รายงานผู้ป่วย

Pedunculated hepatocellular carcinoma : a report of three cases in Thailand

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Pedunculated hepatocellular carcinoma is an unusual entity with its extrahepatic growth, high resectability and good prognosis. Three cases are reported from Thailand with review of available literatures. The 76, 73 and 56 year-old male patients presented with abdominal mass, anorexia and weight loss of at least 1 year-duration. The US and CT of the 3 cases showed protrusion of the mass from inferior surface of the liver. Hepatic angiograms of case No.1 and No.3 revealed arterial supply mainly from left and right hepatic arteries respectively. Awareness of this condition is necessary for early diagnosis and selection of surgical procedure. Presence of pedicle invasion, hepatic or portal vein thrombosis are determining factors for prognosis and adjuvant therapy.

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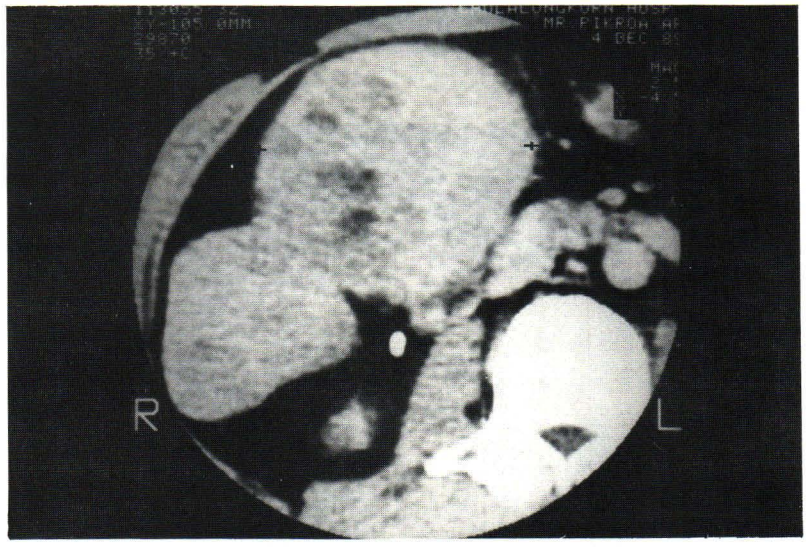
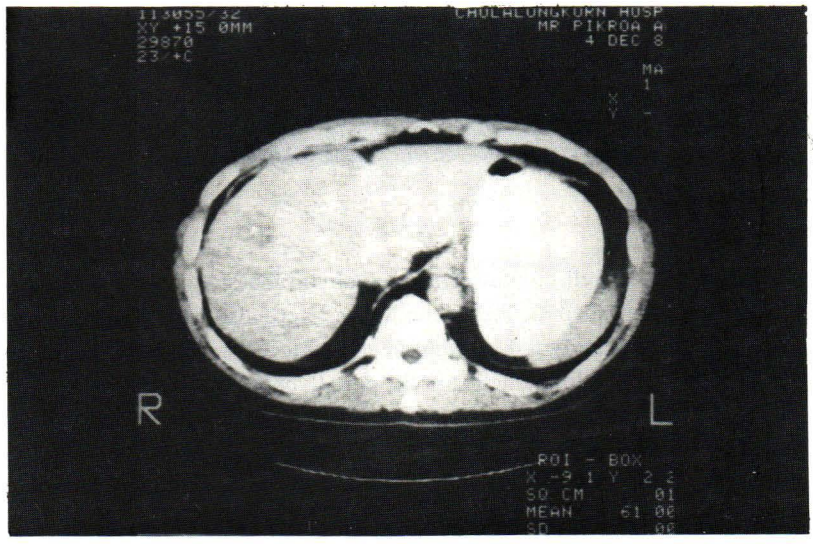
เพชรวรรณ พึ่งรัศมี, ดรุณี บุญยืนเวทวัฒน์, เกียรติ อาจหาญศิริ, พิเชฐ สัมปทานุกุล. พีดังคูเลทแตด เฮพปาโต เซลลูลาร์ คาร์ซิโนมา รายงานผู้ป่วย 3 ราย จากประเทศไทย. จุฬาลงกรณ์เวชสาร 2533 สิงหาคม ; 34 (8) : 613-624

