CARCINOMA OF THE CYSTIC DUCT ASSOCIATED WITH OPISTHORCHIASIS

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INTRODUCTION

Carcinoma of the cystic duct is an uncommon entity (Farrar, 1952; Pack and Teng, 1962; Smith *et al.*, 1962; Parker, 1965). It was called primary if only the malignancy was found in the cystic duct (Farrar, 1952). However, in a larger number of cases in the reported series, carcinoma was found in the extra hepatic duct. The 4 patients described herein had carcinoma of the cystic duct associated with opisthorchiasis *(Opisthorchis viverrini)*. It is possible that the latter may have contributed to the formation of cystic duct carcinoma.

CASE REPORTS

Case 1 : A 63 year-old female from Khonkaen Province, noticed a mass and felt discomfort at the right upper quadrant one week prior to admission to Siriraj Hospital. There was no history of previous jaundice. She is a resident from the northeastern part of Thailand, and for several years in the past had eaten raw fresh-water shrimp and fish. Physical examination revealed a cystic globular mass, 4 finger-breadth below the right costal margin. The liver was not palpable. Peritoneoscopy revealed a markedly enlarged gall bladder extending far beyond the lower edge of the liver. Relevant laboratory values are shown in Table 1. At operation, the gall bladder was markedly enlarged but the common bile duct was not dilated. The surface of the liver was smooth and several dilated bile ducts were present on both lobes. Cholecystectomy was performed.

Grossly, the gall bladder measured 10 centimeters in length and was distended with white bile. The neck was hardened and would not permit any penetration from within (Figs. 1, 2). Histological findings of the cystic duct revealed adenocarcinoma with abundant fibrosis. The gall bladder showed acute and chronic inflammation.

Case 2: A 61 year old female from Khonkaen gave a history of a painless lump at the right side of abdomen for 3 months. She has been a resident of a small village in Khonkaen throughout her life. She used to eat "Koi Pla", more at the younger age. Physical examination revealed a well nourished non-jaundiced female. The gall bladder was felt 4 finger breadths below the right upper quadrant. The liver and spleen were not palpable.

Three stool examinations did not reveal any *Opisthorchis* eggs. The liver scan showed a large defect at the right anterior region, consistent with an enlarged gall bladder. Peritoneoscopy revealed a markedly enlarged gall bladder. The surface on both lobes contained dilated bile ducts and showed diffused fibrosis, the later appearing as whitish tree-like ramification. Cholecystectomy was performed. The common bile duct was not dilated and it was not explored.

Grossly, there was empyema of the gall bladder. The cystic duct as well as the neck were thickened. The histologic section of the cystic duct revealed adenocarcinoma with large amount of fibrosis. Data of other cases are shown in Tables 1 and 2.

Table 1

Summary of clinical profiles and laboratory values.

Age/Sex	Province	Chief complaint	Physical exam.		Haema-tocrit %	WBC	Eosino-phils	Stool exam.	Bilirubin D/T	Alkaline Phos-phatase (Normal 2-4 B.U.)
			Gall Bladder	Liver						
63 F	Khonkaen	Mass, and dis-comfort at the right upper abdomen 1 week	4 FB	Not palpable	32	6,200	11%	*Opisthorchis* (1)*	0.1/0.5	3.2
61 F	Khonkaen	Mass at right upper abdomen 3 months	4 FB	Not palpable	33	7,350	1%	Negative (3)	0.2/0.6	1.2
57 F	Khonkaen	Mass at right upper abdomen 3 months	4 FB	3 FB	30	10,100	12%	*Opisthorchis* (3)	0.3/1.1	21.6
47 M	Nakorn-Ratchsima	Mass at right upper abdomen 5 days	4 FB	3 FB	33	9,550	10%	*Opisthorchis* (1)	0.5/0.8	-

FB = Finger Breath, *Number in parenthesis indicates times of examination.

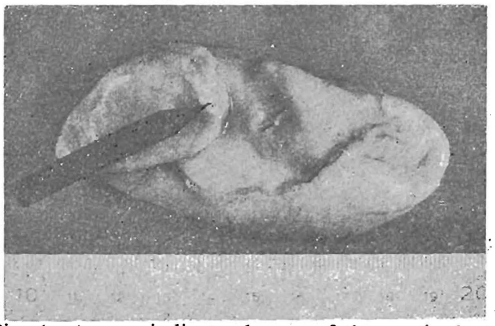

Fig. 1—Arrow indicates lumen of the cystic duct which is obliterated by carcinoma.

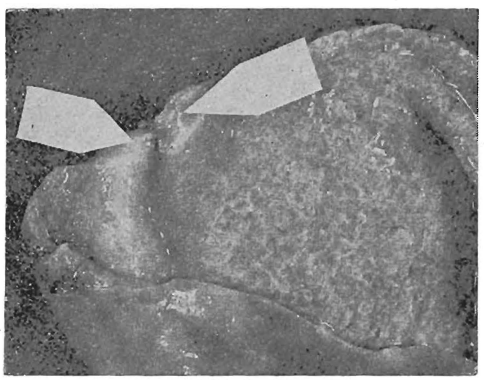

Fig. 2—Arrows indicate carcinoma which obliterated the cystic duct.

