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## Angiography of Gallbladder Cancer

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## 胆のう癌の血管像

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従来、胆のう癌の術前診断は極めて困難であり、種々の胆道系の放射線学的検査によっても、10~30%が診断されたにすぎず、その発見は胆石および胆のう症などの診断の下に偶然発見された場合が少くなかった。

愛知県がんセンター病院において最近8年間に剖検または手術によって確かめられた胆のうの悪性腫瘍48例のうち、選択的腹腔動脈撮影が行われた25例の血管像について詳細な検討が行われた。その内訳は腺癌17、乳嘴状腺癌2、未分化癌4、Mucoepidermoid および Leiomyosarcoma 各1であり、15例に手術が行われたが、うち2例に胆のう切除が出来たにすぎなかった。

胆のう動脈領域における病的血管の拡張は68

%、血管増生は80%、管腔の広狭不整は64%、腫瘍濃染は64%、偏位は32%にみられ、血管像のみからの術前診断は72%であった。その他の胆のう癌の存在に随伴する胃十二指腸動脈の偏位、圧排は40%に、肝転移によるその末梢領域における変化は48%にみとめられた。

腹腔動脈または上腸間膜動脈撮影において、胆のう動脈自体を観察することは決してむづかしいものではなく、その動脈枝を詳細に検討することによって得られる病的所見によつて、高率な術前診断の可能性は今後超選択的血管撮影や拡大撮影の利用によつて、手術可能の胆のう癌の発見に導くことが考えられる。

### Introduction

At Aichi Cancer Center Hospital 48 cases of gallbladder cancer were diagnosed during the last 8

years, all of which were confirmed by subsequent surgery or autopsy.

Gallbladder cancer is extremely difficult to diagnose preoperatively accordingly it has a rather unfavorable prognosis. This study on angiographic findings of gallbladder cancer was made in order to evaluate the usefulness of selective angiography, on the assumption that this technique might be of significant value in the diagnosis of gallbladder cancer.

### Objective and method

Selective celiac angiography was performed in 25 cases who presented with either a palpable tumor in the right hypochondrium or jaundice or both and who were suspected of cholecystopathy.

Clinical findings in these cases are shown in Table 1. Of the 15 operated cases, only 2 underwent cholecystectomy and other 13 had exploratory laparotomy.

Histologically, adenocarcinoma was revealed in 17 cases, papillary adenocarcinoma in 2, anaplastic carcinoma in 4, mucoepidermoid, and leiomyosarcoma in each 1.

Table 1. Clinical Findings of Gallbladder Cancer

No. of cases	Age	Sex	Jaundice	BSP 45min. (%)	Serum Alkali- phosphatase (Unit)	Chole- cystogram	Gallbladder		Location	Surgical procedure	Histology
							Palpable	Stone			
1	55	F	—	17.4	26.2	—	+	—	Entire	Explo. laparotomy	Adenoca.
2	55	F	—		7.9	—	—	+	Fundus	Cholecystectomy	Adenoca.
3	55	M	—	18.5	16.2	—	—	?	Body	—	Adenoca.
4	59	F	—	9.4	5.2	—	+	+	Fundus	Explo. laparotomy	Adenoca.
5	63	F	—		9.7	—	+	+	Neck	—	Adenoca.
6	57	M	+	32.0	57.5	—	+	?	Neck	—	Papillary Adenoca.
7	64	F	+	56.0	66.7	—	+	+	Neck	—	Papillary Adenoca.
8	55	F	—	5.0	3.0	—	—	?	Entire	—	Adenoca.
9	61	F	—		69.0	—	+	+	Neck	Explo. laparotomy	Adenoca.
10	61	F	+	49.0	17.5	—	+	?	Entire	—	Adenoca.
11	52	F	—	15.3	11.7	—	—	+	Entire	—	Mucoepidermoid
12	43	F	+	41.6	50.6	—	+	+	Fundus	External fistula	Ca. simplex
13	69	F	—	7.6	7.2	—	—	+	Entire	—	Adenoca.
14	72	M	—	12.9	6.7	—	+	—	Entire	Explo. laparotomy	Ca. simplex
15	62	M	—	34.0	37.8	—	—	—	Entire	Explo. laparotomy	Adenoca.
16	63	F	—	0.6	35.0	—	—	+	Fundus	Cholecystectomy	Adenoca.
17	53	F	—	12.5	20.6	—	—	+	Entire	Explo. laparotomy	Ca. simplex
18	52	M	—	3.5	9.4	—	+	+	Body	—	Adenoca.
19	62	M	—	5.7	6.0	+	+	+	Fundus	Explo. laparotomy	Ca. simplex
20	51	M	—	13.6	14.8	—	+	—	Entire	Explo. laparotomy	Leiomyosarcoma
21	66	M	—	9.6	15.3	—	—	—	Entire	Explo. laparotomy	Adenoca.
22	56	F	+		69.4	—	+	?	Entire	External fistula	Adenoca.
23	56	F	—	12.5	9.3	—	+	—	Entire	—	Adenoca.
24	63	F	—		24.6	—	+	+	Entire	Explo. laparotomy	Adenoca.
25	61	F	+		100.0	—	+	+	Entire	External fistula	Adenoca.