Pedunculated hepatocellular carcinoma เป็นมะเร็งของตับที่มีลักษณะเฉพาะ คือ เป็นก้อนที่โตยื่นออกภายนอกตับ จึงมักทำให้การวินิจฉัยโรคนี้ไม่ถูกต้องว่าเป็นก้อนของอวัยวะอื่น ๆ ได้แก่ก้อนของถุงน้ำดี ก้อนของกระเพาะอาหารหรือลำไส้ รายงานนี้ได้เสนอผลการตรวจในผู้ป่วย 3 ราย โดยการทำ ซีที สแกน, อุลตราซาวด์ และ angiography ทำให้ได้การวินิจฉัยโรคที่ถูกต้อง เพื่อประโยชน์ในการเตรียมการรักษาที่เหมาะสมต่อไป

CASE No.3

A 56 year-old man presented with asymptomatic mass at right subcostal area of one year-duration. Physical examination revealed a rounded firm mass about 10 cms in size at right subcostal region. The liver function test was normal. HBs Ag was positive. Alfa-fetoprotein was highly elevated. US showed large mass protruding from the inferior surface of right lobe of the liver. Associated multiple small lesions were also noted in right lobe of the liver. CT also showed a large, well-circumscribed exophytic growth connected to the inferior surface of medial portion of right lobe of the liver by a pedicle (Fig.3A) Multiple low density masses were also noted in right lobe of the liver (Fig.3B) Celiac angiogram showed a large hypervascularized mass supplied mainly from right hepatic artery and partly from middle hepatic artery (Fig.3C). Tumor thrombus was evident in superior branch of right portal radical (Fig.3D). Hepatic artery-portal vein shunting was also detected. Exploratory laparotory revealed a large pedunculated mass about 10 cms in size protruding from the inferior surface of right lobe of the liver. Micronodular cirrhosis of left lobe of the liver was observed. The tumor was unresectable due to evidence of metastasis and extension of the mass into to right and left lobes of the liver. Tissue biopsy was performed and histologically, hepatocellular carcinoma was confirmed.





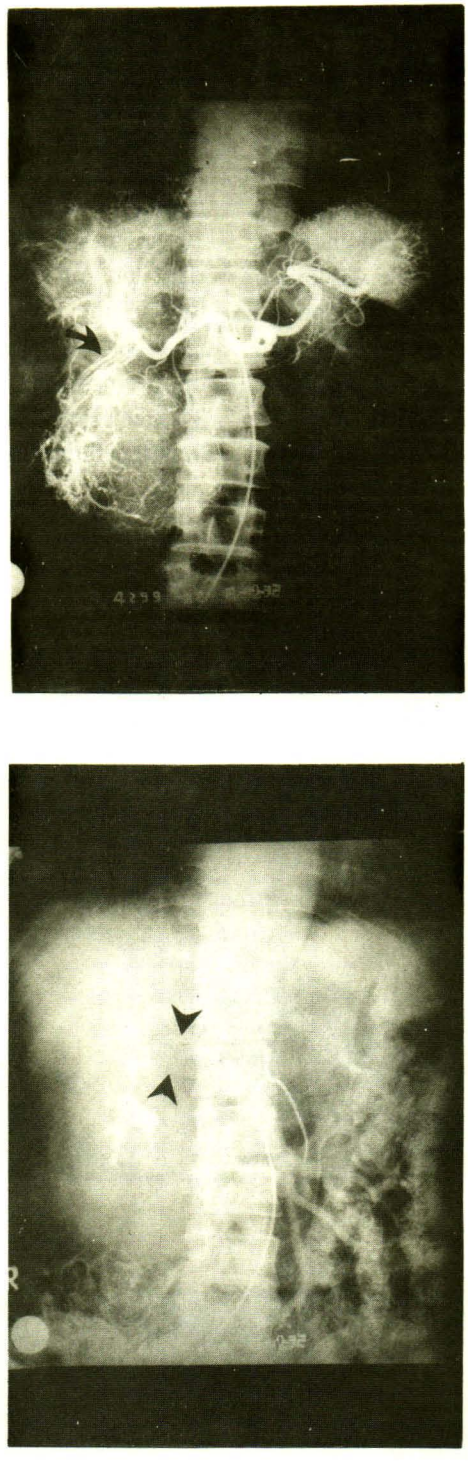
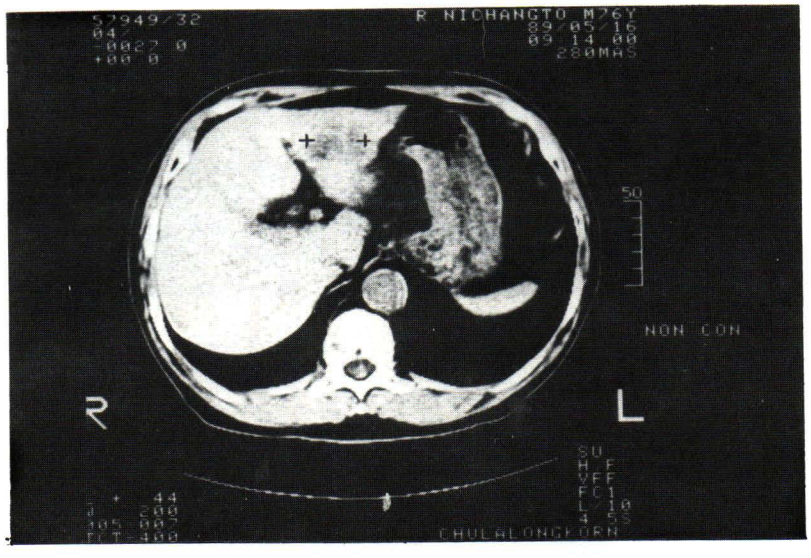


