HEPATIC CARCINOMA WITH OPISTHORCHIASIS

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INTRODUCTION

Primary carcinoma of the liver is a common disease in Thailand (Viranuvatti and Satapanakul,1959; Bhamarapravati and Viranuvatti,1966). Among predisposing factors to be considered are diseases affecting the biliary system such as liver flukes; evidence that the liver fluke *Clonorchis sinensis* may be directly responsible for bile duct carcinoma has been presented by Hou (1956). *Opisthorchis viverrini* is the liver fluke commonly found in northeast Thailand (Vajrasthira and Harinasuta, 1957; Tansurat, 1971), and it has been suggested that malignant change is one of the most serious consequences of opisthorchiasis (Tansurat, 1971). In addition Thai and Thai-Laos, like Mongolians in general, have a high percentage of liver cell carcinoma complicating hepatitis and cirrhosis. This report is based on a review of autopsied cases of primary hepatic carcinoma arising in conjunction with *Opisthorchis viverrini* infection of the liver.

PATHOLOGICAL FINDINGS

In this survey, which spanned 17 years, there were 87 cases of primary hepatic carcinoma in association with *Opisthorchis viverrini* infection of the liver, forming a probably artificial incidence of 56.6% of a total of 154 cases of opisthorchiasis found in this series of autopsies. Fig. 1 shows the age and sex distribution of the 87 patients with primary liver carcinoma, in relation to the age and sex distribution of opisthorchiasis cases. The patients ages ranged from 24 to 77 years, with

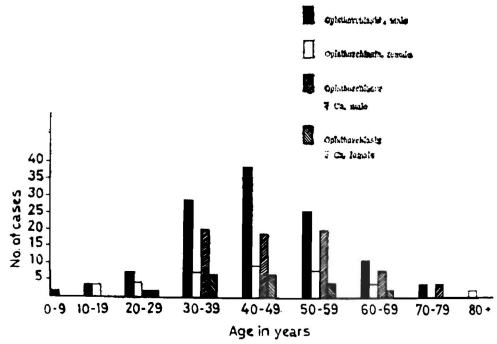

Fig. 1 —Age and sex incidence of opisthorchiasis and hepatic carcinoma.

a mean age of 45.9 years. There were 69 males and 18 females.

The livers ranged in weight from 760 to 6000gm with a mean of 2250gm. The tumours were described as a single mass in 20 cases (25.6%),and as multiple nodules in the remainder. The tumours were located in the right lobe in 22 cases, in the middle in 7, in the left lobe in 6, and generalised in 52. Metastases were found in 71 cases (81%), multiple in 52 (64.4%). Metastases occurred primarily in the regional lymph nodes and lungs. Ascites was present in 66 cases, and jaundice in 57. Liver flukes found on examination of the liver and gall bladder were not counted, but were estimated to be numerous in 36 cases, moderate number in 28, small number in 11, quantity unrecorded in the rest.

On microscopic examination, all the livers showed changes consistent with long standing opisthorchiasis, particularly proliferation of bile duct epithelium, often with pseudo-glandular formation and papillary projections

Table 1

Histologic classification in hepatic carcinoma.

	No.	Per cent
Cholangiocarcinoma	67	77.0
Hepatocellular carcinoma	9	10.3
Mixed hepatocholangiocarcinoma	4	4.7
Unclassified	5	5.7
Squamous cell carcinoma	2	2.3
Total	87	100

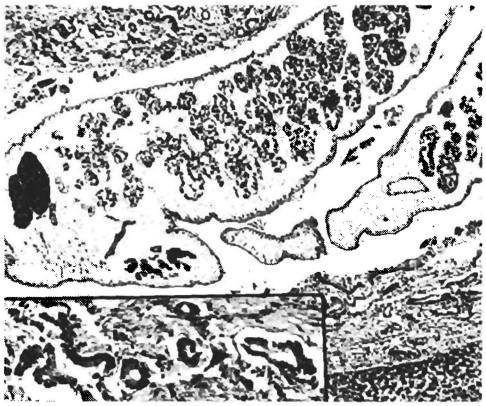

Fig. 2 —Flukes with bile duct proliferation and pseudoglandular formation. H.E. x 35. Inset. Detail of pseudoglandular formation x 100.