### Case reports

Case 4. 59 year old woman.

The patient had persistent dull pain in the right hypochondrium with severe anorexia and weight loss for half a year. A slightly dilated gallbladder was palpable.

Celiac angiogram revealed a slight dilatation and upward displacement of the common hepatic artery. The prominent cystic artery is descending in a large arc and bifurcates at the periphery into the upper, outer and lower, inner branches. In the peripheral region there was moderate hypervascularity of tumor vessels with luminal irregularity, along with an elliptical irregularly patchy tumor-stain in the capillary phase (Figs. 1 and 2).

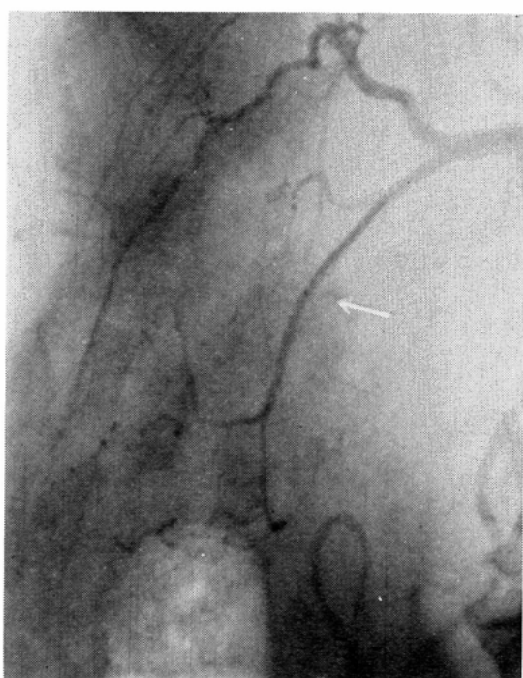


Fig. 1. Case 4. 59 year old woman (Cancer of gallbladder).

The cystic artery (↓) is descending in a large arc and bifurcating at the periphery. Moderate hypervascularity of tumor vessels is revealed in the arterial phase.

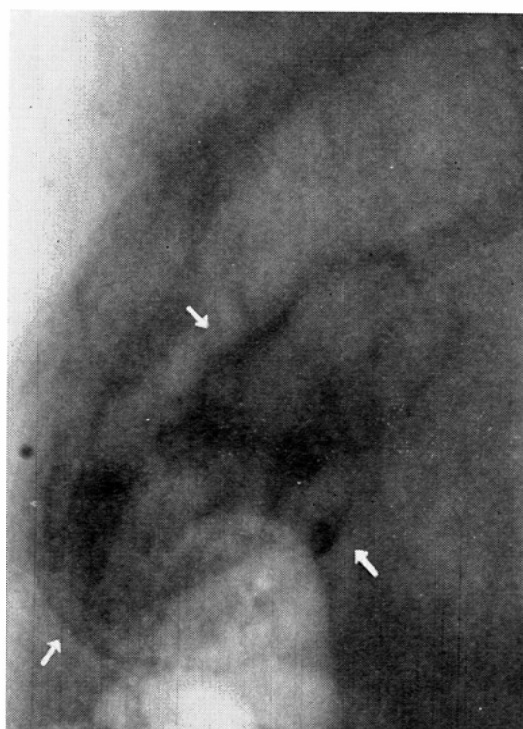


Fig. 2. An elliptical unhomogenous tumor-stain (↓) shows a dilated gallbladder in the capillary phase.

