of nontumorous decrease in ^{99m}Tc-GSA accumulation could not be determined.

Key words: liver, technetium-99m GSA, portal venous flow decrease

INTRODUCTION

Technetium-99m diethylenetriamine-penta-acetic acid-galactosyl human serum albumin (^{99m}Tc-GSA) is an analog ligand to asialoglycoprotein receptor which is used widely for radionuclide imaging of the liver. Uptake of ^{99m}Tc-GSA depends on the presence of normally-functioning hepatocytes.[1–3] Most hepatic neoplasms apart from some tumor-like conditions such as focal nodular hyperplasia[4] show an accumulation defect on hepatocyte-oriented scintigraphy.[5] We previously studied ^{99m}Tc-GSA liver scintigraphy in cases with hepatic regional attenuation/signal intensity differences on CT/MRI.[6,7] The study revealed that nontumorous decreases in ^{99m}Tc-GSA accumulation could occur in cases of decrease in regional portal venous flow and confluent hepatic fibrosis, etc. These decreases were not situated in the tumor itself, but situated in the hepatic parenchyma. A case of localized decrease in ^{99m}Tc-GSA accumulation due to segmental biliary obstruction was also reported.[8] The incidence of these nontumorous decreases in ^{99m}Tc-GSA accumulation and the relative percentages of the various causes are, however, unknown. The aim of this study is to evaluate the possible conditions causing such nontumorous decreases in ^{99m}Tc-GSA accumulation, to clarify the incidences of them, and to calculate the relative percentages of the various causes.

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MATERIALS AND METHODS

Imaging Techniques

The patients were examined in the supine position with a dual-head rotating gamma camera interfaced to a minicomputer (GCA7200A/DI; Toshiba, Tokyo, Japan). A parallel-hole, low-energy, high-resolution collimator was used. Immediately after intravenous administration of 185 MBq of ^{99m}Tc-GSA (Nihon Medi-Physics, Nishinomiya, Japan), dynamic images were acquired in

15-sec frames for 30 min. Next, single-photon emission computed tomography (SPECT) was performed after 35–45 min by the acquisition of 60 projectional images over 360° in a 128 × 128 matrix. Spatial resolution was calculated as 10 mm. The data obtained were reconstructed for transaxial sections 6.9 mm thick. Coronal and sagittal reconstruction was also performed in some more recent cases. A Butterworth filter was used for prereconstruction, and final reconstruction was performed with a Ramp filter. A Chang attenuation correction was applied.

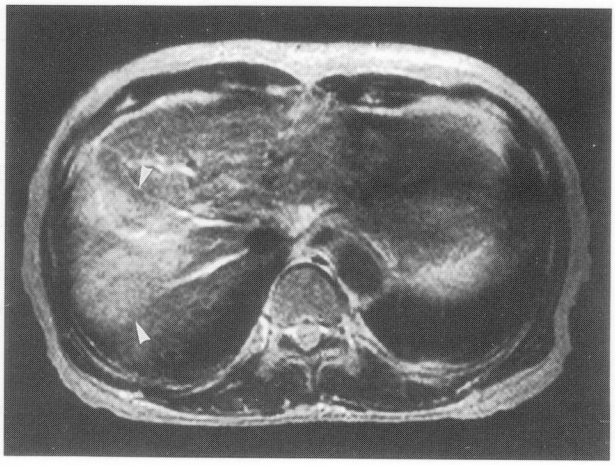
Evaluation

Four hundred and thirty ^{99m}Tc-GSA liver scintigraphies were done at our institution over about four years to evaluate hepatic functional reserve. In this series, 63 patients underwent repeated studies (twice in 46 patients, three times in 13, four times in three, and five times in one), so that 345 patients underwent ^{99m}Tc-GSA liver scintigraphy at least once during this period. Of these 345 patients, 76 were excluded from this study because their ^{99m}Tc-GSA liver scintigrams and/or CT/MRI were not available and therefore could not be evaluated. Two radiologists experienced in radionuclide and liver imaging evaluated the images of the remaining 269 patients. These were 182 men and 87 women aged 19–86 years old. (mean; 57 years). Of these 269 patients, 130 had hepatocellular carcinomas, 46 underwent ^{99m}Tc-GSA liver scintigraphy to evaluate liver cirrhosis, and 19 had cholangiocarcinomas.

