Lipiodol Enhanced CT Scanning of Malignant Hepatic Tumors

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Abstract

From August 1984 to March 1991, 41 patients with malignant liver tumors, 30 males and 11 females, aged 30–75 years were treated at Ramathibodi Hospital with injection of mitomycin-C lipiodol emulsion into the tumor *via* the feeding artery followed by embolization of the feeding artery with gelfoam particles.

The patients comprised 30 cases of hepatocellular carcinoma, 4 cases of cholangiocarcinoma and 7 cases of metastatic tumors of which one was from CA stomach, three were from CA breast, and three from CA colon. The vascularity of the tumor was assessed in angiogram obtained prior to treatment and retention pattern of lipiodol in the tumor was evaluated in lipiodol–enhanced CT scan images taken 2-4 weeks following therapy.

The results showed that lipiodol CT scan images exhibited four patterns of lipiodol retention in the tumor appearing as opacity as follows (1) homogenous (2) heterogeneous (3) ring - like and (4) none. Lipiodol retention pattern appeared to be somewhat related to vascularity of the tumor. Most of the hypervascular tumors such as hepatocellular carcinoma had homogeneous lipiodol accumulation pattern if the tumor size was less than 5 cm. Metastatic tumors and cholangiocarcinoma showed heterogeneous or ring – like pattern of lipiodol accumulation because they were relatively hypovascular. Hypervascular hepatocellular carcinoma may exhibit heterogeneous or ring – like pattern if they are larger than 5 cms, and have multiple feeding arteries, necrosis or AV shunting. Hepatocellular carcinoma with AV shunting may not show any lipiodol accumulation at all.

Key word : Lipiodol CT Scan, Malignant Hepatic Tumors

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Injection of iodized oil (lipiodol) into the hepatic artery for the diagnosis and treatment with anticancer drugs of hepatocellular carcinoma was first described by Nakamura et al in 1979[1]. Several reports have subsequently confirmed the role and usefulness of this new technique[2-4]. It has also been applied in the management of hepatic metastasis[5-7]. Studies with intra-arterial injection of radioactive microsphere[8] or lipiodol[9] to hepatic tumors lend support to the theory that selective uptake of lipiodol by tumors correlates with the distribution of blood to tumors and normal tissues; however, some recent articles have revealed that lipiodol is accumulated in vascular tumors such as hepatocellular carcinoma as well as in poorly vascular tumors, for example, a metastatic tumor[10,11].

For many years, transcatheter oily chemoembolization (TOCE) using lipiodol as a carrier for anticancer drugs has been accepted as the treatment of choice for inoperable hepatocellular carcinoma [4,12,13]. It is also an alternative treatment for liver metastatic tumors, especially from colorectal carcinoma[14].

One routine practice to assess and follow the outcome of treatment of cancer is the tracking of tumor markers such as alfa fetoprotein and carcinoembryonic antigen. In this regard, lipiodol CT scan is another good modality for assessing the results of TOCE and for planning further management of tumors[2,3]. Only a few reports describing the patterns of lipiodol CT scan of different malignant hepatic tumors treated with TOCE have been published[10,15,16]. The present investigation was an additional study to ascertain the usefulness of lipiodol CT scan in determining the patterns of lipiodol CT scan of different malignant hepatic tumors treated with TOCE.

Objective

1. To study the pattern of lipiodol CT scan images of the liver taken 2-4 weeks after TOCE.
2. To evaluate the lipiodol CT scan patterns in relation to the vascularity of the tumor seen in the angiogram.
3. To evaluate the factors such as AV shunting, tumor size, multiple tumor feeder arteries which will modify the lipiodol CT scan patterns of malignant hepatic tumor after treatment with TOCE.