Laparotomy showed marked ascites with milky fluid, the gallbladder contained a stone in the neck and white spotted tumor infiltration was noted at the fundus as well as a mass along the mesentery near the hepato-duodenal ligament and a further mass in the region of the retroperitoneal lymph nodes. The liver was swollen, presenting cirrhosis of Laennec's type. The operation, therefore, ended in exploratory laparotomy only.

Case 5. 63 year old woman.

The patient had occasional localized pain in the epigastrium for one year associated with marked

general fatigue. The presence of ascites and a tumor in the right hypochondrium was noted, there was no jaundice.

In the celiac angiogram, the common hepatic artery revealed moderate dilatation and the branches of the right hepatic artery showed tortuosity in the periphery due to liver cirrhosis. The cystic artery was found to originate just prior to branching of the right hepatic artery from the common hepatic artery, it was markedly distended while descending and formed a hypervascular, dilated stain of tumor vessels meandering significantly in the periphery.

A moderate tumor-stain was shown in the angiogram taken 4 seconds later (Figs. 3 and 4).

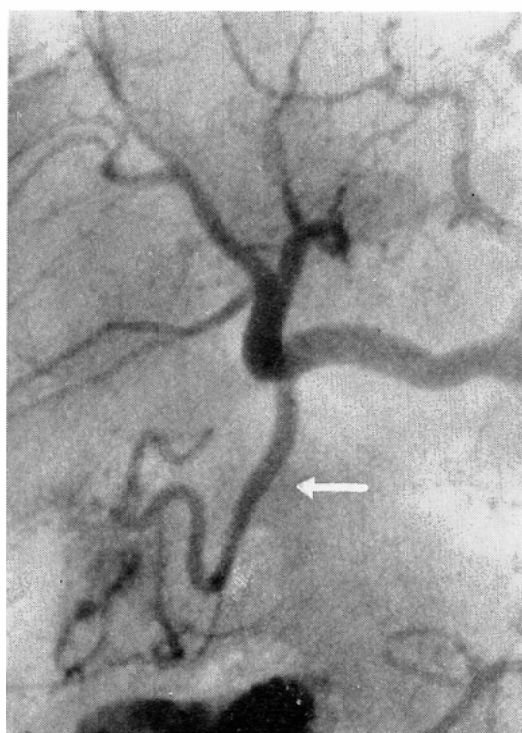


Fig. 3.

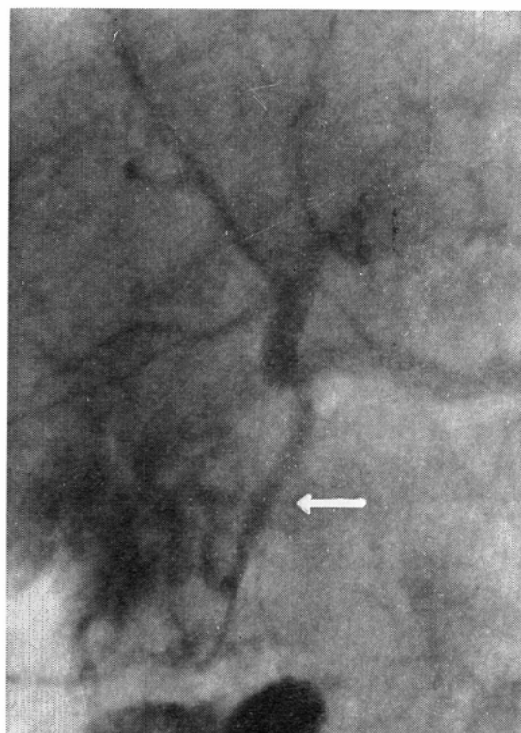


Fig. 4.

