Evaluation of Embolization Effect of Hepatocellular Carcinoma by Hepatic Arterial Flow Study with ^{99m}Tc-MAA SPECT

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=국문 초록=

간암에서 색전술의 효과를 평가하는데 있어서 ^{99m}Tc-MAA SPECT를 이용한 간동맥 혈류 검사의 의의

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본 저자들은 ^{99m}Tc-MAA를 이용하여 정상 간조직에 대한 간암의 상대적인 미세 혈류량을 조사하고 간암 환자에서 간동맥 색전술을 시행 후 상대적인 혈류량의 변화를 검사함으로써 간동맥 색전술의 효과를 알아 보고자 하였다.

여덟명의 간암 환자들을 대상으로 하였는데, 이 중 다섯 명은 조직 생검으로, 그리고 나머지 세 명은 임상적, 그리고 방사선학적으로 진단되었다. 3내지 4 mCi의 ^{99m}Tc-MAA를 2 cc의 생리식염수에 혼합하여 간동맥내에 위치된 카테터(catheter)를 통하여 1분간에 걸쳐 서서히 주입한 후 바로 동적 영상을 4초 간격으로 1분동안 얻었으며, 이어서 정적 영상과 SPECT를 시행하였다.

간동맥 혈관 조영술만을 시행한 세명의 환자에서 ^{99m}Tc-MAA를 주입하자마자 주변 간 조직에서 비해 간암내에 강한 방사능 섭취를 보였으며, 주변 간조직에 대한 간암의 방사능 섭취율은 6.5 이상이었고, 그 범위는 6.5에서 19였으며 평균은 12.5였다.

간동맥 색전술을 시행한 5명 중 4명에서 주변 간조직에 대한 간암의 방사능 섭취율이 심하게 감소하였다(0.5~1.3). 또한 색전된 부위는 색전술 후 시행한 추적 간동맥 혈관 촬영상에서 보다 동위원소 검사에서 잘 관찰되었다. 간동맥 혈관 촬영상에서 완전히 색전된 것으로 생각된 한 환자에서 동위원소 검사상 간암에 강한 방사능 섭취를 보였다(주변 간조직에 대한 간암의 방사능 섭취율 : 7.0). 따라서 본 저자들은 ^{99m}Tc-MAA를 이용한 간 동맥 혈류 검사는 간암에서 색전술의 효과를 정확히 평가할 수 있는 유용한 검사법으로 이용될 수 있으리라 생각한다.

Key Words: Hepatocellular carcinoma, Hepatic-arterial embolization, Radionuclide study

INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most common malignancies in Asia and Sub-Saharan Africa[1~3]. The prognosis of untreated HCC is very poor with a reported survival time of only 1. 6 to 4 months[3,4]. Treatment method is one of the most important factors in prognosis[5]. After hepatic arterial embolization (HAE) began to be applied in the treatment of HCC, the overall survival of patients with inoperable HCC has been improved[6,7]. Hepatic angiography (HAA) has been used to assess devascularization in the tumor immediately after HAE, the radionuclide intraarterial infusion scintigraphy[8,9] with ^{99m}Tc-MAA with single photon emission computerized tomography (SPECT)[10] was proven to be effective for quantifying differences of microvascularity between tumor and normal tissue. These albumin particles, average 30~40 μm in diameter (range of 10~90 μm), are held in the first arteriolar-capillary bed which is the level of the circulation that presumably supplies nutrients vessels for the continued tumor growth. Therefore ^{99m}Tc-MAA activity in the liver should directly reflect the relative density of the microvasculature patency at the time of injection.

The present study demonstrates the density of the functional microcirculation of HCC relative to that of normal liver effectively and provides the information of the effect of HAE (the changes in tumor vascularity).

MATERIALS AND METHODS

Eight patients with HCC [(seven men and one woman: age range, 40~67 yrs (mean, 59 yrs)] were included. The diagnosis of HCC was made by using various imaging techniques (ultrasound, computed tomography, hepatic angiography), positive tests for tumor markers (serum alpha-fetoprotein [AFP]), and/or by histologic examination. All of the patients had a history of chronic liver disease. Six patients had nodular HCC, one had multinodular HCC, and another one had diffuse HCC. The mean diameter of the nodular HCC, as determined by angiograms or computed tomography scans was 5 cm (range: 3~9 cm). Five patients with nodular HCC underwent hepatic angiography followed by chemoembolization using iodized oil (Lipiodol: Andre-Gelbe Laboratories, France) mixed with doxorubocin hydrochloride (Adriamycin: Adria, Dublin, Ohio) and gelatin sponge particles (Gelfoam: Upjohn, Kalamazoo, Mich.) (1 mm^3).