MATERIAL AND METHOD

From August 1984 to March 1991, 41 cases of malignant hepatic tumors, 30 males, 11 females, aged 30-75 years, were admitted to Ramathibodi Hospital for treatment with TOCE. All tumors were proven by histological examination with liver biopsy prior to the procedure. The patients comprised 30 cases of hepatocellular carcinoma, 4 cases of cholangiocarcinoma, and 7 cases of hepatic metastatic tumors of which 1 was from CA stomach, 3 were from CA breast and 3 were from CA colon.

CT scan of the upper abdomen was obtained in every case with and without nonionic water-soluble contrast media given intravenously. The size of the tumor in the enhanced CT scan was measured in transverse and antero-posterior dimensions. On the following days, angiography of the celiac artery and superior mesenteric artery was performed and followed by selective angiography of the right or left hepatic artery that fed the tumor. Next, the angiogram of the tumor was graded for its vascularity by two attending radiologists as hypovascularity, moderate vascularity or hypervascularity. Then, A 2:1 emulsion of iodized oil and mitomycin- C solution was delivered to the tumor *via* the feeding hepatic artery. The emulsion was prepared by shaking manually about ten times, a mixture of 10 ml iodized oil and 3-5 ml solution con-

Fig. 1. Plain film abdomen after TOCE shows lipiodol retained in hepatocellular carcinoma of the liver (arrows).

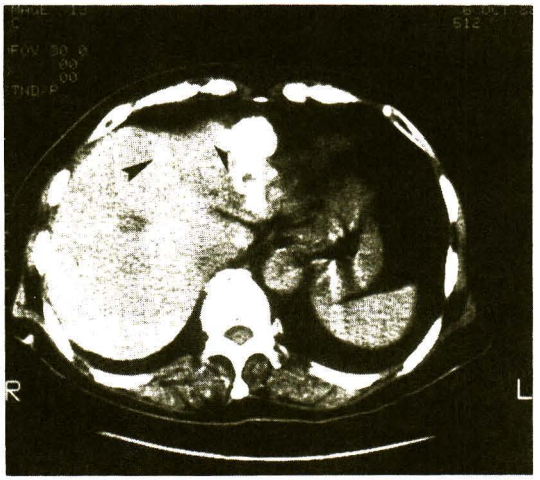

Fig. 2. Lipiodol CT Scan image of hepatocellular carcinoma after TOCE shows lipiodol in a tumor representing necrosis of tumor (small arrow) and in a small daughter of satellite nodule which is not seen in routine CT scan (big arrow head).

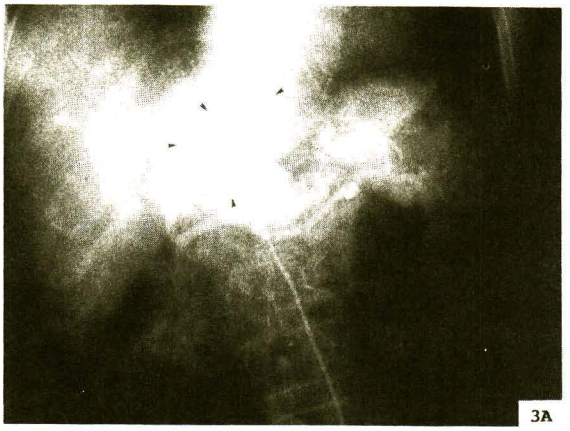

Fig. 3A. Delay capillary phase of celiac angiogram demonstrates hypervascularity of a hepatocellular carcinoma in the left lobe of liver supplied by left hepatic artery (arrow head).

taining 20-30 mg mitomycin-C (Kyowa, Hakko, kogyo, Tokyo) and having a specific gravity equal to that of the iodized oil. The finished emulsion appeared as homogenous to the naked eyes.