DISCUSSION

None of the cases had jaundice and all four patients had palpable gall bladders which led to further investigations. Only on careful examination of the surgically removed gall bladder we able to identify that the enlarged gall bladder was the result of carcinoma of the cystic duct. Gambill *et al.*, (1962) reported 10 cases of hydrops of the gall bladder caused by stones obstructing the cystic duct. In other but rarer instances, the hydrops was caused by carcinoma of the cystic duct (Pack and Teng, 1962; Smith *et al.*, 1962). However, most of these cases also had carcinoma elsewhere in the biliary tree. Furthermore, no report of the cystic duct carcinoma had associated opisthorchiasis.

We would prefer not to call this primary carcinoma of the cystic duct in our patients, since it is possible that malignancy also occurred at other segments of the bile duct but were too small to give rise to any symptoms. The cystic duct however has a smaller lumen and can be obliterated easily. To support this, one of our patients (case 3) came back 3 months after cholecystectomy with obstructive jaundice and cholangiocarcinoma was later found obstructing the common bile duct.

Ujjin (1961) described one similar case of a patient who presented with an abdominal mass. Necropsy revealed hepatoma with cirrhosis and hydrops of the gall bladder caused by obstructing metastatic gland of the cystic duct. Tansurat (1971) mentioned 3 cases of hydrops associated with opisthorchiasis; however, he did not mention the cause of hydrops or whether jaundice was present or absent in his patients.

Our cases came from areas where *Opisthorchis* was endemic (Vajrasthira and Harinasula, 1957; Harinasuta, 1969). As much as 90% of population from some areas were found to have *Opisthorchis* eggs in the stool. Although the presence of *Opisthorchis* eggs in the stool does not imply a cancer/parasite relationship, it is noticed that most of the cholangiocarcinoma patients came from endemic areas of opisthorchiasis. The analysis of 9,694 necropsy cases from 1954-1965 by Stitnimankarn (1966) revealed that, of 42 cases of carcinoma associated with opisthorchiasis, there were 31 cases of cholangiocarcinoma, whereas of 196 cases of carcinoma without opisthorchiasis there were only 19 cases of cholangiocarcinoma. Thus, in spite of a lack of proof by animal experimentation, it would appear that opisthorchiasis is closely associated with cholangiocarcinoma. Hou (1955) in his study believed that clonorchiasis contributes to the malignant transformation of the bile duct either by chronic irritation of the parasite or toxins it produces.

Table 2

Summary of investigations, surgical findings and pathology.

Case	Liver Scan	Peritoneoscopy	Surgical and Pathological findings
1	Not done.	No tumor on the surface of the liver, enlarged gall bladder with dilated bile duct at the liver surface.	Hydrops of the gall bladder and hardened cystic duct. No tumor on the liver. Carcinoma of the cystic duct.
2	Space right lobe probably enlarged gall bladder.	No tumor on the surface of the liver, enlarged gall bladder with dilated bile duct at the liver surface.	Empyema of the gall bladder and hardened cystic duct. Carcinoma of cystic duct.
3	Space at right lobe, superior aspect.	Enlarged gall bladder with dilated bile duct at the liver surface.	Hydrops of the gall bladder, hardened cystic duct, with some nodular appearance at the wall of gall bladder. Carcinoma of cystic duct and gall bladder.
4	No space occupying lesion of the liver, enlarged left lobe.	Enlarged gall bladder with dilated bile duct at the liver surface.	Hydrops of the gall bladder with stone at the neck. Hardening of the cystic duct, with normal liver. Carcinoma of cystic duct.

One of our patients (case 2) did not have *Opisthorchis* eggs in the stool after repeated examinations. Generally, patients with opisthorchiasis will reveal eggs on repeated stool examination particularly when there is no biliary obstruction (Harinasuta, T., pers. comm.). However, the negative stool findings should not exclude the infection. This patient as well as others had dilatation of the bile ducts accompained by fibrosis on the surface of the liver. These are usually pathognomonic for opisthorchiasis in our experience with patients who presented with cholangiocarcinoma or jaundice.

Cholecystectomy without operative cholangiography was done in all of our patients. This might not be adequate if other portions of biliary tree were involved. It is suggested that operative cholangiography should be performed in all patients who were suspected of having carcinoma involving the cystic duct so that suitable surgical procedures could be done. In examining a non-jaundiced patient with a palpable gall bladder coming from an opisthorchiasis endemic area one should carefully look for the presence of cystic duct carcinoma.

SUMMARY

Four patients who had obstructing carcinoma of the cystic duct and who presented themselves with enlarged and palpable gall bladders but without jaundice are reported.

All patients came from endemic areas of opisthorchiasis and had evidence of *Opisthorchis* infection by peritoneoscopic and surgical findings. All but one had *Opisthorchis* eggs in the stool. The pathogenesis and management was discussed.

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