Case 5. 63 year old woman (Cancer of gallbladder).

The cystic artery (↓) is descending and forming hypervascularity of tumor vessels in the arterial phase. A moderate tumor-stain is shown in the angiogram taken 4 seconds later.

Autopsy revealed the presence of polygonal adenocarcinoma in the neck of gallbladder, with a metastasis in retroperitoneal lymph nodes and intrahepatic cholangitis due to stasis of bile.

Case 6. 57 year old man.

The patient had heartburn for 2 years, which was followed by jaundice and hepatomegaly and was diagnosed as liver cancer later. The liver was 5 fingers breadth enlarged in the right hypochondrium. Direct serum bilirubin was 11.6 mg/dl, serum alkaline phosphatase, 57.5 unit/dl.

Celiac angiogram revealed dilatation of the common hepatic artery as well as a large arc like upward displacement of the right hepatic artery the lower margin of the swollen liver.

Peripheral branches of these arteries showed luminal irregularity and hypervascularity with minute tumor vessels.

The cystic artery was found bifurcating after branching from the common hepatic artery. The outer ramus was significantly dilated giving rise to a considerable number of small vessels forming a network. The inner ramus was smaller than the outer, being markedly displaced in an arc to the left. These two rami of the cystic artery depicted the gallbladder which was enlarged to the size of an adult's fist. Irregular tumor stain was noted also in the capillary phase. The gastroduodenal artery was also slightly displaced to the left (Figs. 5 and 6).

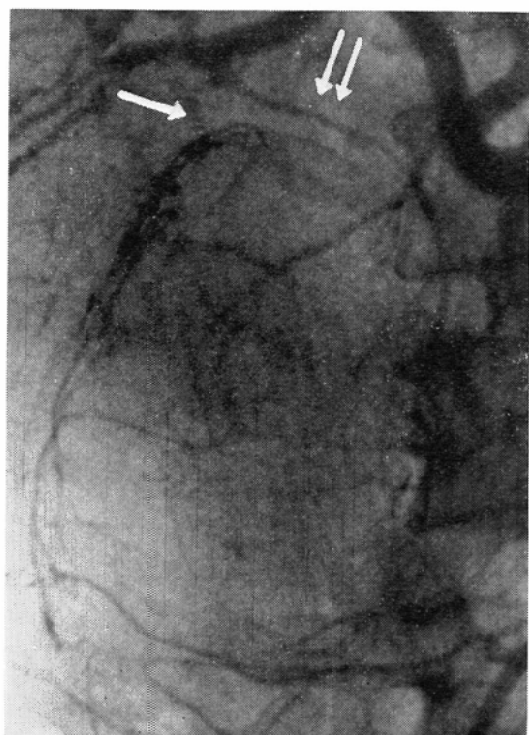


Fig. 5.

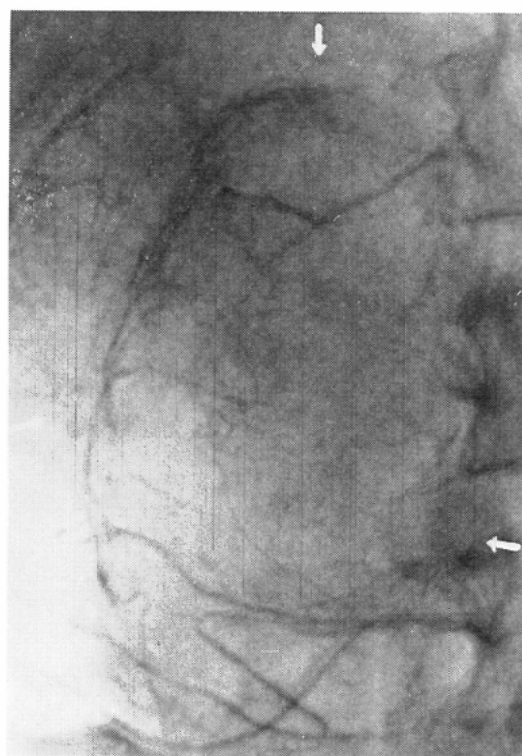


Fig. 6.