Selective angiography without chemoembolization was performed in remaining three patients (1 nodular, 1 multinodular, and 1 diffuse). When the blood flow of the segmental branches supplying the tumor ceased on angiograms, the embolization procedure was finished. After HAE or HAA, the catheter was secured in position at the feeding artery for HAE, and common hepaic artery for HAA and the patient was transported to nuclear medicine department for a MAA perfusion scan. Briefly, the MAA flow studies were performed within 1 hr of HAA or HAE. Three to four mCi (111~148 MBq) of ^{99m}Tc-MAA in 2 cc of saline was injected through the catheter at a rate of 50~100 ml/hr with aid of an external infusion pump and then flushed with 2 cc saline for a minute. Following the dynamic serial images with every 4 sec per frame for 1 minute, static images with total counts of 500,000 counts were obtained.

SPECT was performed using a Siemens Orbiter 7500 (Siemens), 64 views was obtained at 5.6 degree angular increment with an acquisition time of 10 seconds per view. Three tomographic images of transverse, coronal, and sagittal views were reconstructed by a filtered back projection method using a Butterworth filter (cut of frequency 0.5 cycle/cm, order No. 5). The images were displayed in a 64×64 matrix size.

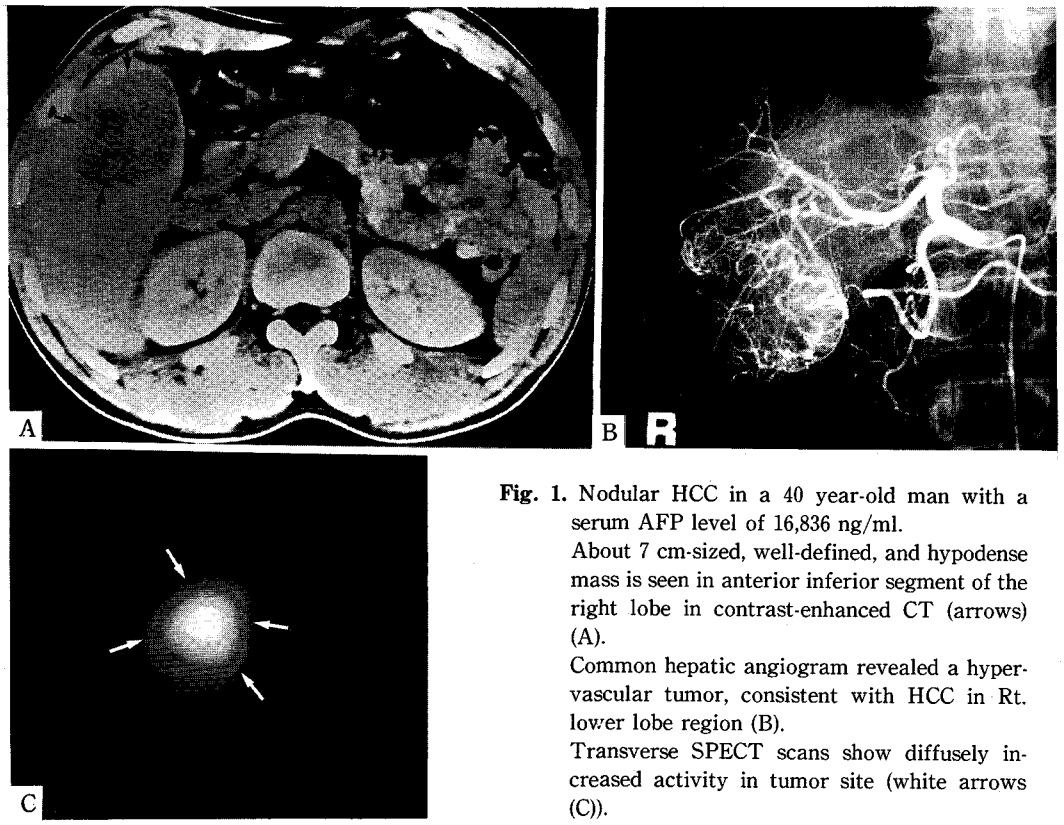

Fig. 1. Nodular HCC in a 40 year-old man with a serum AFP level of 16,836 ng/ml.
About 7 cm-sized, well-defined, and hypodense mass is seen in anterior inferior segment of the right lobe in contrast-enhanced CT (arrows) (A).
Common hepatic angiogram revealed a hypervascular tumor, consistent with HCC in Rt. lower lobe region (B).
Transverse SPECT scans show diffusely increased activity in tumor site (white arrows (C)).