Finally, selective embolization of the tumor vascular feeders was performed with gel-

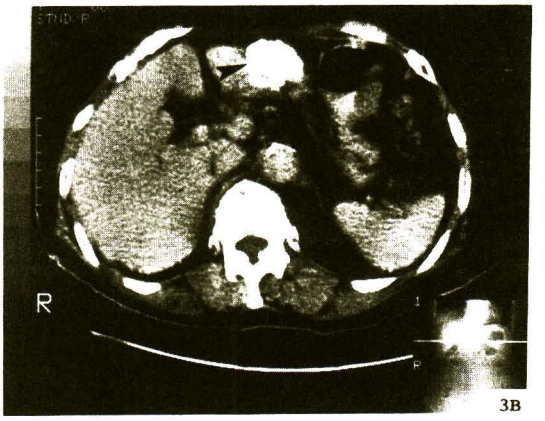

Fig. 3B. Lipiodol CT Scan of the same liver shown in Fig. 3 A shows homogenous accumulation of lipiodol.

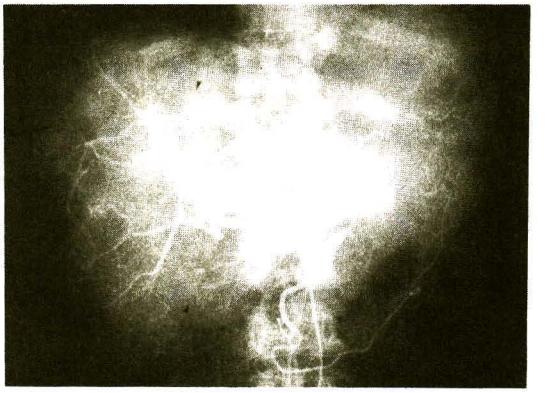

Fig. 4A. Selective proper hepatic angiogram of cholangiocarcinoma shows a hypovascular mass in the right lobe of the liver (arrow).

foam particles (gelatin sponge) size 1x1 mm gradually until cessation of arterial blood flow.

Two to four weeks after TOCE, lipiodol CT scan of the liver with and without intravenously administered water-soluble contrast media was carried out with GE 9800 and its accumulation patterns were evaluated by two interventional radiologists.

RESULTS

Tumor uptake of lipiodol

During fluoroscopy, lipiodol would be visualized after intra-arterial injection to move quickly towards the periphery and could be seen in

plain radiograph (Fig. 1). Hepatocellular carcinoma and metastatic tumor appeared as dense areas in CT scan images. Satellite nodules of hepatocellular carcinoma were detected in lipiodol CT scan images (Fig. 2) but may not appear in CT scan images with and without water soluble contrast intravenously.

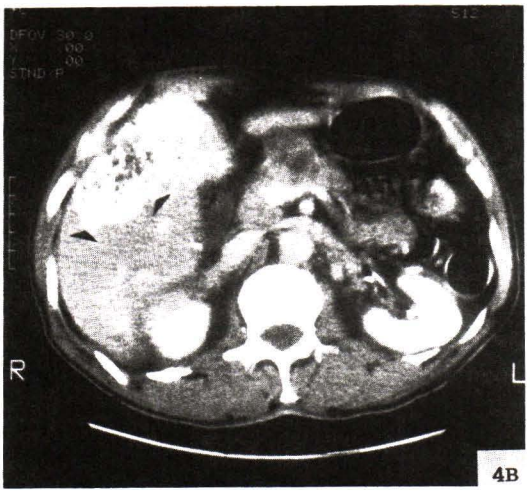

Fig. 4B. Lipiodol CT scan of the same liver shown in Fig. 4 A taken 2 weeks after TOCE reveals heterogenous accumulation of lipiodol in right lobe liver (arrow head).