Case 6. 57 year old man (Cancer of gallbladder).

The outer ramus of the cystic artery (↓) is significantly dilated while deriving a lot of small vessels forming a network. The inner ramus (↑↑) is displaced in an arc to the left in the arterial phase. These two rami depicted the gallbladder and unhomogenous tumor-stain is noted in the capillary phase.

Autopsy revealed hypertrophy of serous menbrane of the gallbladder which contained little bile, but with plenty of necrosed substance from the tumor as well as tumor infiltration from the porta hepatis into the left liver lobe, resulting in a tumor as large as a child's head. The tumor invaded the lumen

of a vein at the site adjacent to the descending aorta. Papillary adenocarcinoma was proven histologically.  
Case 9. 61 year old woman.

The patient had right hypochondriac pain and anorexia. The gallbladder was palpable as a hard tumor.

Celiac angiogram revealed a somewhat dilated common hepatic artery as well as cystic artery bifurcating as if surrounding the gallbladder and forming a reticular pattern. There was remarkable hypervascularity corresponding to the bottom of the reticular pattern.

In the angiogram taken 6 seconds later, tumor-stain in the lower part and the bottom of the gallbladder showed up (Figs. 7 and 8).

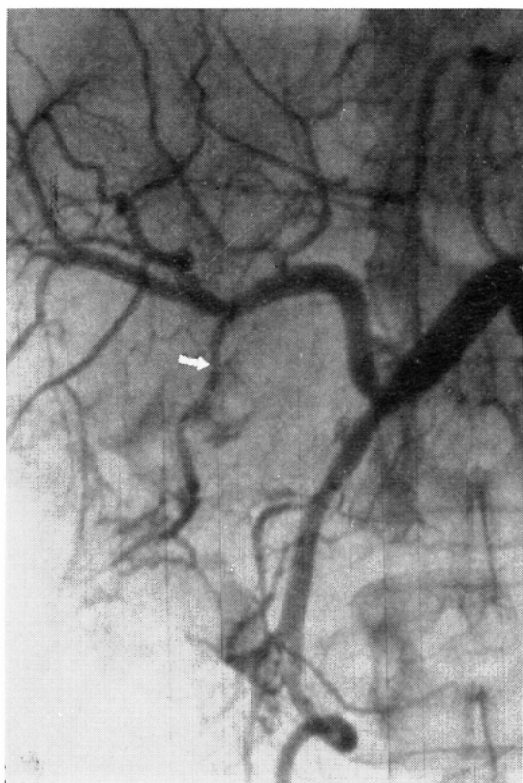


Fig. 7.

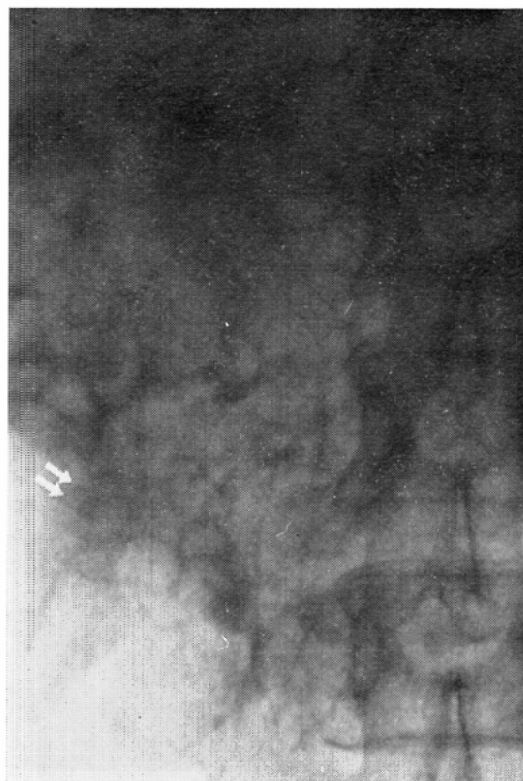


Fig. 8.

