Hepatic Arterial Collaterals After Transcatheter Oily Chemoembolization of Hepatocellular Carcinoma

CHARINDR EURVILAICHIT, M.D.*,
CHAMAREE CHUAPETCHARASOPON, M.D.**

Abstract

From July 1989 to June 1999, 100 patients, 76 male and 24 female, were admitted for treatment of hepatocellular carcinoma (HCC) with transcatheter oily chemoembolization (TOCE) using lipiodol 10 ml mixed with an anticancer drug (mitomycin C 20 ml) and gelfoam particles, described by Nakamura H et al[1].

The periodic follow-up angiogram showed hepatic collaterals which developed according to the mode of embolization. For peripheral hepatic arterial embolization such as segmental or lobar arterial embolization, the intrahepatic collaterals were commonly demonstrated. However, for more proximal hepatic arterial embolization of the tumor feeder arteries such as the proper hepatic artery and the common hepatic artery, the extrahepatic collaterals were commonly demonstrated with fine, small tortuous vasculatures, rendering a repeat TOCE more difficult. The hepatic collaterals are presented.

Key word : Hepatic Arterial Collaterals, Hepatocellular Carcinoma, Transcatheter Oily Chemoembolization

EURVILAICHIT C & CHUAPETCHARASOPON C
J Med Assoc Thai 2001; 84: 75-84

Because of the increasing role of transcatheter oily chemoembolization (TOCE) of hepatocellular carcinoma (HCC) in Ramathibodi Hospital, Bangkok, Thailand, we have had the opportunity to study various hepatic collaterals by TOCE. The collateral routes which were postulated by Michels [2], Charnsangavej et al[3] and Plengvanit et al[4] have been observed in our cases.

* Department of Radiology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400,
** Department of Radiology, Smithivej 2 Hospital, Bangkok 10250, Thailand.

The purpose of this paper was :

(1) To illustrate and classify the collateral pathways following TOCE of hepatocellular carcinoma.

(2) To demonstrate the time intervals, the frequency of TOCE in developing the collateral pathways. The impact of tumor size in developing the collateral pathways are emphasized.

(3) The significance of the collateral pathways are discussed.

MATERIAL AND METHOD

One hundred patients, 76 men and 24 women, aged 17 to 80 years, were examined. All were proved by biopsy to be hepatocellular carcinoma. CT scans of upper abdomen were obtained in all patients with and without water soluble contrast media prior to angiographic procedure. In doing TOCE, the initial celiac, superior mesenteric and selective right, middle and left hepatic angiography were routinely performed in all patients. The angiogram was thoroughly evaluated by the interventional radiologists for the feeders of the tumor. The patency of the portal vein was also accessed by celiac and superior mesenteric angiogram. The TOCE was performed selectively using a mixture of an iodized oil (Lipiodol; Andre' Guerbet, Aulnay-sous-bios, France) 10 cc with Mitomycin c 20 mg together with gelfoam sponge for hepatic embolization. The arterial embolization of the feeders was performed with superselective segmental or lobar arterial embolization as peripheral as possible. However, many patients had a large tumor (size more than 10 cm) with multiple tumor feeder arteries and the proper hepatic arteries together with other extrahepatic collaterals (demonstrated prior to TOCE) had to be embolized.

All patients were followed with periodic alfafetoprotein titers, Lipiodol CT scan every month. A repeat TOCE was obtained every 6 weeks if there was residual tumor demonstrated in the CT scan[5].

RESULTS

The patterns of the collateral circulation were evaluated in relation to the site of arterial embolization (peripheral *vs* proximal) and were classified as intrahepatic and extrahepatic collaterals. (Tables 1-3)

Intrahepatic Collaterals

1. Interlobar collaterals. These vessels were demonstrated immediately in 25 patients (Table 1) who were under TOCE with lobar arterial

Table 1. Frequency of intrahepatic collaterals in 100 patients.

Type of collateral	No. of vessels
Perivascular	10
Interlobar	25
Intralobar	5
Combination of perivascular, interlobar, intralobar	16
Total	56

Table 2. Frequency of extrahepatic collaterals in 100 patients demonstrated in the first session (prior to TOCE).