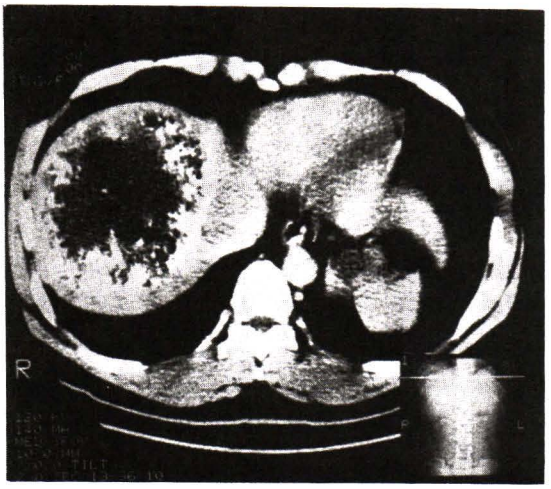

Fig. 5. Lipiodol CT Scan of a tumor metastasized from CA colon shows peripheral accumulation of lipildol with center defect.

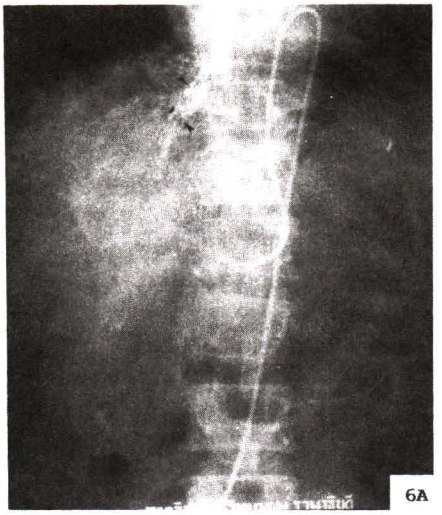

Fig. 6A. Late capillary phase of selective proper hepatic angiogram of hepatocellular carcinoma (case 5, Table 3) shows AV shunt from right hepatic artery to hepatic vein (big arrow) with tumor cast seen (small arrow head).

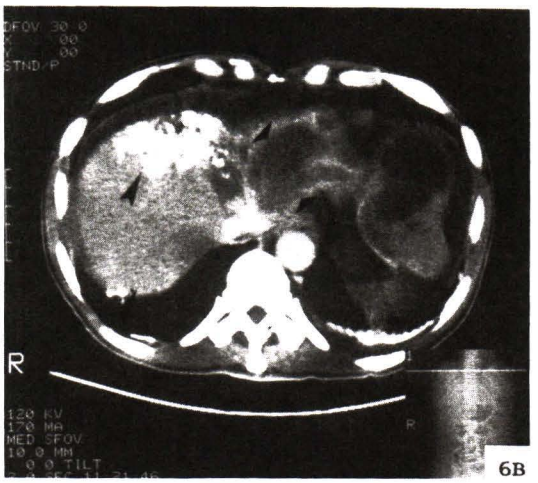

Fig. 6B. Lipiodol CT scan of the same liver shown in Fig. 6 A taken 4 weeks after TOCE shows heterogenous retention of lipiodol in the right lobe of the liver (big arrow head) and no accumulation of lipiodol in left lobe liver due to AV shunting as seen in Fig. 6A (small arrow head).

Pattern of lipiodol CT scan of tumor

Lipiodol CT scan images taken two to four weeks after TOCE showed different patterns of opacity representing residual lipiodol, as follows.

1. Homogenous opacity.
2. Heterogenous opacity.
3. Peripheral or ring-like opacity and
4. No opacity.

They are shown in Fig. 3, 4, 5, and 6 respectively.

The relationship of tumor vascularity and lipiodol CT scan accumulation patterns are summarized in Table 1 and Table 2. Factors which may influence accumulation of lipiodol in the tumor are tabulated in Table 3.

DISCUSSION

Lipiodol is composed of iodinated ethyl esters of fatty acids of poppy seed oil. It contains 37 per cent iodine and has been used for several

Table 1. Vascularity of tumor seen in angiogram and accumulation pattern of lipiodol seen in CT scan image of different types of tumor in the liver.