The readers first reviewed the CT/MRI of the 269 patients and recognized the contour of the liver, and masses when such existed. They then reviewed ^{99m}Tc-GSA SPECT for the presence of nontumorous decreases in ^{99m}Tc-GSA accumulation.[6] In patients with repeated ^{99m}Tc-GSA scans, abnormality was defined to exist when nontumorous decrease in ^{99m}Tc-GSA accumulation was seen in at least one study. The site, size and relationship with hepatic masses were recorded. Causes of these nontumorous decreases in ^{99m}Tc-GSA accumulation were clarified as far as possible by reviewing CT/MRI and/or angiograms and by checking surgical records. The incidence of each cause was calculated and variously compared.

RESULTS

Nontumorous decreases in ^{99m}Tc-GSA accumulation were seen in 32 of 269 patients (12%). The distribution of the decreases were lobar in 13 (2 in the right lobe and 11 in the left lobe), segmental in 6, subsegmental or less in 7, and non-segmental in 6 patients. In 16 patients (6%), nontumorous decreases in ^{99m}Tc-GSA accumulation corresponded to regional decrease in portal venous flow (Fig. 1). Portal vein stenosis or occlusion was seen on angiography in 12 of the 16 patients and confirmed on surgery in



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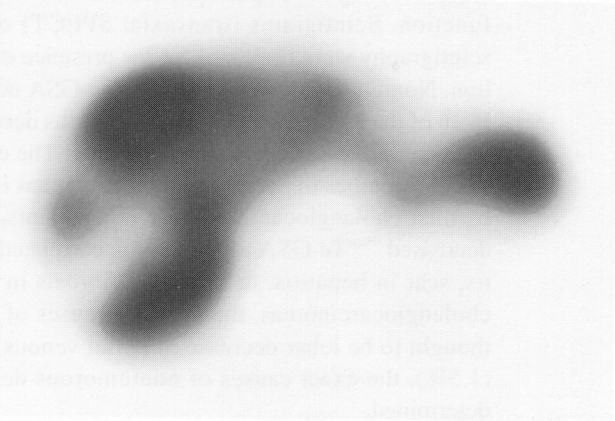

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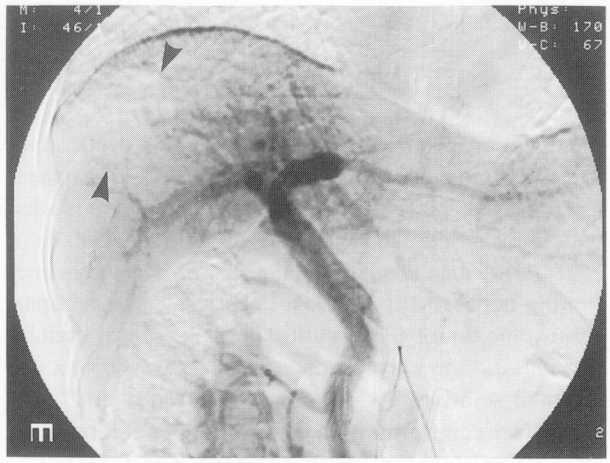

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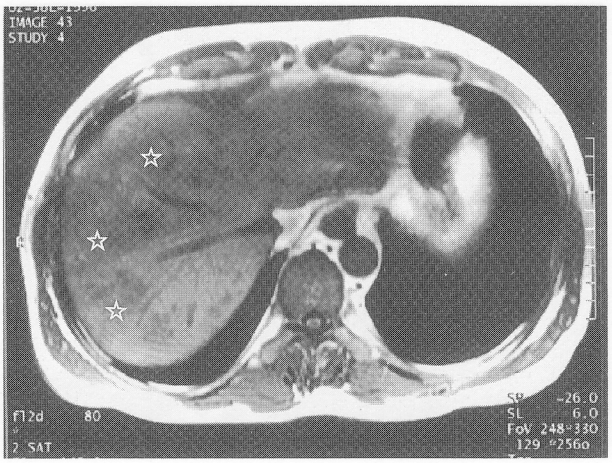
Fig. 1 A 68-year-old woman with hepatocellular carcinoma and thrombus in the right anteriosuperior portal vein. a: T2-weighted MR image shows segmental hyperintensity in the anteriosuperior segment (arrowheads). b: Obvious decrease in ^{99m}Tc-GSA accumulation in the segment is seen on transaxial SPECT. c: On portogram via superior mesenteric artery, the right anteriosuperior branch and portal perfusion in the corresponding segment were absent (arrowheads).