Type of collateral	No. of vessels	Other feeders of tumor	No. of other feeders	Tumor Size (average) in cm
Retroduodenal a.	3	Proper hepatic a.	2	14
		Right hepatic a.	1	14
Inferior phrenic a.	(Rt) 3	Right hepatic a.	3	12
	(Lt) 1	Left hepatic a.	1	12
		Accessory hepatic a.	1	12
		Cystic a.	1	12
Cystic a.	3	Right hepatic a.	3	18
		Inferior phrenic a.	2	18
Accessory hepatic a. (from SMA)	1	Proper hepatic a.	1	10
Total	11			

a. = artery; SMA = superior mesenteric artery; Rt = Right; Lt = Left

Table 3. Frequency of extrahepatic collaterals in 100 patients (demonstrated after TOCE).

Type of collateral	No. of vessels	Frequency of TOCE (average)	Intervals from first TOCE (Months)
Retroduodenal a.***	7	4	9.4
Inferior phrenic a.	13	4.6	4.8
Accessory hepatic a.*** (from SMA)	4	3.3	3.5
Cystic a.*** (from SMA)	1	3	6
Omental branch	1	4	4
Right paracolic gutter a.	1	3	6
Internal mammary a.	2	4	4
Intercostal a.	1	4	6
Capsular branch of the right renal a.	1	4	6
Left gastric route	1	4	4
Pancreaticoduodenal arcade	1	4	4
Total	33	4*	5.9**

* Extrahepatic collaterals in all cases demonstrated after average 4 sessions of TOCE
** Extrahepatic collaterals in all cases demonstrated after average 5.9 months intervals from first TOCE
*** Periportal routes

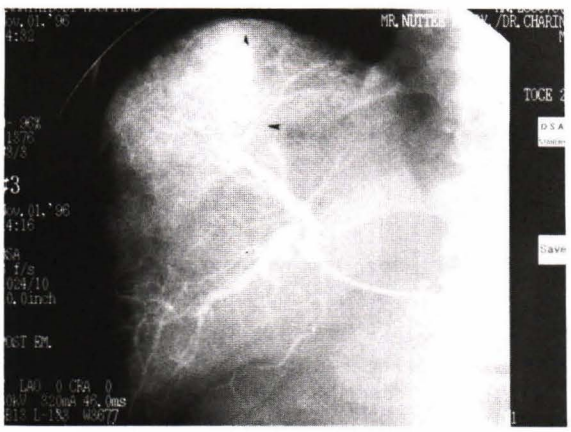

Fig. 1. Hepatic angiogram reveals HCC right lobe (small arrow) supplied by right hepatic artery (big arrow).

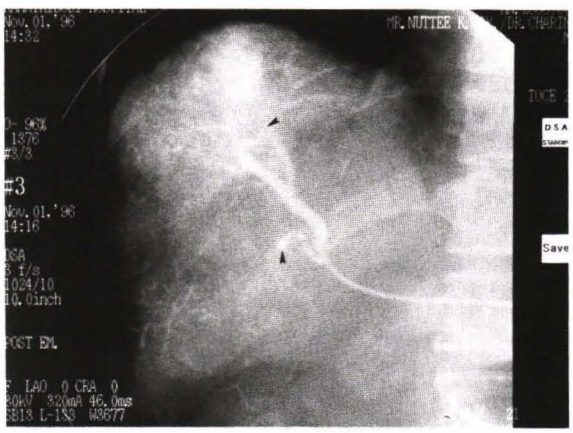

Fig. 2. Right hepatic arteries are occluded (arrow) by TOCE.

embolization in either right hepatic, middle hepatic or left hepatic arterial embolization (Fig. 3).

2. Perivascular. These collaterals were demonstrated in 10 patients (Table 1) about 4 weeks after segmental arterial embolization (Fig. 3).

3. Intralobar. These collaterals were seen in 5 patients 4 weeks after TOCE (Table 1, Fig. 3).

4. Combination of intrahepatic collaterals. Sometimes, the intrahepatic collaterals were demonstrated in the same patient following TOCE which were seen in 16 patients. (Fig. 1-3, Table 1)

Extrahepatic Collaterals

These collaterals were usually demonstrated after repeated TOCE. Usually, the lobar arteries were already occluded and more proximal embolization such as proper hepatic or common hepatic arteries had to be used as the embolized arteries. Eventually, these arteries were injured or