Tumor	N	Vascuarity Appeared in angiogram	Accumulation pattern of lipiodol CT scan image			
			Hemogenous	Heterogenous	Ring-Like	None
Hepatocellular carcinoma	24	Hypervascular	19	4	1	
	4	Moderate hypovascular	1	1	2	
	2	Mild hypovascular		1		1
Stomach metastasis	1	Moderate hypovascular		1		
Breast metastasis	3	Moderate hypovascular	1	2		
Colon metastasis	3	Moderate hypovascular		1	2	
Cholangiocarcinoma	4	Mild hypovascular		4		

N = Number of patient

Table 2. Relation between accumulation pattern of lipiodol CT scan images and vascularity of tumors appeared in angiogram.

Tumor Type	Lipiodol CT scan Pattern	Vascularity Appeared in Angiogram
Hepatocellular carcinoma	Homogenous	Hypervascular
Colon metastasis	Ring - like opacity	Moderate hypovascular
Breast metastasis	Heterogenous opacity	Moderate hypovascular
Stomach metastasis	Heterogenous opacity	Moderate hypovascular
Cholangio carcinoma	Heterogenous opacity	Mild hypovascular

Table 3. Tumor size and certain features of the hepatocellular carcinoma.

Case	Size (cm)	Artery feeding	Vascularity	Lipiodol CT scan Pattern	Miscellaneous
1	16 x 16	IFA, RHA	Hypervascular	Ring – Like	Necrosis
2	9 x 6	RHA, MHA	Hypervascular	Heterogenous	AV shunt
3	9 x 8	RHA	Hypervascular	Heterogenous	
4	12 x 10	RHA, MHA, IFA	Hypervascular	Heterogenous	
5	5 x 5 (Rt)	RHA, MHA	Hypervascular	Heterogenous	
	7 x 6 (Lt)	LHA	Mild hypovascular	None	AV shunt
6	8.3 x 5.3	RHA	Hypervascular	Heterogenous	

IFA = Inferior phrenic artery; RHA = Right hepatic artery; MHA = Middle hepatic artery; LHA = Left hepatic artery

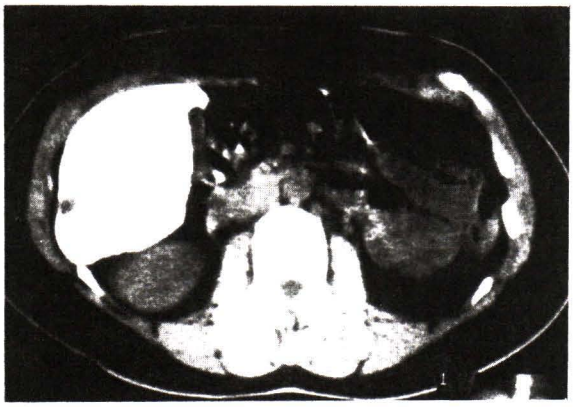

Fig. 7. Lipiodol CT scan of hepatocellular carcinoma taken only one week after TOCE shows the entire liver opacified with lipiodol, which makes it impossible to identify the exact location of the tumor.

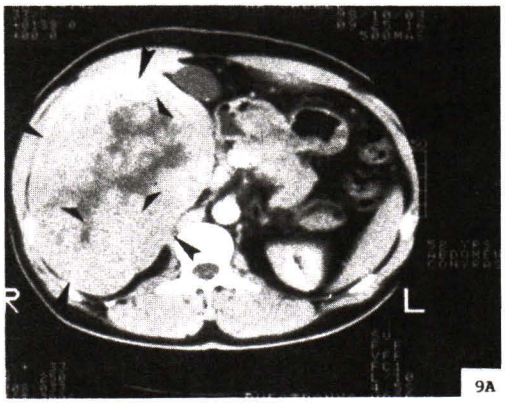

Fig. 9A. Contrast enhanced CT scan of liver shows a big necrotic hepatocellular carcinoma. (big arrow head) The small arrow points to the center of necrosis.