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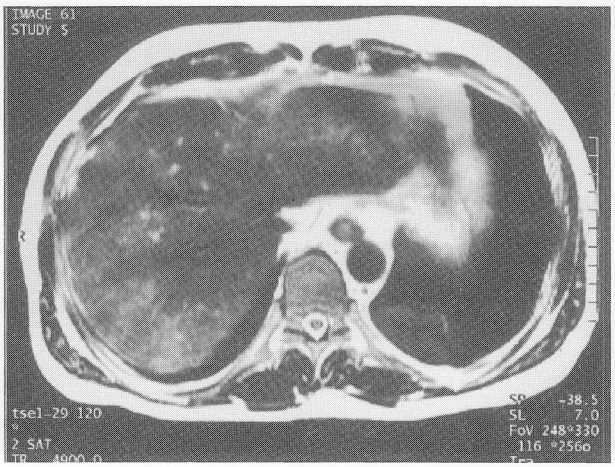

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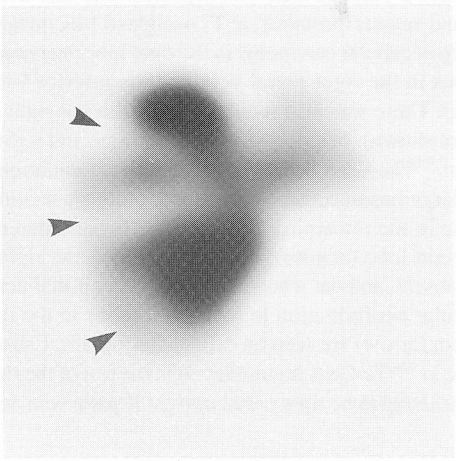

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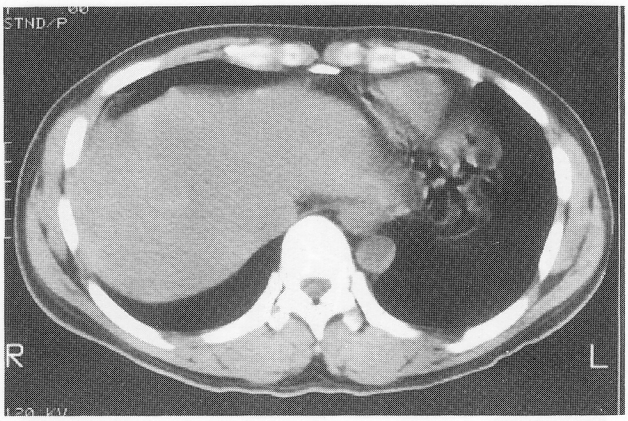
Fig. 2 A 51-year-old man with confluent fibrosis in advanced cirrhosis. a: T1-weighted MR image shows wedge-shaped hypointensities in the periphery of the right hepatic lobe (stars). b: The regions are slightly hyperintense on T2-weighted images. c: Wedge-shaped decreases in ^{99m}Tc-GSA accumulation are shown on transaxial SPECT (arrowheads).



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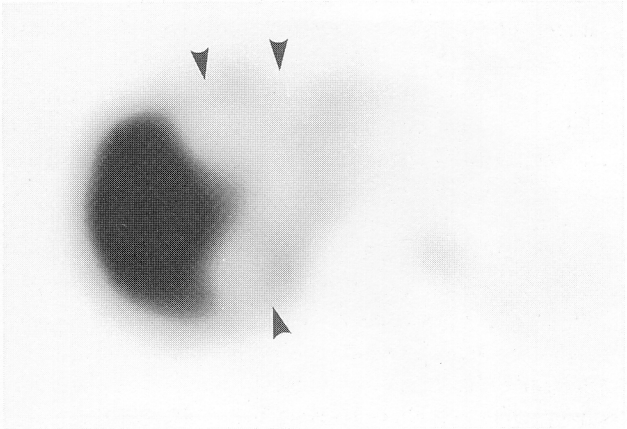