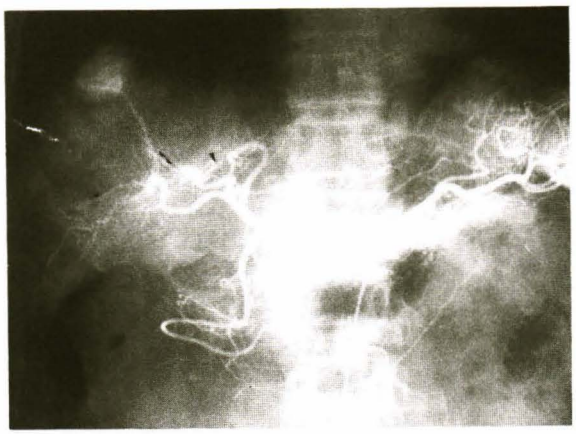

Fig. 3. Post-TOCE for 4 weeks, celiac angiogram reveals perivascular collateral (small arrow), interlobar collateral (two small arrows) and intralobar collateral (big arrow).

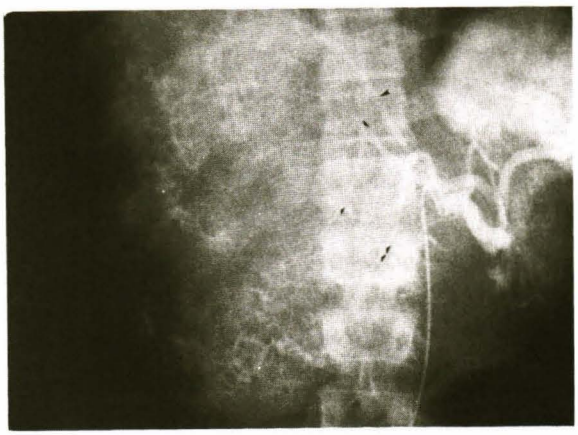

Fig. 4. Big size of HCC (about 18 cm) supplied by right hepatic artery (small arrow) cystic artery (two small arrows) and inferior phrenic artery (big arrow).

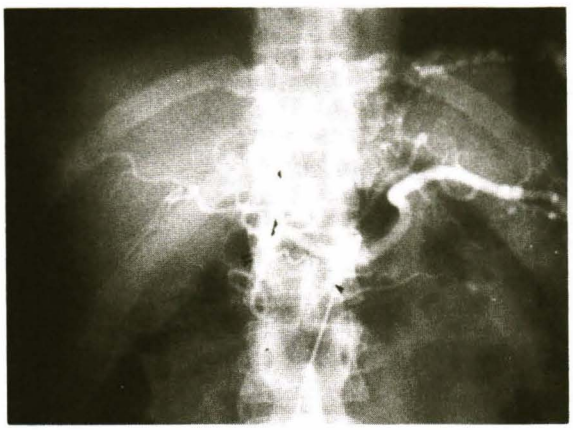

Fig. 5. Celiac angiogram shows occlussion of left hepatic artery (small arrow) and proper hepatic artery (two small arrows) from TOCE. There is a collateral route from dorsal pancreatic artery (big arrow) and retroduodenal artery (two big arrows).

occluded intentionally or inadvertently with the extrahepatic collaterals then being demonstrated. There were 33 patients with extrahepatic collaterals demonstrated after 4 sessions of TOCE or about 5.9 months from the first TOCE (Table 3).

However, there were 11 patients who had extrahepatic collaterals demonstrated at the first session of TOCE due to the big tumor size with multiple tumor feeder arteries (Table 2, Fig. 4).

The extrahepatic collateral pathways included:

1. Pancreaticoduodenal arcade. This route was seen in 1 patient (Table 3) with proper or common hepatic arteries occlusion; these were collaterals from the dorsal pancreatic artery to the liver (Fig. 5).

2. Periportal route. These collaterals were seen in 12 patients (Table 3), 7 of whom demonstrated collaterals which were the retroduodenal artery (Fig. 5). The accessory hepatic branch arising from the superior mesenteric artery entering the liver was demonstrated in 4 patients (Fig. 6), and the cystic artery arising from the superior mesenteric artery was demonstrated in 1 patient (Fig. 10).

3. Left gastric route. This vessel was seen in 1 patient along the lesser curvature of the stomach between the right gastric artery and left gastric artery, and was demonstrated in one patient with occlusion of the left hepatic artery (Fig. 7, 8).