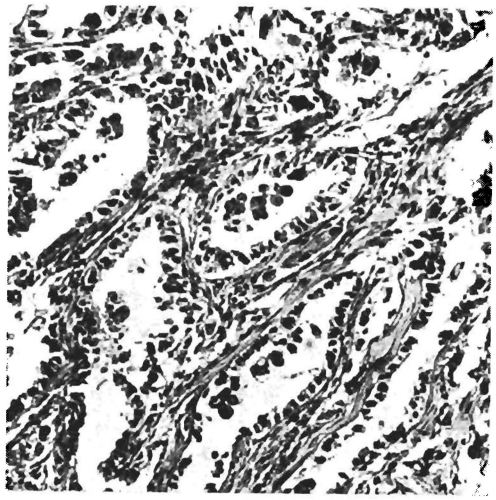

Fig. 4 —Cholangiocarcinoma, well-differentiated. H.E. x 100.

Fig. 3 —Marked papillary proliferation of bile duct epithelium. H.E. x 100.

Fig. 5 —Cholangiocarcinoma, well-differentiated, with marked mucin production. H.E. x 100.

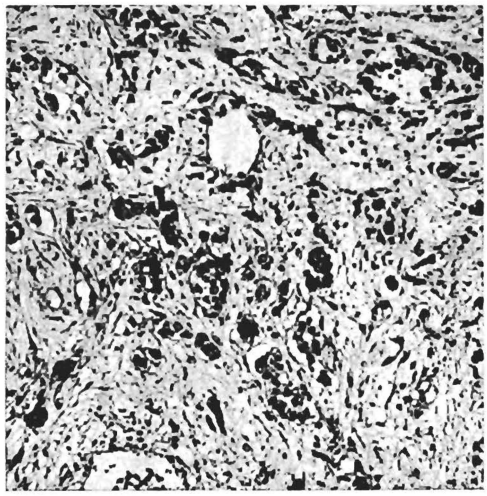

Fig. 6 —Cholangiocarcinoma, moderately differentiated. H.E. x 100.

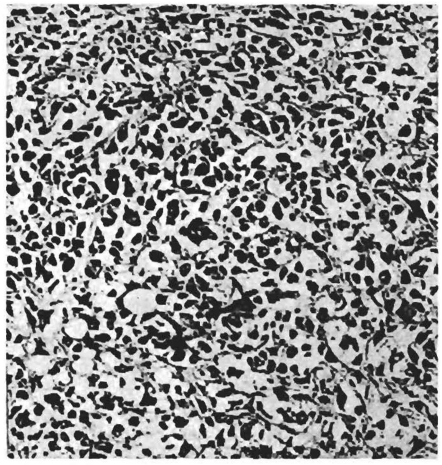

Fig. 8 —Anaplastic large cell carcinoma. H.E. x 100.

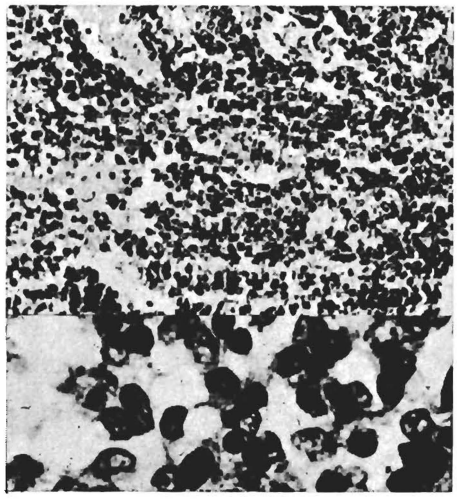

Fig. 7 —Cholangiocarcinoma, poorly differentiated, with mucin production. H.E. x 100. Inset. Detail of the above. x 100.

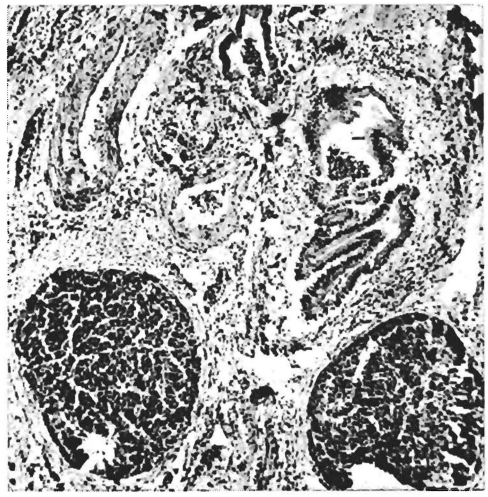

Fig. 9 —Hepatocellular carcinoma with fluke changes in adjacent bile ducts (flukes elsewhere). H.E. x 35.