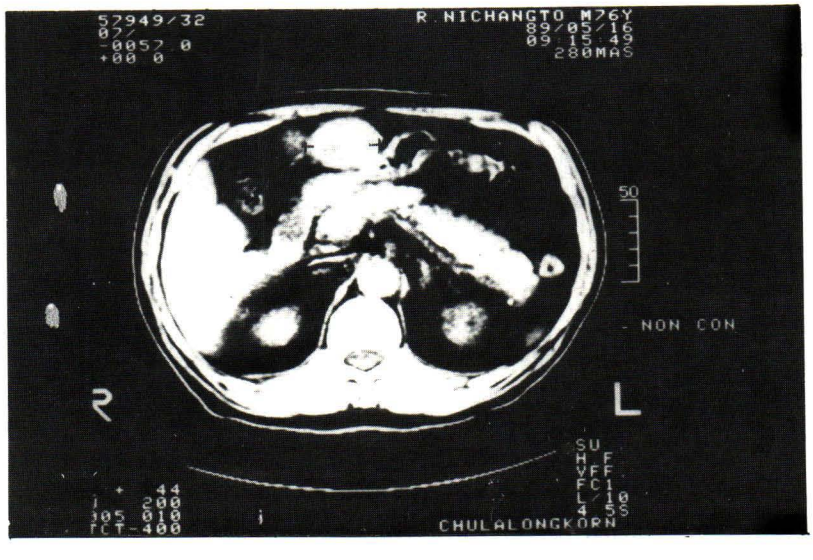
Figure 3A-D. (case No.3)
Contrast CT scan (3A) revealed large, well-circumscribed exophytic mass attached to inferior portion of right lobe of the liver by a pedicle (++). Intrahepatic metastatic lesions were also noted (3B). Celiac angiogram (3C) showed hypervascularity of the tumor mainly fed by right hepatic artery (arrow). Venous phase of the superior mesenteric arteriogram (3D) demonstrated filling defect in the portal venous system, representing tumor thrombus (arrow heads)

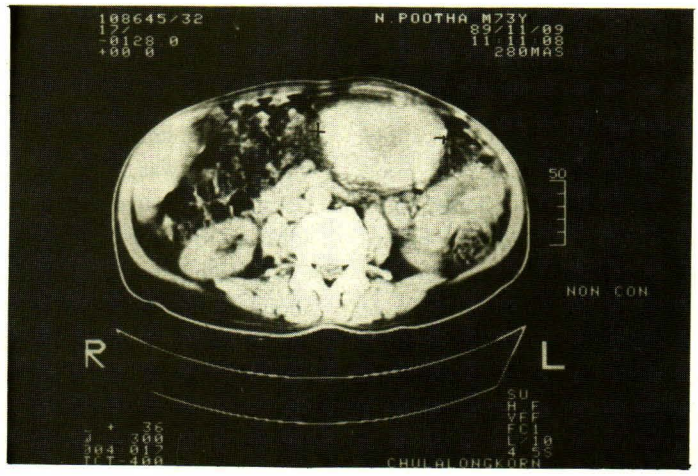
Pedunculated hepatocellular carcinoma, regarded by Edmondson[1] in 1954 as a tumor growing extrahepatically and connected with the liver by a pedicle, was suggested by Horie et al in 1983[2] to be a distinct entity characterized by a high resectabillity rate and good prognosis. Formerly, a diagnosis of pedunculated hepatocellular carcinoma had been difficult[3] before exploratory laparotomy or postmortem autopsy. But after 1970, celiac angiography has enabled preoperative diagnosis, and recently, CT and US have enabled preangiographic diagnosis. Thirty-seven cases from literature review had already been reported. Additional three cases from Thailand are presented.