4. Inferior phrenic artery. These collateral pathways were seen in 13 patients who had

Fig. 6. Superior mesenteric angiogram following repeated TOCE shows accessory hepatic branch (periportal route) entering the liver (arrow).

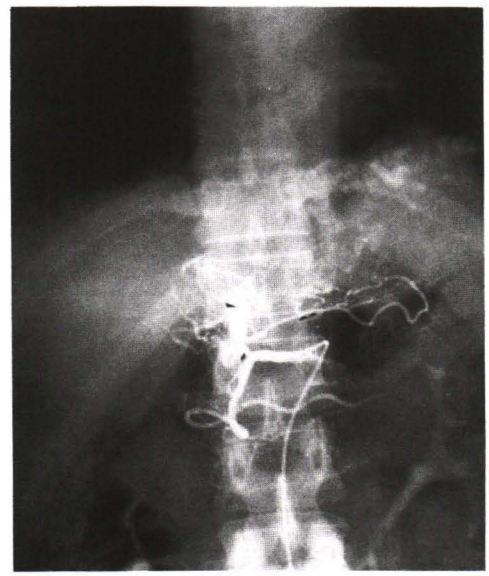

Fig. 7. Common hepatic angiogram post repeated TOCE with occlusion of proper hepatic artery (small arrow) and left hepatic artery (big arrow), the right gastric artery connects with the left gastric artery and enters left lobe liver (two small arrows).

occlusion of the common or proper hepatic arteries. The left inferior phrenic artery was seen in 2 patients after occlusion of the left hepatic artery (Fig. 9). There were 4 patients with a big size of HCC who had the inferior phrenic arteries demonstrated in the first session of TOCE together with other tumor feeders (Fig. 4, Table 2).

5. Right paracolic gutter route. Branches from the right colic artery arising from the superior mesenteric artery supplying the right lobe of liver was seen in 1 patient (Fig. 10, Table 3).

6. Omental branch or epiploic branch. Omental branch or epiploic branch from the right gastroepiploic artery supplying the right lobe of liver, was seen in 1 patient (Fig. 11, Table 3).

7. Internal mammary artery. These collaterals were seen in 2 patients after occlusion of proper hepatic arteries (Table 3, Fig. 12, 14).

8. Intercostal artery. This vessel was seen in 1 patient.

9. The capsular branch of the right renal artery. This artery was seen in 1 patient (Fig. 15).

DISCUSSION

Basing his study on dissection of 200 cadavers, Michels[2] described 26 possible pathways for arterial supply to the liver following hepatic artery ligation. These included replaced and accessory hepatic arteries arising from the celiac and superior mesenteric arteries and their branches as well as potential collateral pathways in and around the pancreas, duodenum, stomach and diaphragm. Charnsangavej in 1982 and many subsequent investigators reported hepatic collaterals after transarterial embolization[3]. He classified the collateral pathways into the intrahepatic and extrahepatic types. We tried to perform peripheral embolzation such as segmental and lobar hepatic arterial embolization which found a high incidence of intrahepatic collaterals (56%) after TOCE in the first few sessions. We found interlobar collaterals to be the most common intrahepatic collaterals (25%), corresponding well with other literature[6]. These collaterals usually developed immediately following TOCE accom-

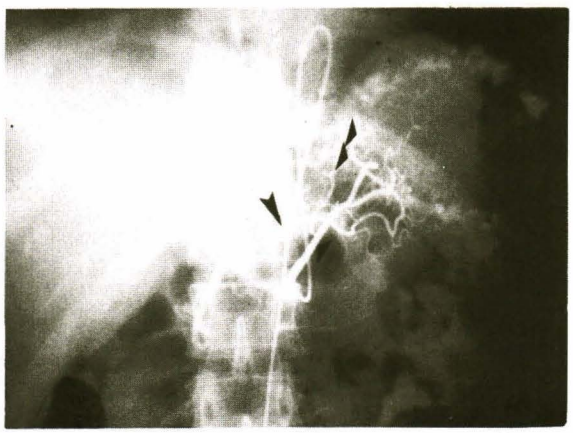

Fig. 8. Same patient as Fig. 7, left gastric angiogram (small arrow) shows connection from left gastric artery to right gastric artery (big arrow) and enters the HCC left lobe (two arrows).