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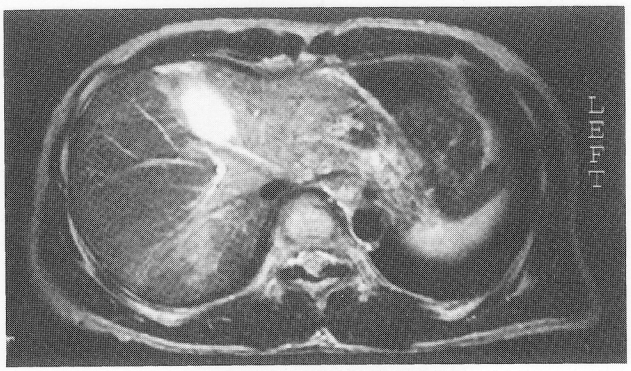

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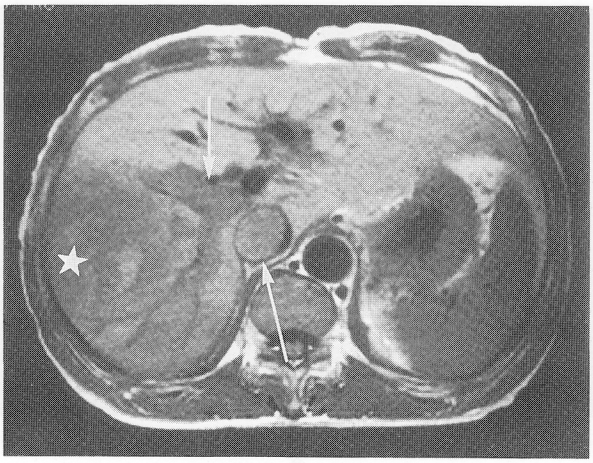
Fig. 3 A 39-year-old man with massive hepatic necrosis in fulminant hepatitis. a: Unenhanced CT performed near the onset of the disease show no attenuation abnormality in the liver. b: ^{99m}Tc-GSA transaxial SPECT performed about one month after CT shows decreases in accumulation in the right posterior segment and the left lobe (arrowheads). c: T2-weighted MR image obtained 5 months after CT shows hyperintensity in the corresponding regions. ^{99m}Tc-GSA scan might be able to predict regions which might develop massive hepatic necrosis in fluminant hepatitis.



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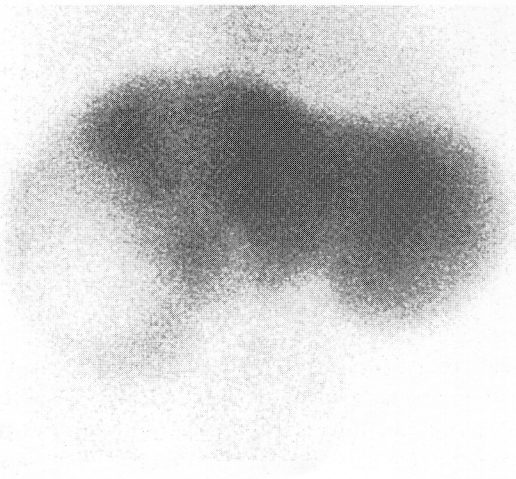

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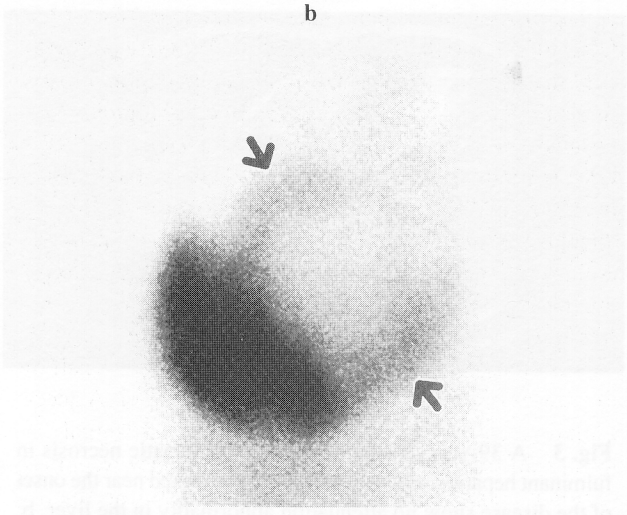