(Figs. 2-3). The histological classification of the tumours, following that given by Edmonson, is shown in Table 1. The overwhelming majority, 67 cases (77%), were cholangiocarcinoma. Abundant mucin production was frequently seen, apparently independent of the degree of differentiation. There were 9 cases (10.3%) of hepatocellular carcinoma. Figs. 4-9 demonstrate the histology representative of the tumours found in this series. The age and sex distribution of the two main groups, cholangiocarcinoma and hepatocellular carcinoma, and their relation with liver flukes and cirrhosis, are shown in Fig. 10.

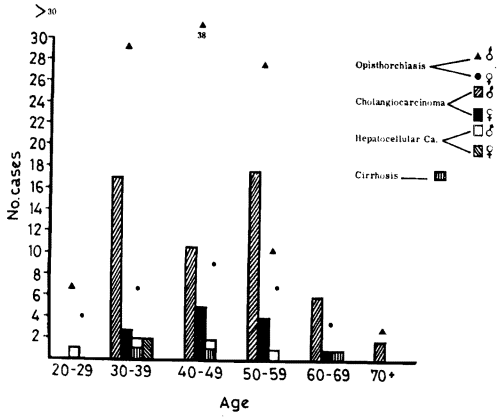

Fig. 10—Age and sex incidence of cholangiocarcinoma versus hepatocellular carcinoma, in relation to opisthorchiasis and cirrhosis.

DISCUSSION

Opisthorchiasis is an important human infection in northeastern Thailand and Laos. In northeastern Thailand, from 72-87 % of the population have been reported as infected with *Opisthorchis* as a result of the habit of eating raw fish (Vajrasthira and Harinasuta, 1957; Tansurat,1971).

Tumours classified histologically as cholangiocarcinoma formed more than three-quarters of the whole series. More males (80.8 %) were affected than females. The patients had a mean age of 45 years. This is in contrast to cholangiocarcinoma in general which seems to affect females more than males, in late or middle life. Metastasis was most commonly to the regional lymph nodes and lungs. There were numerous or moderate numbers of liver flukes in most cases.

Cholangiocarcinoma is a relatively uncommon malignant tumour. In the Far East cholangiocarcinoma often develops in livers infected with the flukes *Clonorchis sinensis* and *Opisthorchis viverrini.* It is hoped that the incidence of this tumour will be reduced if liver fluke infection can be controlled.

As for hepatocellular carcinoma, the role played by opisthorchiasis in its pathogenesis is uncertain; it may be that a concomitant parasitic state favours persistent antigenaemia in a less specific or additive fashion, especially in a population selectively favoured by non-recognition of hepatitis antigens or hepatocytes infected and altered by the virus with subsequent malignant induction.

These findings were compared with a 3-year autopsy study in Udorn in northeast

Table 2

Comparison of Siriraj and Udorn autopsy series of hepatic carcinoma and opisthorchiasis.

	Bangkok	Udorn
Total no. of autopsies	15,461	146
No. years studied	21	3
Cases with opisthorchiasis	154	123
	(0.99 %)	(85 %)
Cases with opisthorchiasis with primary liver cancer	87	11
% of cases of opisthorchiasis with cancer	56.6	9
Cholangiocarcinoma	67	8
% of opisthorchiasis cases	43.6	6.5
% of primary liver cancer	77	73
Hepatocellular carcinoma	9	3
% of opisthorchiasis cases	5.8	2.4
% of primary liver carcinoma	10.3	27

Thailand. In this series of 146 autopsies, there were 123 cases of opisthorchiasis, or 85%. Among the patients with liver fluke infection there were 11 cases (9%) of hepatic carcinoma; 8 of these were cholangiocarcinoma with a male to female ratio of 7:1; the mean age was 44 years, the youngest being a 15-year-old boy with well-differentiated cholangiocarcinoma. Of the 3 cases of hepatocellular carcinoma, 2 were males and one female; 2 had post-hepatitic cirrhosis; the average age was 51 (Table 2).

It is conjectural which represents the true incidence of hepatic carcinoma co-existing with opisthorchiasis; most probably neither as patients with serious diseases tend to come to Bangkok.

SUMMARY

Eighty-seven cases of primary hepatic carcinoma associated with opisthorchiasis were reviewed. The prevalence of liver carcinoma among 154 cases of liver fluke infection was 56.6%. The tumours were classified histologically as cholangiocarcinoma in 67 cases (77%), hepatocellular carcinoma in 9 (10.3%), mixed hepatocholangiocarcinoma in 4, squamous carcinoma in 2, and undifferentiated carcinoma in 5. Metastases, found in 71 cases, occurred most frequently in the regional lymph nodes and lungs. There were numerous or moderate numbers of liver flukes in most of these cases.

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