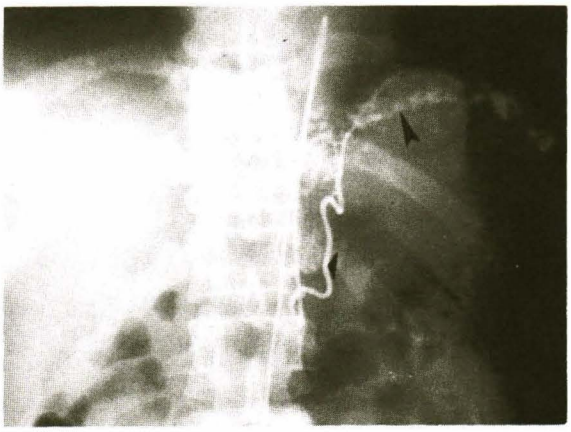

Fig. 9. Left inferior phrenic angiogram post repeat TOCE shows left inferior phrenic artery entering tumor left lobe (small arrow) note Lipiodol stain in left lobe from TOCE (big arrow).

Fig. 10. Superior mesenteric angiogram post repeated TOCE reveals right paracolic gutter route from right colic artery supplies HCC right lobe (big arrow), there is also a cystic artery route entering the liver (small arrow).

panying other intrahepatic collaterals (Fig. 3). For intrahepatic collaterals, a repeated TOCE was easily performed and catheterization of the intrahepatic collaterals was easily obtained.

With repeated TOCE for 4 sessions or more, the hepatic arteries most often showed narrowing, stenosis, spasticity or occlusion. Yu YQ et al[7] described absent or weakening of hepatic arterial pulsation due to injection of chemotherapeutic agents or due to catheter induced arteritis leading to arterial stenosis or occlusion. Proximal TOCE had to be performed with eventual occlusion of proper or common hepatic arteries leading to the development of extrahepatic collaterals. We commonly found retroperitoneal vessels such as inferior phrenic arteries as the major extrahepatic collaterals which was compatible to literature in Japan[8] and Thailand[4] which may be due to greater hypervascularity of the tumor (Fig. 4) compared to those found by Charnsangavej[3], commonly seen around hepatoduodenal ligament. The main cause of inferior phrenic artery supplying the HCC is due to the anatomic location of the tumor adjacent to the bare area and suspensory ligament of the liver[9]; attenuation or occlusion of the hepatic artery may exaggerate the degree of collateral circulation (Fig. 16, 17). This artery may anastomose with other extrahepatic collaterals, such as the internal mammary artery or intercostal artery[10] (Fig. 13, 14). The periportal collateral (Table 3) was the second most common extrahepatic collateral in our patients. These

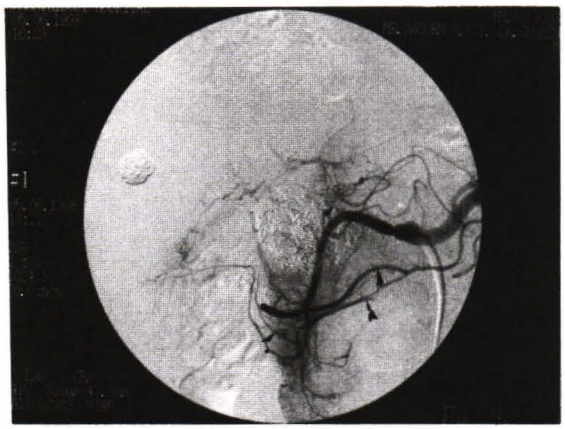

Fig. 11. Celiac angiogram post repeated TOCE reveals occlusion of proper hepatic artery (small arrow), the omental epiploic artery is seen entering the liver (big arrow).

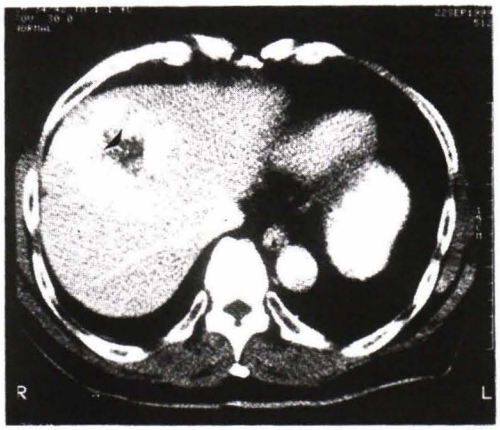

Fig. 12. Lipiodol CT scan post TOCE of hepatic artery shows residual tumor (not opacified by Lipiodol) in right lobe liver (arrow).