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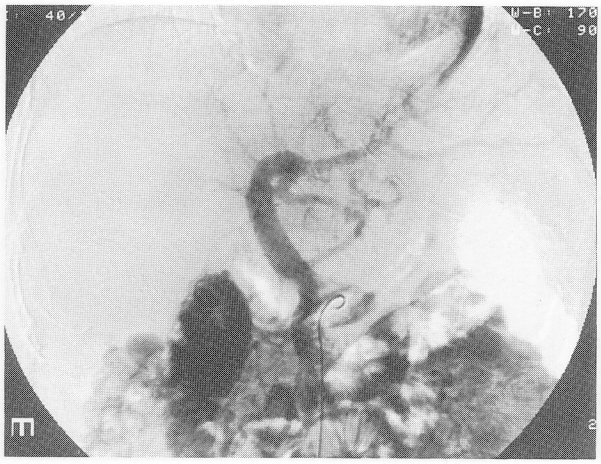

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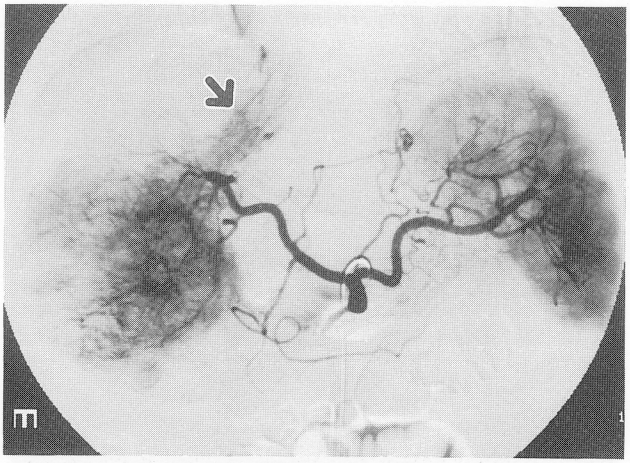

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Fig. 4 A 62-year-old man with hepatocellular carcinoma with portal and venous thrombus. a: T1-weighted MR image shows large hepatocellular carcinoma in the right lobe (star) and tumor thrombus in the right portal vein and the inferior vena cava (arrows). There was also tumor thrombus in the right hepatic vein (not shown). b, c: Right anterior oblique and right lateral views of ^{99m}Tc-GSA scintigraphy show accumulation defect due to large hepatocellular carcinoma. Note an accumulation decrease in the remaining nontumorous hepatic parenchyma in the right lobe (arrows). d: On portogram, the right portal vein is absent, and the whole right lobe lacks portal perfusion. e: Vascular neoformation in tumor thrombus in the right hepatic vein (arrow) are seen on celiac arteriogram. Cause of the decrease in ^{99m}Tc-GSA accumulation in the rest of the right lobe was considered to be right portal or right hepatic vein occlusion or both.

two patients. In one patient with idiopathic portal hypertension, portal vein stenosis was not seen, but portal perfusion decrease was seen in the periphery of the liver.[7] In two patients, portal vein stenosis was recognized on postcontrast CT. In one patient, portal vein stenosis was confirmed by contrast-enhanced MR portography.

The causes of such a decrease in portal venous flow were portal thrombus of hepatocellular carcinomas in eight patients, portal venous stenosis or occlusion by hilar cholangiocarcinomas in five, portal venous stenosis by hepatic abscess in one, portal venous thrombosis in one, and there was one patient with idiopathic portal hyperten-

sion.[7] Most regions with a decrease in portal venous flow were hypodense on precontrast CT, hypointense on T1-weighted MR images, and hyperintense on T2-weighted images. Most of them had regional enhancement in the arterial phase of dynamic CT/MRI.