Case 9. 61 year old woman (Cancer of gallbladder).

The cystic artery (↓) is dilated and irregular. Hypervascularity and tumor-stain are seen in the periphery (↑↑).

Nodular stains in the right lobe of the liver suggest existence of liver metastasis. These findings were proven by laparoscopy. Autopsy revealed the presence of adenocarcinoma in the whole gallbladder and its metastasis in the liver.

Case 20. 51 year old man.

This patient had a dull pain in the epigastrium accompanied by loss of weight for two years. A round non-tender tumor of the size of an adult's fist was palpable in the right hypochondrium. Radiological examination by means of barium meal suggested the existence of a fistula formation between the irregularly dilated duodenal loop and the gallbladder (Figs. 9 and 10).

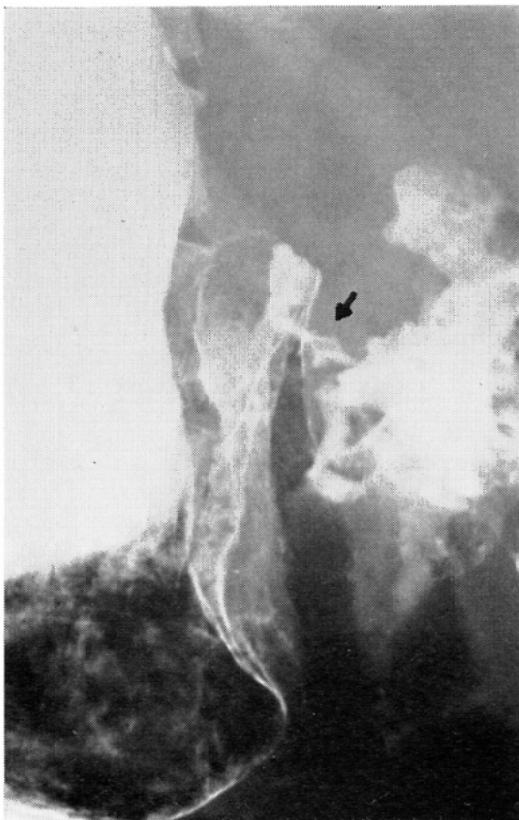


Fig. 9. Case 20. 51 year old man (Leiomyosarcoma of gallbladder).

The stomach is compressed widely in the greater curvature of the antrum and irregular shaped fistula is revealed in the duodenal bulb (↓). (P-A view).



Fig. 10. A-P view in the same case.

The bulb is strongly deformed and the duodenal loop is remarkably shifted to the left by a huge tumor of the gallbladder.

A fistula (↑) is noted between the bulb and gallbladder.

The cystic artery was significantly dilated and showed luminal irregularity. Especially, the inner ramus was dilated, from it issued a large number of dilated vessels forming a network. The outer ramus was smaller than the inner, though hypervascularity was very marked. These two rami of the cystic artery surrounded the gallbladder which was enlarged to the size of a child's fist. A homogeneous tumor-stain in the capillary phase was also noticed. The gastroduodenal artery was displaced sharply to the left (Figs. 11 and 12).

Autopsy revealed a large amount of necrotic tumor substance as well as tumor infiltration from the porta hepatis into the right liver lobe, resulting in a tumor mass as large as an adult's fist.