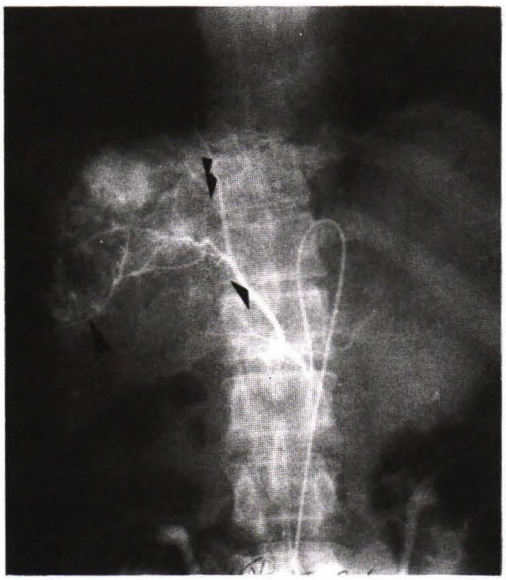

Fig. 13. Same patient as Fig. 12 after TOCE of hepatic artery, inferior phrenic angiogram (small arrow) shows lateral branch of inferior phrenic artery supply HCC (big arrow), the medial branch does not supply HCC (two small arrows).

included the retroduodenal artery (Fig. 5), the accessory hepatic artery (Fig. 6) and the cystic artery (Fig. 10). These collaterals are also considered by Charnsangavej[3] to be the most common and potential extrahepatic collaterals.

The rare collateral pathways -- including the omental branch from the gastroepiploic artery (Fig. 11), right paracolic gutter route (Fig. 10) and left gastric route (Fig. 7, 8) -- were seen in the patients after repeated TOCE for several sessions. These vessels may enter the liver by triangular ligament, hepatorenal ligament or lesser omentum. The capsular branch of the renal artery is also one of extrahepatic collaterals not demonstrated by Charnsangavej[3] but was seen in one patient (Fig. 15), it probably entered the liver *via* the hepatorenal ligament. There was no report in the Thai literature regarding collateral circulation following TOCE of hepatocellular carcinoma. The paper by Plengvanit U[4] which demonstrated the collateral arterial pathways of a hepatic tumor after hepatic artery ligation also had the most common extrahepatic collateral from the inferior phrenic artery which was quite compatible to our study. However, we encountered many rare extrahepatic collateral pathways not mentioned by Plengvanit including the omental route, the right paracolic gutter route, the capsular branch of the right renal artery as well as the internal mammary artery pathway. The present study found about 56 per cent of patients with intrahepatic collateral pathways which was not mentioned in

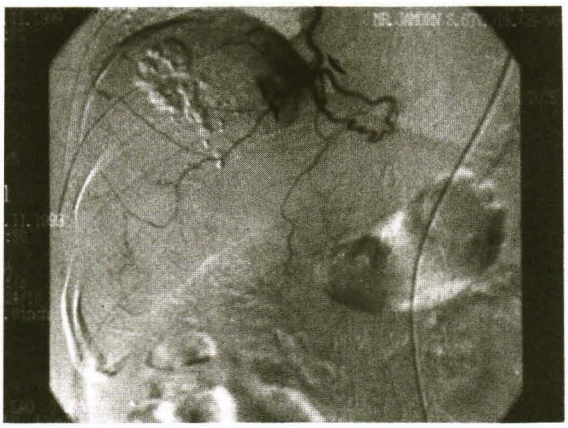

Fig. 14. Same patient as Fig. 12, internal mammary angiogram (small arrow) supplies HCC at antero-superior portion of right lobe liver (two small arrows) and probably anastomosed with superior branch of inferior phrenic artery (see Fig. 13).

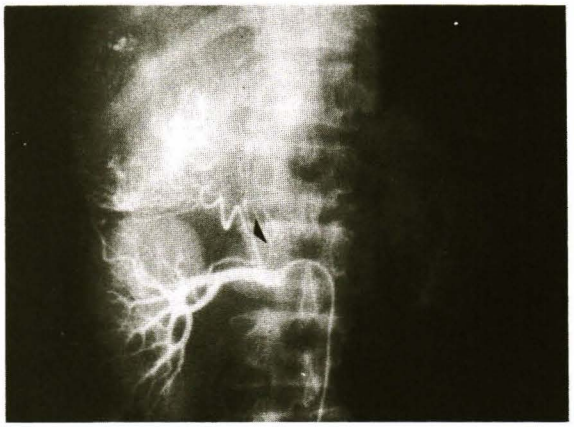

Fig. 15. Right renal angiogram post repeated TOCE shows capsular branch of right renal artery supplies HCC right lobe liver (small arrow).