In eight patients (3%), the regions with decreased ^{99m}Tc-GSA accumulation were wedge-shaped or band-like in the periphery of the liver. They were hypoattenuating on precontrast CT, hypointense on T1-weighted MR images, and hyperintense on T2-weighted images. Of these eight patients, six had suffered from advanced liver cirrhosis (Fig. 2), one had developed fulminant hepatitis (Fig. 3), and one had suffered from autoimmune hepatitis. In one patient with advanced cirrhosis, confluent fibrosis was confirmed during surgery for hepatocellular carcinoma.

In two patients (0.7%) with hilar cholangiocarcinomas, lobar decrease in ^{99m}Tc-GSA accumulation was seen. Ipsilateral portal vein obstruction was seen on angiography. On CT, the bile duct was dilated in both hepatic lobes but predominant in the lobe with decreased ^{99m}Tc-GSA accumulation. In one patient (0.4%), with intrahepatic stones, bile duct dilatation was seen in the left lobe. In one patient (0.4%) with hepatocellular carcinoma, ^{99m}Tc-GSA accumulation was decreased in the right lobe, and both the right portal vein and the right hepatic vein were occluded. In this case, the cause was considered to be a decrease in portal venous flow or occlusion of the hepatic vein or both (Fig. 4). Figures 1–4 show representative cases of each cause. In four patients (1.5%), the causes of nontumorous decrease in ^{99m}Tc-GSA accumulation could not be determined. Of these four, one patient with a decrease in ^{99m}Tc-GSA accumulation in the left lobe had hepatocellular carcinomas, but there was no evidence of a decrease in the portal venous flow in the left lobe. Two patients had hepatocellular carcinomas and metastatic tumors, respectively. Decreases in ^{99m}Tc-GSA accumulation were seen in the peripheral hepatic parenchyma to the tumors. Portal vein or hepatic vein stenosis or occlusion by the tumors was the suspected cause. This, however, could not be confirmed. One patient with liver cirrhosis had a decrease in ^{99m}Tc-GSA accumulation in the left lobe and right anterior segment. The cause of this decrease could not be determined.

DISCUSSION

Nontumorous decrease in ^{99m}Tc-GSA accumulation has been poorly covered in the literature. Understanding of this phenomenon is, however, important for evaluating regional hepatic reserve. In order to properly evaluate the phenomenon, all serial cases, including those with homogeneous ^{99m}Tc-GSA accumulation needed to be reviewed. This we did for all available cases undergoing ^{99m}Tc-GSA liver scintigraphy over a period of about four years. In this study, the incidence of nontumorous decrease in ^{99m}Tc-GSA accumulation proved to be surprisingly high (12%). These nontumorous decreases in ^{99m}Tc-GSA accumulation can often be misdiagnosed for hepatic masses on the scintigrams alone. Moreover, such inhomogeneity of ^{99m}Tc-GSA accumulation directly suggests inhomogeneity of regional hepatic function and this indicates some possible problems when dealing with hepatic diseases.

In the first place, these inhomogeneities may cause a discrepancy between hepatic reserve evaluation by ^{99m}Tc-GSA and by other anatomical methods such as CT volumetry.[9] CT cannot express regional function or functional density of the liver, because it estimates regions of poor function as normal parenchymal volume and may overestimate these regions. Moreover, to know these functional inhomogeneities of the liver is essential in planning therapy for hepatic disease. In cases with biliary stasis, percutaneous biliary decompression or stent insertion should be performed preferentially to save a region or lobe rich in ^{99m}Tc-GSA accumulation which retains better function than other regions or lobes. In planning surgery too, such functional inhomogeneity needs careful consideration. Lobectomy which resects a lobe with poor function and ipsilateral to the mass may have few serious consequences. When extended lobectomy is planned, on the other hand, one should be careful because it resects part of a contralateral lobe which still functions well.

In this study, decrease in portal venous flow was defined as existing when stenosis or obstruction of a portal branch was seen on angiograms or enhanced CT. Biliary stasis was defined as existing when dilatation of the intrahepatic bile duct was recognized on CT/MR images at that time or before percutaneous drainage. When dilatation of the intrahepatic bile duct is obviously predominant in a region, it has been established that biliary stasis in the region was more severe than in other regions, so it became a candidate cause for a relative decrease in ^{99m}Tc-GSA accumulation. In two cases, the causes of a decrease in ^{99m}Tc-GSA accumulation were thought to be a lobar decrease in portal venous flow, lobar biliary stasis, or both. As for the other pathological conditions, each typical finding on CT/MRI previously reported[10–14] was referred to.