The radionuclide flow studies and SPECT were evaluated in regard to the segmental or lobar distribution, the relative intensity of radionuclide in the tumor to the adjacent uninvolved liver and the changes in the patterns of arterial distribution, particularly in patients who underwent HAE. The patterns of blood flow distribution and vascularity were compared with those of hepatic angiograms.

The ratios between the ^{99m}Tc-MAA entrapment in the center of a tumor nodule and that in the adjacent uninvolved liver were obtained on static views.

RESULTS

1. Nonembolized HCC

The ^{99m}Tc-MAA hepatic-arterial dynamic flow studies revealed marked increased radioactivity in hepatoma relative to extratumoral liver in all of the three patients. The ratio of radioactivity in HCC relative to extratumoral liver (T/E ratio) on static views were greater than 6.5 (mean: 12.5).

Nodular HCC showed homogeneously increased activity almost exclusively within the tumor area, but little activity in remaining areas of the normal liver (Fig. 1). In multinodular HCC with arteriovenous (hepatic and portal) shunts, the microcirculation density of hepatocellular carcinoma was lower than that in uninvolved left liver parenchyme in dynamic flow image, but greater in late static image (T/E ratio, 12). Diffuse HCC with portal vein thrombosis showed greater radioactivity in the tumor areas than those in eithr nodular or multinodular HCC (T/E ratio, 19) on both dynamic and delayed images.