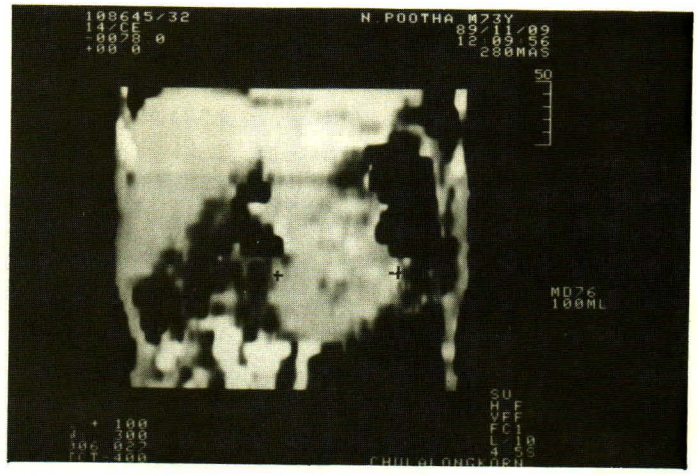
CASE No.1

A 76 year-old man presented with history of anorexia of two year-duration and weight loss of about thirteen kilograms within one year. He developed epigastric distention with palpable mass for ten days before admission. Physical examination revealed irregular mass of five cms. in size at the epigastric region. Liver function test was of normal values. HBs Ag was negative. US showed an irregular, heterogenous hypoechoic mass adhered to inferior surface of left lobe of the liver. CT revealed an irregular heterogenous low density mass about 4 cms in size, bulging from inferior surface of lateral segment of left lobe of the liver (Fig.1A-B). Celiac angiography showed tumor vascularity fed mainly from left hepatic artery (Fig.1C). At surgery, the hard mass was noted at epigastrium arising from left lobe of the liver. Enlarged lymph nodes at celiac axis were also found. The tumor was removed by wedge excision. Histological diagnosis of well-differentiated hepatocellular carcinoma on non-cirrhotic liver background was reported.









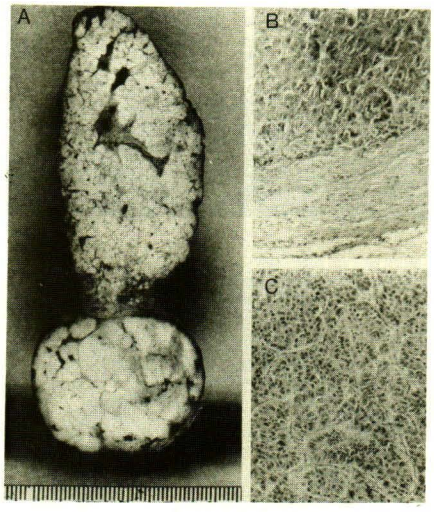


Figure 2A-D. (case No.2)
US (2A) revealed mixed echoic lesion attached to inferior border of left lobe of the liver (++). CT (2B) showed well-marginated extrahepatic lesion growing from inferior aspect of lateral segment of left lobe (++). Reconstruction in coronal planes (2C) clearly demonstrated the figure of pedunculated tumor (++). Pathological examination (2D) A : Gross specimen in sagital section, peripheral cut. Note the well-circumscribed exophytic mass of 4 cms in size connected to inferior aspect of lateral segment of left lobe of the liver by a pedicle. B : (H & E × 400) Peripheral fibrous tumor was depicted. C : (H & E × 400) Well-differentiated hepatocellular carcinoma arranging in pseudoglandular pattern.