A decrease in portal venous flow accounted for half of the causes of nontumorous decrease in ^{99m}Tc-GSA accumulation. In evaluating regional attenuation/signal intensity differences on CT/MRI, we previously reported regional decrease in ^{99m}Tc-GSA accumulation due to a decrease the portal venous flow.[6,7] This was thought to correlate with the phenomenon where hepatic parenchyma with decreased portal venous flow becomes hypoattenuating on precontrast CT, hypointense on T1-weighted MR images, and hyperintense on T2-weighted images. Edema, hepatocyte depletion, and fibrosis often occur in regions of decreased portal venous flow. As a result, hepatic attenuation/intensity abnormalities occur on CT/MRI. Normally-functioning hepatocytes may de-

crease due to these histological changes and ^{99m}Tc-GSA accumulation in the region may also fall.[6] We previously evaluated cases where both lobar decrease in portal venous flow and lobar biliary stasis existed. Hilar cholangiocarcinomas often involve both the portal vein and the bile duct. In such cholangiocarcinomas, lobar decrease in ^{99m}Tc-GSA accumulation correlated better with the decrease in portal venous flow than with the severity of biliary stasis.[15] These phenomena resembled the lobar atrophy following obstruction of the ipsilateral portal vein from hilar cholangiocarcinoma which was reported by Takayasu et al.[16] and Hann et al.[17]

The interrelationship of massive hepatic necrosis in fulminant hepatitis,[10] scar in hepatitis of insidious onset and/or without definite coma,[11] and confluent hepatitis in cirrhotic liver[12,13] has not been properly clarified. They do, however, appear similar on pre- and postcontrast CT and MRI.[11] In this study, we dealt with them as a single pathological condition. In these regions, decreases in ^{99m}Tc-GSA accumulation were seen, and making up one fourth of all causes of nontumorous decrease in ^{99m}Tc-GSA accumulation, they were the second most frequent cause (after portal venous flow decrease). The number of hepatocytes tends to manifest a sharp decrease in these necrotic or scar-like lesions. In the same manner as on CT/MRI, these lesions can be misdiagnosed as neoplasms. Knowledge of CT/MRI findings typical of these conditions and any clinical history of fulminant hepatitis or long-term cirrhosis is essential. In the case of fulminant hepatitis, a decrease in ^{99m}Tc-GSA accumulation was seen in the region of massive necrosis at a relatively early stage when precontrast CT was unable to show any abnormality. This appears to suggest that ^{99m}Tc-GSA liver scintigraphy is better able to predict at an earlier stage those regions which might develop massive hepatic necrosis.

In one case ^{99m}Tc-GSA accumulation was decreased in the left lobe and the cause was thought to be lobar biliary stasis. In the patient with hepatocellular carcinoma, ^{99m}Tc-GSA accumulation was decreased in the right lobe, and both the right portal vein and the right hepatic vein were occluded. The cause of the decrease was considered to be right portal or right hepatic vein occlusion or both. Differences in the regions on CT which correspond with the right portal vein and right hepatic vein were well described by Murata et al.[18] In our case, however, deformity of the liver by hepatocellular carcinoma and the limited spatial resolution of SPECT made it difficult to distinguish between the two regions, and closer determination of the possible cause proved impossible.

Several limitations were perceived with this study. First, we failed to review 76 of 345 patients due to the unavailability of CT/MRI or ^{99m}Tc-GSA scintigrams. This did not seem to produce any significant bias, however, in patient population or proportion. During the study, we confined ourselves to introducing the basic principle of hepatic functional inhomogeneity expressed by ^{99m}Tc-GSA. More accurate prediction of postoperative hepatic reserve and any safe extension of hepatectomy indication with regard to these phenomena need to be further evaluated and discussed.

In conclusion, we reviewed ^{99m}Tc-GSA scintigrams of a series of 269 patients and studied the incidence and causes of nontumorous decrease in ^{99m}Tc-GSA accumulation, a surprisingly not uncommon occurrence. Half of these decreases correlated with regional decrease in the portal venous flow.

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