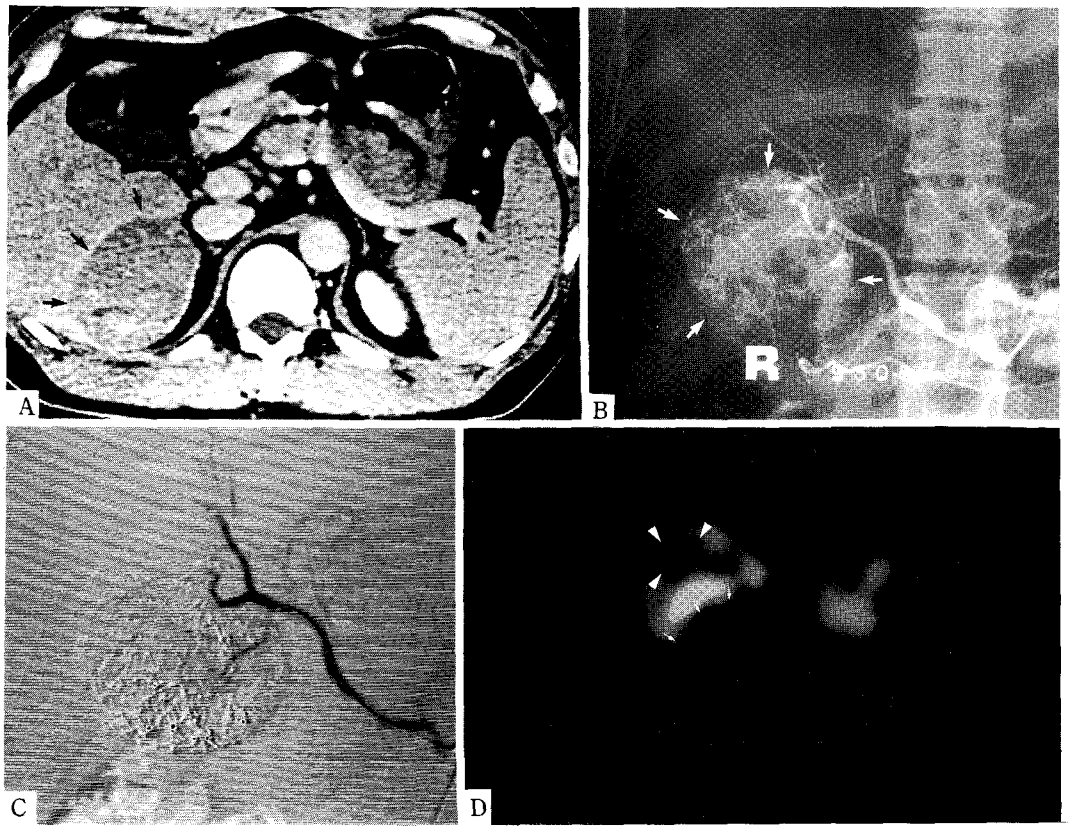

Fig. 2. Nodular HCC in a patient of 36 year-old man with a serum AFP level below 3 ng/ml.
About 6 cm-sized, well-defined, and hypodense mass is seen in posterior inferior segment of the right lobe on CECT (arrows) (A).
Celiac angiograms show hypervascular and nodular mass supplied from the posterior segmental artery of the right hepatic artery (arrows) (B).
On digital subtraction angiograms, there is no blood flow into the tumor and remaining segmental arteries are well opacified (C).
After HAE, transverse scan reveals remarkably decreased radioactivity in the tumor site (white arrows) with markedly increased radioactivity in the non-embolized hepatic segments (T/E ratio; 0.5) and also demonstrates markedly decreased radioactivity in anterior inferior portion of right lobe of liver (white arrowheads) (D).

2. Embolized HCC

In four of the five patients who underwent HAE, T/E ratio were remarkably decreased (0.5~1.3) and reflux of radiotracer into the nonembolized hepatic segment were found. The embolized areas were better delineated in radionuclide study than in post-embolization HAA (Fig. 2).

In the one who considered to be embolized completely in HAA, an area of strong radiouptake within the tumor was disclosed in the radionuclide study (T/E ratio: 7.0) (Fig. 3).

DISCUSSION

Early report demonstrated that the arteriolar density in hepatocellular carcinoma evaluated by a SPECT study was approximately 20~30 times greater than that of the surrounding normal tissue and uniform. Our study also showed increased activ-