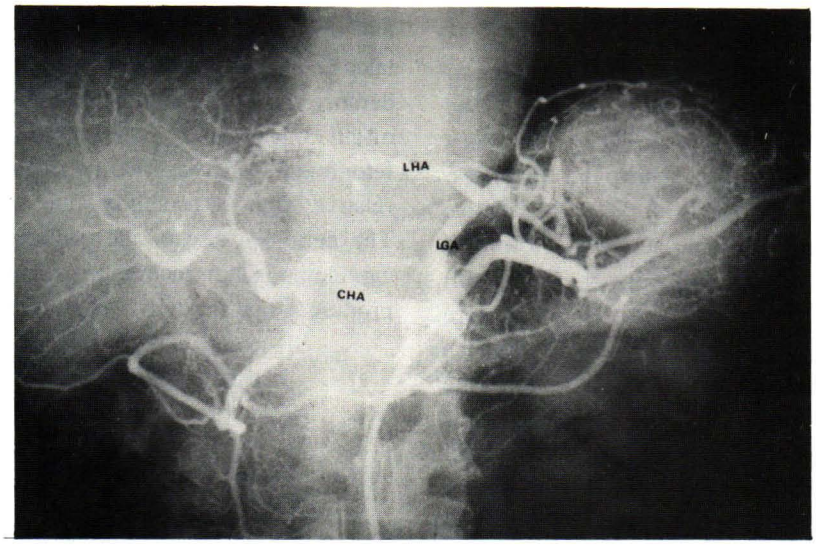
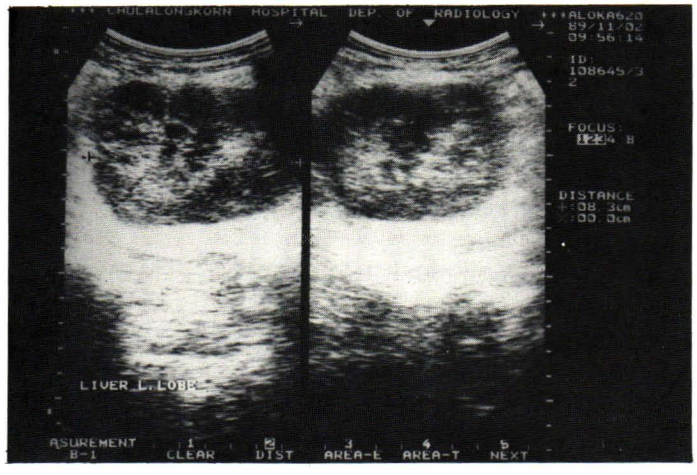


Figure 1A-C. (case No.1)
Non-contrast CT scan, 10 mm-slice interval (1A-B) showed inhomogenous low density lesion protruding from inferior aspect of left lobe of the liver, located very close to the stomach (++). Celiac angiogram (IC) revealed vascularity of the mass, mainly fed by dilated left hepatic artery-LHA. Note the variation of hepatic vascular supply; LHA is replaced from left gastric artery-LGA which is also dilated in this case.

CASE No.2

A 73 year-old man presented with asymptomatic with progressively enlarging mass at epigastrium for more than 2 years. He has developed symptoms of anorexia and weight loss for 5 months before admission. Physical examination revealed a palpable mass about 5 cms in size at epigastrium. Laboratory findings showed normal liver function test. HBs Ag was positive. Alfafetoprotein and CEA values were highly elevated. Liver scintigram (^{99m}Tc-RBC) showed highly increased uptake at the area just inferior to the left lobe of the liver. US revealed large mixed echoic mass at mid abdomen (Fig.2A). The upper border of the mass was contiguous to inferior surface of lateral segment of left lobe of the liver. CT confirmed that the mass about 9 cms in size, extended from inferior surface of lateral segment of left lobe of the liver with marked peripheral enhancement and central low density,representing area of necrosis (Fig.2B-C). The mass was resected together with lateral segmentectomy of left lobe of the liver. Gross pathological examination showed that the well-circumscribed exophytic mass was connected to inferior surface of lateral segment of left lobe of the liver by a pedicle (Fig.2D-A). Histological examination revealed the tumor to be well-differentiated hepatocellular carcinoma arranged in pseudoglandular pattern with peripheral fibrous capsule (Fig.2D,B-C)