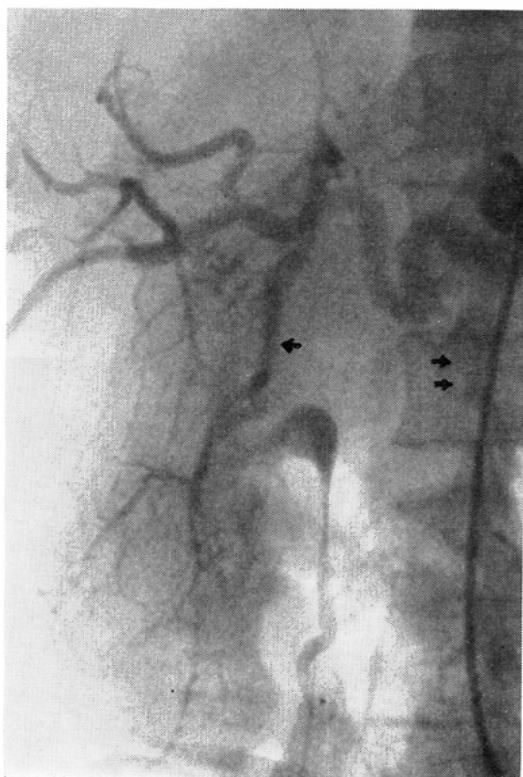


Fig. 11. (Leiomyosarcoma in the gallbladder)

The cystic artery (↑) is remarkably dilated and hypervascularity with numerous dilated tumor-vessels in the periphery and the formed network suggests a huge tumor.

The gastro-duodenal artery is strongly shifted to the left (↑↑).



Fig. 12. In the capillary phase a faint tumor-stain is noted in the same region.

Leiomyosarcoma of low grade originating from the gallbladder was confirmed.

#### Summary of angiographic findings of gallbladder cancer (25 cases)

The results of selective angiography may be summarized as shown in Table 2.

Cystic artery itself presented vasodilatation in 17 cases (68%), hypervascularity to different extent in 20 cases (80%) and tumor-stain in 16 cases (64%).

These blood vessels had the character of tumor vessels with luminal irregularity and stiffening in 16 cases (64%) and displacement or interruption due to swelling of the gallbladder were seen in 8 cases (32%). 11 cases (44%) presented a slight displacement to the left of the gastroduodenal artery attributable to swelling of retroperitoneal lymph nodes, enlargement of the choledochus, or infiltration of the tumor into the liver or pancreas. Three cases (12%) presented stenosis or interruption of the gastroduodenal artery or proliferation of minute blood vessels.

Liver metastasis was angiographically observed in 12 (48%) and liver cirrhosis in 4 cases, both agreeing with laparotomic findings.

Table 2. Angiographical Findings of Gallbladder Cancer

No. of cases	Gastro-duodenal artery	Cystic artery					Hepatic artery	Angiographical diagnosis
	Displacement	Dilatation	Hyper-vascularity	Luminal irregularity	Displacement	Tumor stain	Metastasis	
1	—	+	+	+	—	—	+	Ca. of Pancreas
2	—	+	+	—	—	+	+	Ca. of Gallbladder
3	—	+	+	—	—	+	—	Ca. of Gallbladder
4	—	+	+	—	—	+	—	Ca. of Gallbladder
5	—	+	+	+	+	+	—	Ca. of Pancreas
6	+	+	+	+	—	+	—	Ca. of Gallbladder
7	—	—	+	+	+	—	+	Ca. of Gallbladder
8	+	—	—	—	—	+	—	?
9	—	+	+	+	+	+	+	Ca. of Gallbladder
10	—	—	+	+	—	+	—	Ca. of Gallbladder
11	+	+	+	+	+	+	+	Ca. of Gallbladder
12	+	+	+	—	—	+	+	Ca. of Gallbladder
13	—	+	+	+	+	+	—	Cholelithiasis
14	—	+	—	—	—	—	—	Ca. of Gallbladder
15	—	+	+	—	—	—	+	Ca. of Gallbladder
16	—	—	+	+	—	+	+	Ca. of Gallbladder
17	+	+	+	+	—	—	—	Ca. of Gallbladder
18	+	+	—	+	—	—	+	?
19	+	+	+	—	—	+	+	Ca. of Gallbladder
20	+	+	+	+	+	+	+	Ca. of Gallbladder
21	—	—	+	+	+	—	—	?
22	—	—	+	+	—	—	—	Ca. of Gallbladder
23	+	—	+	+	+	+	—	Ca. of Gallbladder
24	+	+	—	—	—	+	+	Ca. of Gallbladder
25	—	—	—	+	—	—	—	Ca. of Pancreas
Ratio of Pathological Findings	40%	68%	80%	64%	32%	64%	48%	Accuracy rate 72%

### Discussion

Gallbladder cancer is seldom of epidermoid nature but mostly adenocarcinoma, tending to be of the scirrhous type in the majority of cases. There may be an infiltration into extrahepatic region of bile duct in relatively early stage, metastatic lesions in bile duct is also an early manifestation, similarly with metastatic lesions in the surrounding organs, abdominal cavity or the lung. This is by means of transportation into the venous system through lymphatic or portal circulation. Prognosis is unfavorable, ending in death of the patient within 1 year in most cases.