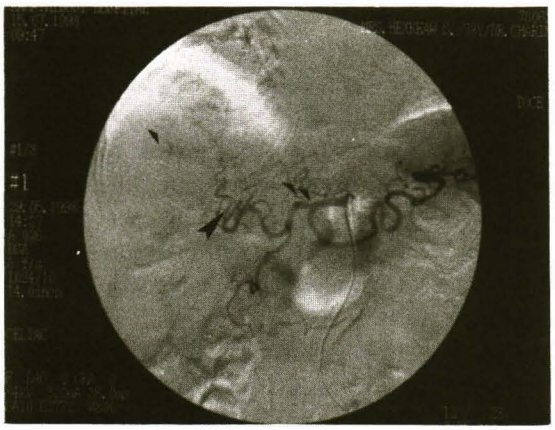

Fig. 16. Celiac angiogram prior to the first TOCE reveals HCC (small arrow) supplied by right hepatic artery (big arrow), note the inferior phrenic artery is normal in size and not supplying the tumor (two small arrows).

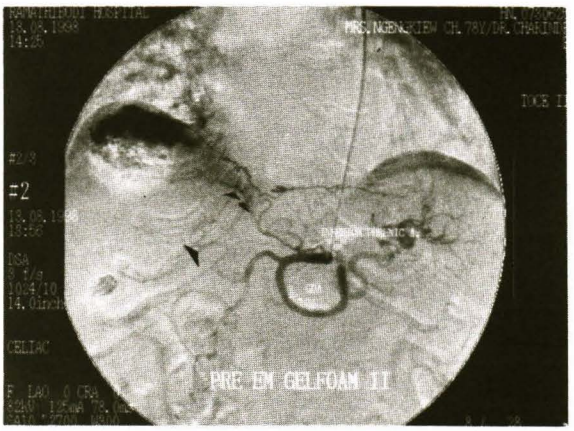

Fig. 17. Celiac angiogram (same case as Fig. 16) shows occlusion of right hepatic artery from last TOCE (small arrow), the inferior phrenic artery is now enlarged supplying the HCC (two small arrows).

Plengvanit's report. This intrahepatic collaterals pathway occured secondary to more peripheral hepatic embolization following TOCE which was different from the hepatic arterial ligation done by Plengvanit (proximal occlusion of the hepatic artery).

In conclusion, the ideal TOCE is to perform TOCE by peripheral embolization with

intrahepatic collaterals demonstrated[11] after TOCE and easily controled by repeated TOCE if recurrent HCC occur. However, by repeating TOCE for more than 4 sessions, extrahepatic collateral may develop which is difficult to catheterise. Every attempt should be made to detect these extrahepatic collaterals and TOCE should be performed in these collaterals. The extrahepatic collateral is suggested when a large tumor is detected or residual tumors are detected by Lipiodol CT scan or rising titer of alfafetoprotein is found following TOCE.

(Received for publication on April 28, 2000)