LITERATURE REVIEW

A total of 37 cases of pedunculated hepatocellular carcinoma were reported during the 1897-1988 period (Table I). The average age of these patients was 60.2 years (range 35-85). There were 11 females and 26 males. Associated cirrhosis was found in 76.9%. Positive HBs Ag was found in 3 of 18 measurements. Elevated alfa-fetoprotein (minimal positive value = 200 ng/ml) was noted in 8 of 19 measurements. Tumors were attached to the right lobe in 21 cases, to the left lobe in 11 cases, to the caudate lobe in 3 to the quadrate lobe in 1 and to the Riedel's lobe in 1. The size of the tumors ranged from 3 to 25 cms. The average weight of the tumors was 1,039.6 grams (range 100-3,050). Operations (palliative or partial or total resection) were performed in 23 cases. Duration of well-being after resection ranged from 4 months to 5 years. As compared to the ordinary hepatocellular carcinoma (Table II); the figures in common include the peak patient age and the cirrhotic association. Chief characteristics of pedunculated hepatocellular carcinoma are reduced male preponderance, relative lack of symptom and minimal invasion of adjacent organs, less positivity of HBs Ag and alfa-fetoprotein, relative difficulty in preoperative diagnosis, relative high resectability rate and good prognosis. The definite cause of the pedunculated hepatocellular carcinoma is still uncertain. At least 4 hypotheses were proposed, that the tumor may arise from

1. congenitally displaced lobules in the capsule of Glisson[4].
2. ectopic liver tessue[5-7]
3. accessory lobe[5-7]
4. protruding site of liver cirrhosis[11]

Malignancy of the accessory lobe or the protruded cirrhosis can explain most features of the pedunculated hepatocellular carcinoma.

TABLE 1 REPORTED 40 CASES OF PEDUNCULATED HEPATOCELLULAR CARCINOMA*

Case No. Author	Age/Sex/ race	Site	Size (cm)	Weight (gm)	AFP (ng/ml)	HBsAg	Cirrhosis
1. Roux 1897	54/F Italian	caudate	hen's egg				-
2. Goldberg 1934	35/M US	left lobe	grapefruit				+
3. Katoh 1957	46/M Japanese	right lobe	13×10×7	680			+
4. Chen-Huang 1960	83/F Taiwan	right lobe	child's head				-
5. Maki 1963	77/F Japanese	right lobe	fist				
6. Nakatsuka 1967	52/M Japanese	left lobe	man's head				
7. Teruya 1968	60/M Japanese	right lobe	13×10×7				+
8. Shimoyama 1973	63/M Japanese	right lobe	16×14×9.5	1,080	18		+
9. Hirayama 1977	70/M Japanese	right lobe	21×15×8	1,400	-	-	+
10. Manes 1977	67/M US	caudate	7	-			+
11. Miyatani 1977	80/M Japanese	right lobe	12×12×7	1,045	7.3	-	+
12. Miyoshi 1977	67/M Japanese	right lobe	3	-	4,000	-	+

Table 1. (cont'd)

Case No. Author	Age/Sex/ race	Site	Size (cm)	Weight (gm)	AFP (ng/ml)	HBsAg	Cirrhosis
13. Gyotoku 1980	53/F Japanese	left lobe	11×7×7	200	510	+	+
14. Ninomiya 1980	58/M Japanese	right lobe	15×12×8	-	116.7	-	+
15. Baer 1981	66/M US	right lobe	9	-	214	-	+
16. Horie 1983	41/F Japanese	left lobe	9.5×8×5.5	330	86,800	-	-
17. Horie 1983	44/M Japanese	right lobe	25×20×12	3,050	409,000	+	+
18. Horie 1983	54/M Japanese	right lobe	15×12×8	1,000	< 40	+	+
19. Cunningham 1984	66/F US	right lobe	8×8×6	-	-	-	
20. Caielli 1984	74/F French	right lobe	9×7×5	280		-	-
21. Nobusawa 1984	59/M Japanese	left lobe	4.5×4×3.4	-	200→5,100 5,100		+
22. Nobusawa 1984	61/M Japanese	left lobe	3×2.3×7 and 1	-	110	-	+
23. Ichikawa 1984	51/M Japanese	left lobe					
24. Ichikawa 1984	57/M Japanese	left lobe					
25. Ichikawa 1984	52/M Japanese	right lobe					
26. Ichikawa 1984	40/F Japanese	left lobe					
27. Ichikawa 1984	74/M Japanese	right lobe					
28. Ichikawa 1984	52/M Japanese	caudate					
29. Komaki 1984	67/M Japanese	right lobe	hen's egg	-	190,000		
30. Shimoyama 1986	63/M Japanese	right lobe	16×14×9	-	18	-	+
31. Shimoyama 1986	53/M Japanese	right lobe	21×11×20	-	-	-	+
32. Shimoyama 1986	83/M Japanese	left lobe	7×6×5	-	-	-	-
33. Shimoyama 1986	57/M Japanese	quadrate	10×10×10	-	4.3	-	+
34. Anthony 1987	65/F UK	Riedel 1.5 cm pedicle	6×3×2	100		-	+