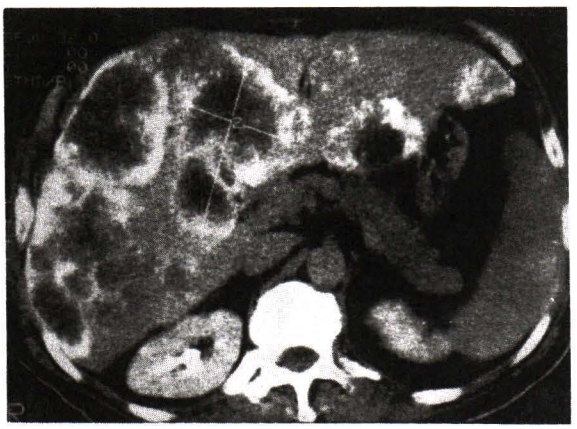

Fig. 8. Lipiodol CT scan of a tumor metastasized from CA colon to the liver after TOCE, demonstrates typical ring-like deposit of lipiodol in the tumor.

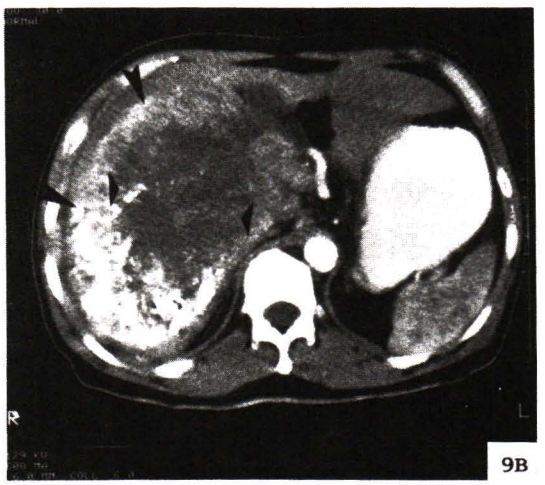

Fig. 9B. Lipiodol CT scan, the same liver shown in Fig. 9A, taken 4 weeks after TOCE, shows peripheral accumulation of lipiodol with central defect due to tumor necrosis seen in Fig. 9A (small arrow points necrotic area, big arrow points to lipiodol accumulation in the tumor).

years for the diagnosis and treatment of hepatic malignancy[2-6,10,17]. When a mixture of lipiodol and anticancer drug such as mitomycin-C was injected into the feeding hepatic artery, it was initially distributed throughout the entire liver. The lipiodol completely opacified the whole liver as evident from lipiodol CT scan images taken within one week; this hindered evaluation of the tumor (Fig. 7). The lipiodol droplets in normal hepatic parenchyma were phagocytized by kupffer cells of the liver and were washed out from the normal hepatic tissue *via* hepatic lymphatic system and portal vein in about 2 to 4 weeks. Due to lack of lymphatic system and leaky characteristic of the neovasculatures of the tumor, the lipiodol was still

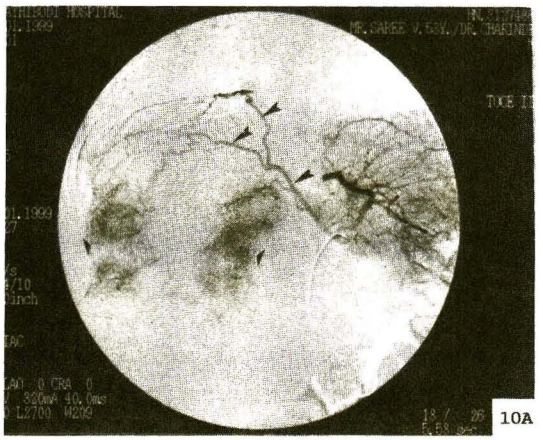

Fig. 10A. Selective angiogram of the same liver shown in Fig. 9A and 9B shows multiple tumor arterial feeders, from inferior phrenic arteries (big arrow head) and lipiodol accumlation (small arrow head) are illustrated.