Preoperative diagnosis of gallbladder cancer is often difficult, since radiography of this organ is not feasible with routine X-ray procedure, and the disease may be suggested fluoroscopically only as a displacement of the descending portion of the duodenum. Even laparoscopy<sup>4)5)</sup>, direct cholecystography using the laparoscope or percutaneous transhepatic cholangiography<sup>6)7)</sup> can only reveal the presence of disease with difficulty. Successful diagnosis is possible in only 10–30% of cases. Even if diagnosed

as gallbladder cancer, most cases are ordinarily subjected to exploratory laparotomy but no further action is taken. Radical operation is mostly performed when an incorrect diagnosis of cholelithiasis or cholecystopathy is at hand, in other words, by chance.

In fact, the preoperative diagnosis in our series pointed to gallbladder cancer in 18, cholelithiasis in 1, and pancreatic cancer in 3 each, and obstructive jaundice, choledochus stone and retropentoneal tumor in 1 each out of 25 cases of gallbladder cancer. Angiography revealed the cancer in 18 out of 25 cases (72%), thereby significantly contributing to its preoperative diagnosis.

Only a limited number of reports is available on angiographic findings of this condition, some of which were presented by Ödman<sup>8)</sup>, Abrams<sup>1)</sup>, Deutsch<sup>3)</sup>, Chudáčěk<sup>2)</sup>, Rösch<sup>10)</sup> and Reuter<sup>9)</sup>. The cystic artery is bifurcated from the right hepatic artery: anterior outer and posterior inner branches, which are further ramified into small branches that cover the surface of cholecystic wall. The presence of a malignancy is expressed, as in other organs, by features of tumor blood vessel, i. e. and irregular size of the lumen, proliferation of abnormal vessels such as hardened, interrupted, dilated or tortuous vessels, or tumor-stain, which undoubtedly indicate an infiltrated wall of the gallbladder. Deutsch et al.<sup>3)</sup> found vascular proliferation in all of 5 cases, stating that an irregular width of the cholecystic wall is of great diagnostic significance. Abrams et al.<sup>1)</sup> found dilatation and proliferation of cystic artery together with interruption of its branching and some stains in 6 cases of gallbladder cancer.

Among our series, 18 cases were diagnosed preoperatively by angiography as gallbladder cancer and 3 erroneously as cancer of the pancreas, in one of which it might have been not difficult to make a diagnosis of gallbladder cancer. Thus, angiography enables a high rate of successful diagnosis. The fact should be stressed that most of these patients had an advanced cancer not permitting radical operation.

This is partly due to preoperative failure of angiography in many cases but also and this is significant to the fact that angiographer's attention is apt to be concentrated on abnormalities of blood vessels distributed in organs such as the liver, spleen or pancreas but not on those in the area of the cystic artery. When one pays special attention to the cystic artery the presence of such abnormalities, and hence of any pathological picture of the artery, may be readily detected.

The normal gallbladder has its thin wall depicted by peripheral branches of the cystic artery. In acute cholecystitis, dilatation or hypervascularity of the vessel may occur, but its lumen is regular. When the condition gets chronic, the vessel becomes narrow and scanty, mostly lacking in reticular formation. In case of empyema, displacement is considered to be a main finding, although this remains largely obscure.

Selective celiac or superior mesenteric angiography should be carried out promptly for a detailed examination of cystic artery in women aged over 50 suffering from cholelithiasis, high phosphatase level and not undergoing cholecystography.

The procedure must be regarded to be of greater diagnostic aid in gallbladder cancer, than other previously practiced examinations.

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