Table 1. (Cont'd)

Case No. Author	Age/Sex/ race	Site	Size (cm)	Weight (gm)	AFP (ng/ml)	HBsAg	Cirrhosis
35. Anthony 1987	63/M UK	right lobe 2 cm pedicle	17×17×12	1,960			
36. Moritz 1988	69/F US	right lobe	15×20×8	1,350		-	+
37. Moritz 1988	51/F US	left lobe	8×8×7		163,314 282,809		+
38. current case No.1	76/M Thai	left lobe	4	-		-	-
39. current case No.2	73/M Thai	left lobe 2 cm pedicle	9	-	1,043 IU/ml	+	+
40. current case No.3	56/M Thai	right lobe 4 cm pedicle	10	-	> 100,000 IU/ml	+	+

* adapted from Nobusawa et al[11], Anthony et al[18] and Moritz et al[19]

TABLE 2. COMPARISON BETWEEN ORDINARY AND PEDUNCULATED HEPATOCELLULAR CARCINOMA

	Ordinary HC*	Pedunculated HC**
Gross classification	Eggel's[20] : massive/nodular/diffuse	Ichikawa's[21] : protrusive/pedunculated
Incidence	US 3.6-4.8/100,000 Afr 19.2-28.4/100,000	Okuda 0.3%[22] Horie 2.4%[2]
Sex male : female	1.67-6.7 : 1	2.36 : 1 Nobusawa 2.35 : 1[11]
Age	peak at 6° decade	average 60.2 years Nobusawa 58 years[11]
Associated cirrhosis	83-89.2%	76.9% Nobusawa 80%[11]
Positive HBs Ag	40-80% Pongpipat 56.1%[23]	16.7%
Positive AFP	Hasegawa 73.1%[24] Pongpipat 78.1-100%[23]	42.1% Nobusawa 65%[11]
Resectability	3-24% Okamoto 40% or more[25]	82.1%

* from Cunningham et al[16], except specified as others.

** from literature review, except specified as others.

DISCUSSION

When a patient presents with abnormal mass located outside the hepatic area, the diagnosis of hepatocellular carcinoma is less uaually considered. Some of the early case of pedunculated hepatocellular carcinomas were misdiagnosed as empyema of gallbladder[12], retroperitoneal tumor[3], omental or mesenteric sarcoma[14] or even adrenal tumor[15]. Generally, celiac angiography provides the definite diagnosis of hepatocellular carcinoma by the demonstration of tumor vessels from hepatic artery. In case No.1, exophytic gastric tumor cannot be definitely excluded eventhough angiography was performed, due to anatomic variation of vascular supply to liver. In addition to hepatic arteries supplying the tumor, tumor vessels from lumbar[16], middle adrenal[17], renal and inferior phrenic arteries[15] have been reported. Like other malignancies, early detection of the tumor and proper management bring good result. Recognition of this unusual entity is required for early diagnosis. In case No.2, the preoperative diagnosis was made with more confidence without angiography. US and CT provided the helpful datas for preoperative surgical planning. Pedunculate hepatocellular carcinoma provided good prognosis owing to its slow growth, extrahepatic location, and encapsulation[18]. Intrahepatic metastasis is related to the degree of invasion at pedicle. CT and US play an important role in detection of pedicle invasion and may serve as a guide for more extended operation together with adjuvant therapy[11]. US, CT and angiography can help to demonstrate evidences of liver metastases and tumor thrombi in portal vein. Intraoperative US is also essential to exclude residual tumors and tumor thrombi in portal vein for proper management[11]. In case No.3, angiographic evidences of tumor thrombus in portal system precluded the choice of extended or radical resection of the tumor. Besides, the elevation of AFP level is an important clue in establishing the diagnosis of hepatocellular carcinoma, but is not sensitive enough for use as a screening tool to detect early cases[16].

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