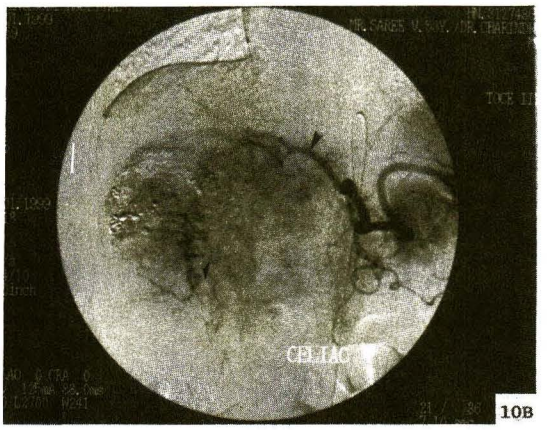

Fig. 10B. Feeder from right hepatic artery (big arrow) and lipiodol accumulation (small arrow) are illustrated.

retained in the tumor while the lipiodol in the normal hepatic parenchyma had already been washed out from the liver. The lipiodol remaining in the tumor could be seen in plain films and even better in CT scan images. For hepatocellular carcinoma it could remain longer in the tumor and could be followed by CT scan for up to 6-12 months. In a hypovascular metastatic tumor and cholangiocarcinoma, the lipiodol was only retained for up to 3 months. Accordingly, the optimal time to perform lipiodol CT scan after TOCE should be 4 weeks for hepatocellular carcinoma[17], and 2 to 4 weeks for hypovascular metastatic tumors or for cholangiocarcinoma[5].

As compared in Tables 1 and 2, tumor vascularity seen in the angiogram correlated with opacity in lipiodol CT scan images. Most of the hepatocellular carcinoma with hypervascularity appeared as homogenous opacity in lipiodol CT scan images. Due to hypovascularity, metastatic tumors and cholangiocarcinoma presented them selves in lipiodol CT scan images as heterogenous or ring like opacity, a pattern similar to that reported by Raby N. and Karani[15].

Hepatic tumor metastasized from carcinoma of the colon may present itself in lipiodol CT scan images as a typical pattern of ring-like opacity as shown in Fig. 8. Miller DL and Timothy J[16]. believed that the ring-like opacity was due to accumulation of lipiodol in the peritumor hepatic sinusoids and not in the tumor itself. A histological study has revealed lipiodol droplets plugging the sinusoids and permeation of tumor cells into these sinusoids[16]. It has been shown that hepatic metastasis can cause peritumoral congestion[7], or dilatation[18], which may account for the peritumoral or ring-like opacity seen in lipiodol CT scan images.

Referring to Table 3, some hepatocellular carcinomas with hypervascularity appeared as heterogenous opacity in lipiodol CT scan images or as ring-like pattern as in case 1. These patterns were mostly due to a combination of factors, namely, tumor size over 5 centimeters, tumors with necrotic center as in case 1 and case 2 (Fig. 9), multiple feeding arteries (Fig. 10), and vascular shunting from hepatic artery to portal vein or hepatic vein as seen in case 2 also is an important factor to modify lipiodol CT scan images. In case 5, the left lobe of the liver did not show any opacity in the lipiodol CT scan as a result of shunting of blood through the hepatic vein (Fig. 6).

In summary, lipiodol CT scan is useful for differential diagnosis between hypervascular tumor and hypovascular tumor. Most hepatocellular carcinomas exhibit homogenous opacity in lipiodol CT scan images while metastatic tumors or cholangiocarcinoma show heterogenous or ring-like opacity. The pattern seen in lipiodol CT scan images depends on many factors such as size of the tumor, necrosis, number of tumor feeding arteries and AV shunting.

The pattern of lipiodol accumulation after TOCE may be an adjunct for differentiating the type of malignant hepatic tumor if liver biopsy is not performed initially for histological examination.