REFERENCES

1. Nakamura H, Hashimoto T, Oi H, Sawada S. Transcatheter oily chemoembolization of the hepatocellular carcinoma. Radiology 1989; 170: 783-6.
2. Michels NA. Collateral arterial pathways to the liver after ligation of the hepatic artery and removal of the celiac axis. Cancer 1953; 6: 708-24.
3. Charnsangavej C, Chuang VP, Wallace S, Soc CS, Bewers T. Angiographic classification of hepatic arterial collaterals. Radiology 1982; 144: 485-94.
4. Plengvanit U, Chearanai O, Sindhvananda K, Damrongsak D, Tuchinda S, Viranuvatti V. Collateral arterial blood supply of the liver after hepatic artery ligation, angiographic study of twenty patients. Ann Surg 1972; 175: 105-10.
5. Itai Y, Nishikawa J, Tasaka A. Computed tomography in the evaluation of hepatocellular carcinoma. Radiology 1979; 131: 165-70.
6. Kochler RE, Korobkin M, Lewis F. Arteriographic demonstration of collateral arterial supply to the liver after hepatic artery ligation. Radiology 1975; 117: 49-54.
7. Yu YQ, Xu DB, Zhou XD, Lu JZ, Tang ZY. Experience with liver resection after hepatic arterial chemoembolization for hepatocellular carcinoma. Cancer 1993; 71: 62-5.
8. Iwata Y, Endo J, Saito T, Iwata T. Hepatic embolization through extrahepatic collateral pathways after hepatic arterial embolization for the hepatocellular carcinoma. Tokai J Exp Clin Med 1996; 21: 177-83.
9. Chung JW, Park JH, Han JK, Choi BI, Kim TK, Han MC. Transcatheter oily chemoembolization of the inferior phrenic artery in hepatocellular carcinoma : the safety and potential therapeutic role. JVIR 1998; 9: 495-500.
10. Duprat G, Charnsangavej C, Wallace S, Carrasco H. Inferior phrenic artery embolization in the treatment of hepatic neoplasms. Acta Radiologica 1988; 29: 427-9.
11. Doppman JL, Girton M, Kalrn ER. Proximal *versus* peripheral hepatic artery embolization : experimental study in monkeys. Radiology 1978; 128: 577-88.

การเกิดหลอดเลือดข้างเคียงขึ้นตามหลังการอุดกั้นหลอดเลือดของตับเพื่อการรักษามะเร็งของตับชนิดปฐมภูมิ

ชรินทร์ เอื้อวิไลจิต, วท.บ., พ.บ.,*
*จามรี เชื้อเพชรโสภณ, วท.บ., พ.บ.***

ตั้งแต่กรกฎาคม 2532 จนถึงมิถุนายน 2542 มีผู้ป่วยที่ทำการศึกษาในโรงพยาบาลรามาธิบดีทั้งหมด 100 ราย เป็นผู้ป่วยชายไทย 76 ราย ผู้ป่วยหญิงไทย 24 ราย ทุกรายได้รับการรักษาโดยการใส่หลอดสวนเข้าหลอดเลือดของตับแล้วฉีดสารพวกไมโดไมซิน ซี ซึ่งเป็นยาต้านมะเร็ง ผสมกับลิพิโอดอลซึ่งเป็นสารทึบรังสีจำพวกไขมัน ตามหลังด้วยการอุดกั้นหลอดเลือดตับด้วยสารเจลโฟม ซึ่งเป็นสารอุดกั้นหลอดเลือดชนิดชั่วคราว การติดตามผู้ป่วยด้วยการทำการฉีดสารทึบรังสีในหลอดเลือดตับ พบว่ามีการเกิดหลอดเลือดข้างเคียงขึ้นตามตำแหน่งของการอุดกั้นหลอดเลือด ถ้าอุดกั้นหลอดเลือดของตับส่วนปลายใกล้กับมะเร็งตับ จะเกิดหลอดเลือดข้างเคียงภายในตับขึ้น ซึ่งสามารถควบคุมและทำการรักษาด้วยวิธีดังกล่าวได้ง่าย แต่ถ้าอุดกั้นหลอดเลือดตับตรงตำแหน่งต้น ๆ ใกล้ส่วนต้นของหลอดเลือดของตับ มักจะเกิดหลอดเลือดข้างเคียงชนิดภายนอกตับขึ้น ซึ่งพบว่าการผ่านหลอดสวนไปหลอดเลือดที่กล่าวมาชนิดหลังนี้มีความยากลำบากมาก หลอดเลือดข้างเคียงแต่ละชนิดดังกล่าวยังแบ่งออกเป็นชนิดต่าง ๆ ดังจะได้กล่าวถึงในรายงานนี้

คำสำคัญ : หลอดเลือดข้างเคียง, อุดกั้นหลอดเลือดตับ, มะเร็งตับปฐมภูมิ

ชรินทร์ เอื้อวิไลจิต, จามรี เชื้อเพชรโสภณ
จดหมายเหตุทางแพทย์ ฯ 2544; 84: 75–84

* ภาควิชารังสีวิทยา, คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี, มหาวิทยาลัยมหิดล, กรุงเทพฯ 10400
** ภาควิชารังสีวิทยา, โรงพยาบาลสมิติเวช, กรุงเทพฯ 10250