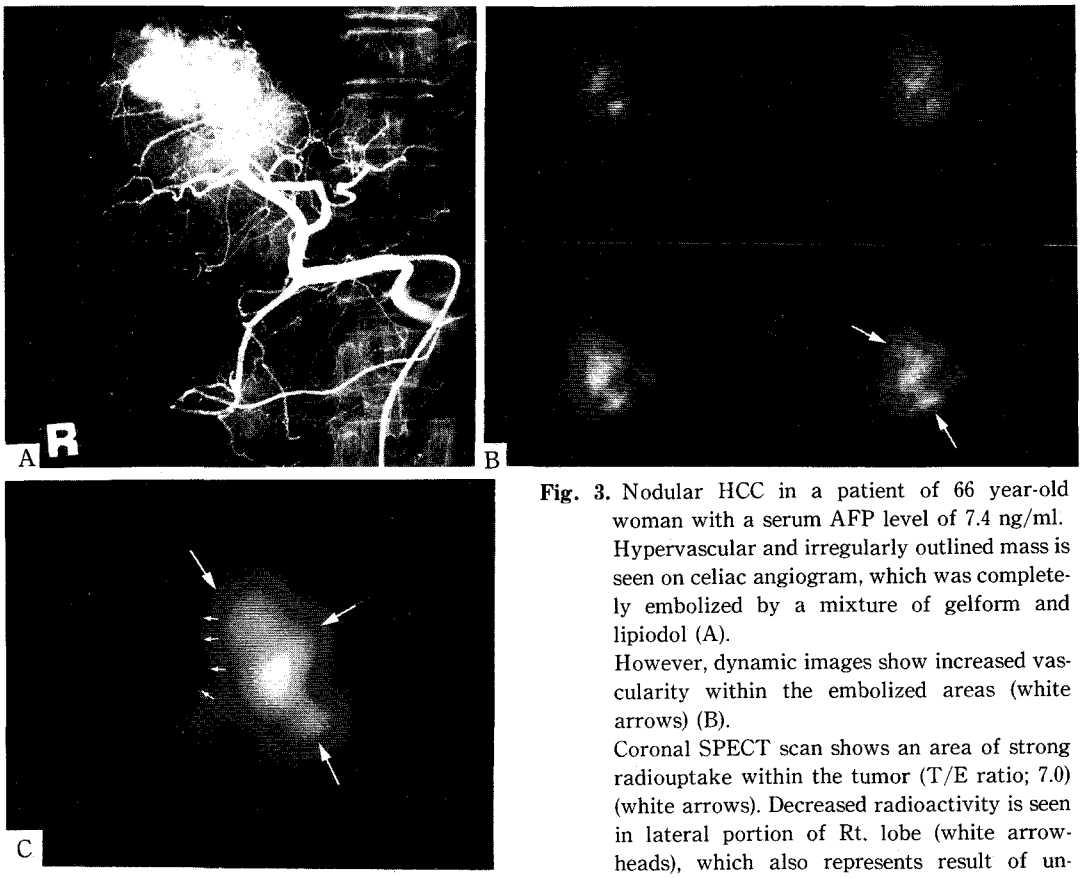

Fig. 3. Nodular HCC in a patient of 66 year-old woman with a serum AFP level of 7.4 ng/ml. Hypervascular and irregularly outlined mass is seen on celiac angiogram, which was completely embolized by a mixture of gelform and lipiodol (A).
However, dynamic images show increased vascularity within the embolized areas (white arrows) (B).
Coronal SPECT scan shows an area of strong radiouptake within the tumor (T/E ratio; 7.0) (white arrows). Decreased radioactivity is seen in lateral portion of Rt. lobe (white arrowheads), which also represents result of unexpected embolization (C).

ity within tumor areas[11].

Nodular hepatoma showed increased activity in both early and delayed images, while multinodular hepatomas being A-V shunt showed decreased perfusion on early stage, but high tracer uptake on delayed image. Diffuse HCC with portal vein thrombrosis (PVT) showed much greater radioactivity in tumor areas than those in either nodular and multinodular. The A-V shunt and PVT may affect the radionuclide density in tumor areas[12], accurate mechanisms remain to be resolved.

In the patients who underwent HAE, several methods have been used to document hepatic arterial flow distribution. Standard cut-film angiography require injection of contrast medium at a rate of 4~6 ml/sec. This injection rate may give misleading information about hepatic arterial flow dynamics and it may be difficult to document hepatic perfusion into the hepatic tumor because previously deposited lipiodol density in HCC may mask tumor staining. On the other hand, DSA, if performed with a low flow rate (0.5 ml/sec)-which still greater than that of the radionuclide study-has enabled to evaluate arterial flow pattern satisfactorily. It should be noted, however, that DSA performed through the pump side port may not depict the small branches of the hepatic artery because of difficulty in injection of an adequate volume of contrast material. Planar hepatic perfusion scanning has been used to evaluate hepatic flow distribution in hepatic tumors followed by HAE. It can show variable distribution patterns[13]. SPECT combined with planar hepatic perfusion

scanning in our study to evaluate the changes in vascularity of HCC followed by HAE showed not only the changes in the tumor vascularity, but also the embolized areas which were better delineated than post-embolization HAA (Fig. 2, 3).

In conclusion, we suggest that hepatic-arterial flow study and SPECT using ^{99m}Tc-MAA can be a valuable method to assess the embolization effect in HCC. We will further evaluate the existence of residual tumor and time to revascularization of tumor after HAE.

SUMMARY

This study was aimed to compare the density of the functional microcirculation of hepatocellular carcinoma (HCC) with normal liver and to investigate the effect of hepatic-arterial oily chemoembolization (HAE) by radionuclide examination.

Methods : Eight patients with HCC proven by biopsy in five, and clinically and radiologically in three were included. The mixture of 2 cc normal saline with three to four mCi of ^{99m}Tc-MAA was infused through a hepatic-arterial catheter for a minute. Dynamic images were obtained at a rate of 4 sec per frame for a minute, and static images and SPECT were followed.

Results : In three patients who underwent hepatic arterial angiography (HAA) alone, radioactivity was markedly increased in tumors compared to the adjacent liver immediately after infusion of ^{99m}Tc-MAA. The ratios of tumoral and extratumoral uptake (T/E ratio) were above 6.5 (range; 6.5~19, mean; 12.5). In four of the five patients who underwent superselective HAE, T/E ratio were remarkably decreased (0.5~1.3). The areas of embolization were better delineated in radionuclide study than in postembolization HAA. In the other one who was considered to be embolized completely on HAA, strong radiouptake in the tumor was disclosed (T/E ratio; 7.0).

Conclusions : Therefore hepatic-arterial flow study with radionuclide imaging using ^{99m}Tc-MAA can be a valuable method to assess the accurate embolization effect in HCC.

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