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ลิพิโอดอล–ซีทีสแกนในการวินิจฉัยมะเร็งตับทั้งชนิดปฐมภูมิและทุติยภูมิ

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จากเดือนสิงหาคม พ.ศ.2527 ถึงเดือนมีนาคม พ.ศ.2534 ได้รักษาผู้ป่วยที่เป็นมะเร็งตับชนิดต่าง ๆ 41 ราย ซึ่งเป็นมะเร็งตับชนิดปฐมภูมิ 30 ราย มะเร็งท่อน้ำเหลืองของตับ 4 ราย มะเร็งทุติยภูมิของตับจากมะเร็งกระเพาะอาหาร 1 ราย จากลำไส้ใหญ่ 3 ราย และจากมะเร็งเต้านม 3 ราย โดยการใส่หลอดสวนเข้าไปในหลอดเลือดแดงของมะเร็งเหล่านี้ แล้วใช้สารลิพิโอดอล (ซึ่งเป็นสารทึบรังสีใช้ในการตรวจต่อมน้ำเหลืองตามแขนขา) เขย่าเข้ากับสารเคมีที่ใช้รักษาโรคมะเร็งคือ ไมโตไมซินซี แล้วฉีดเข้าไปในหลอดเลือดแดงของตับที่ไปเลี้ยงมะเร็งดังกล่าว แล้วอุดตันหลอดเลือดนี้ด้วยสารเจลโฟม ผู้ป่วยทุกรายได้รับการวินิจฉัยในการติดตามผู้ป่วยด้วยการถ่ายภาพทีซีสแกนของตับใน 2 ถึง 4 สัปดาห์ หลังการรักษาดังกล่าวมาแล้ว จะพบว่าสารลิพิโอดอลเมื่อไปอยู่ที่มะเร็งตับชนิดต่าง ๆ สามารถจับกับมะเร็งได้มากน้อยขึ้นกับความมากน้อยของหลอดเลือดของมะเร็งชนิดนั้น ๆ จะพบว่ามะเร็งตับซึ่งมีหลอดเลือดแดงไปเลี้ยงมาก จะมีการจับของสารลิพิโอดอล เป็นแบบสม่ำเสมอทั่วทั้งก้อนมะเร็ง ในขณะที่มะเร็งของตับที่มาจากมะเร็งลำไส้ มะเร็งกระเพาะอาหาร มะเร็งเต้านม หรือมะเร็งท่อน้ำเหลืองนี้มีหลอดเลือดแดงไปเลี้ยงน้อยกว่ามะเร็งตับชนิดปฐมภูมิ จึงมีการจับของสารลิพิโอดอลซีทีสแกนเป็นชนิดไม่สม่ำเสมอกัน บางแห่งในก้อนมะเร็งไม่พบสารลิพิโอดอล มะเร็งลำไส้ใหญ่จะพบการจับของสารลิพิโอดอล ในซีทีสแกนอยู่ตามขอบ ๆ เป็นรูปวง ๆ ซึ่งอาจเป็นลักษณะจำเพาะของลิพิโอดอลซีทีสแกนของมะเร็งชนิดนี้ สำหรับมะเร็งตับชนิดปฐมภูมิที่มีก้อนโตมากเกิน 5 เซ็นติเมตร หรือมีบางส่วนของมะเร็งที่แสดงการตายเน่าของเนื้อเยื่อหรือมะเร็งที่มีหลอดเลือดแดงมาที่ก้อนทูมหลายเส้น หรือมะเร็งที่มีส่วนต่อของหลอดเลือดแดงและหลอดเลือดดำของตับโดยตรง มักจะมีลักษณะลิพิโอดอลซีทีสแกนเป็นชนิดไม่สม่ำเสมอกันหรืออาจไม่มีลิพิโอดอลไปจับที่ก้อนมะเร็งเลยก็ได้

คำสำคัญ : มะเร็งตับ, การวินิจฉัย, ลิพิโอดอล–ซีทีสแกน

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