HUMAN PATHOLOGY OF *OPISTHORCHIS VIVERRINI* INFECTION: A COMPARISON OF ADULTS AND CHILDREN

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INTRODUCTION

The liver fluke infection by *Opisthorchis viverrini* is prevalent in the northeastern part of Thailand. It has been estimated that about 5 million people in this area harbour the flukes (Preuksaraj, 1982). The worms stay mainly in the biliary tree. They do not kill the host unless there are superimposed complications such as cholangitis, cholangiohepatitis or cholangiocarcinoma (Koompirochana, 1978; Kurathong, 1985). The human pathology of mild infection and infection in children has not been described. This paper reports on autopsy findings from patients of all age groups who had *O. viverrini* infection and died from either complications of opisthorchiasis or from other causes. The findings in adults and children will be compared.

MATERIALS AND METHODS

Autopsy was performed in 29 patients with opisthorchiasis at the Bangkok Hospital for Tropical Diseases during 1969 to 1988. There were 22 adults aged 20 to 68 years and 7 children aged 7 to 15 years. All of them came from the northeastern part of Thailand and had *O. viverrini* in the bile ducts. The causes of death in these patients were pneumonia, falciparum malaria with pulmonary edema, cerebral malaria, congestive heart failure, cardiac tamponade, acute hemorrhagic fever, massive intra-abdominal hemorrhage, bile peritonitis secondary to spontaneous rupture of dilated subcapsular bile ducts and carcinoma of the liver.

All autopsies were performed within 13 hours of death. A total of 1,740 slides (approximately 60 slides for each case) were examined. These included slides prepared with routine hematoxylin and eosin stain, phosphotungstic acid hematoxylin (PTAH) stain for fibrin, Masson's trichrome stain for fibrous connective tissue, periodic acid Schiff's (PAS) stain for glycogen, Mayer's mucicarmine stain for mucin and Hall's bilirubin stain for bile (Lee and Luna 1968).

RESULTS

O. viverrini flukes were found in the bile from the liver or gallbladders of all cases.

There were few flukes recovered in children while numerous flukes were found in adults.

The gross pathology of the liver is shown in Table 1. All except one case had enlargement of the liver weighing double the normal value. The patient who had a small liver died from falciparum malaria with pulmonary edema and acute liver necrosis.

The gross pathological findings consisted of icteric stained liver (65%), dilatation of intrahepatic and subcapsular bile ducts (55%), fibrosis at the portal area and along the wall of intrahepatic bile ducts (24%), and liver congestion (17%). The occurrence of these findings in adults and children were similar equal. Intrahepatic tumor was found in 10 adults and none in children.

Abnormal gallbladders were found in 7 adults. They were dilatation in 6 cases and fibrous adhesion in 1 case. The gallbladders of all children appeared normal.

Ascites was detected in adults only, 70% were associated with intrahepatic tumor.

Histopathological findings are summarized in Table 2. *O. viverrini* adults were found in the sections of the liver of all cases. The pathological changes were confined to the large and medium-sized bile ducts where the flukes were located (Fig.1). Only minimal cellular infiltration was seen in the small interlobular bile ducts which were less than 30 μ in diameter. Pericholangitis of the large and medium bile ducts with fibrous tissue infiltration of the wall was observed. The cellular infiltration consisted of lymphocytes, monocytes, eosinophils and some plasma cells. Cholestasis in the liver cells was found in cases who had obstructive jaundice clinically.

Table 1

Gross pathology of the biliary system in Opisthorchiasis in adults and children

Gross appearance	Adults n = 22 (%)	Children n = 7 (%)	Total n = 29 (%)
The liver			
Enlargement of the liver	21 (95.5)	7 (100)	28 (96.6)
Dilatation of bile duct			
Intrahepatic	11 (50.0)	5 (71.4)	16 (55.2)
Subcapsular	10 (45.5)	3 (42.9)	13 (44.8)
Fibrosis			
At portal area	5 (22.7)	2 (28.6)	7 (24.1)
Periductal	3 (13.6)	1 (14.3)	4 (13.8)
Congestion of the liver	4 (18.2)	1 (14.3)	5 (17.2)
Intrahepatic tumor	10 (45.5)	0 (0)	10 (34.5)
The gallbladder			
Dilatation	6 (27.3)	0 (0)	6 (20.7)
Fibrous adhesion	1 (4.5)	0 (0)	1 (3.4)
Ascites	10 (45.5)	0 (0)	10 (34.5)
Jaundice	14 (63.6)	5 (71.4)	19 (65.5)
Carcinoma of liver	10 (45.5)	0 (0)	10 (34.5)

Table 2

Comparison of Histopathology due to oposthorchiasis in adults and children.

Gross appearance	Adults n = 22 (%)	Children n = 7 (%)	Total n = 29 (%)
Pericholangitis	21 (95.5)	7 (100)	28 (96.6)
Fibrous tissue infiltration at the wall of bile duct	20 (90.9)	7 (100)	27 (93.1)
Adenomatous formation	18 (81.8)	7 (100)	25 (86.2)
Dilatation of bile duct	18 (81.8)	6 (85.7)	24 (82.8)
Hyperplasia of epithelium	15 (68.2)	6 (85.7)	21 (72.4)
Desquamation of epithelium	15 (68.2)	5 (71.4)	20 (69.0)
Proliferation of epithelium	13 (59.1)	6 (85.7)	19 (65.5)
Dense fibrous tissue at the portal area	13 (59.1)	3 (42.9)	16 (55.2)
Dilatation of portal vein	10 (45.5)	2 (28.6)	12 (41.4)
Cholestasis	10 (45.5)	2 (28.6)	12 (41.4)
Chronic cholecystitis	7 (31.8)	0 (0)	7 (24.1)
Adenocarcinoma of bile duct	8 (36.4)	0 (0)	8 (27.6)
- Well differentiated	6 (27.3)	0 (0)	6 (20.7)
- Poorly differentiated	2 (9.1)	0 (0)	2 (6.9)
Hepatocellular carcinoma	2 (9.1)	0 (0)	2 (6.9)

Chronic inflammation of the gallbladder was found only in adults. Other findings were adenomatous formation, dilatation of the bile ducts, hyperplasia, desquamation and proliferation of the epithelial lining cells. There were approximately the same numbers of glandular formation beneath the surface epithelial lining, 38-73 (mean 51.5) and 37-85 (mean 68) per medium power field in adults and children respectively, and the amount of fibrous connective tissue infiltration was also moderate to marked in both groups.

Chronic inflammation of the gallbladder was observed only in adults.

Carcinoma of the liver was found in 10 adults aged 36-68 (mean 51) years but not in children. They are located in the right lobe. Their diameters ranged from 5 to 20 cm. (mean 10.8). Six of 10 cases were well differentiated, mucin-producing adenocarcinoma; two were poorly differentiated carcinoma and two were hepatocellular carcinoma, one of which was of the trabecular type and the other exhibited peritheliomatous arrangement. All carcinomas had evidence of local and multiple extensions into the liver parenchyma. Distant metastasis was observed in 80%. The most common metastatic organ was lymph node (porta hepatic, hilar, peripancreactic, mesenteric, paraaortic, periadrenal and coeliac lymph nodes), followed by diaphragm, adrenal glands, striated muscle, thymus and small intestine. Less common involved organs were other parts of gastrointestinal tract, urinary bladder, heart, bones, portal vein and nerve. Metastatic carcinoma to the wall of gallbladder was found in 4 cases, three of

Fig. 1–Adult liver fluke in the lumen of a large dilated bile duct. Note hyperplasia, desquamation and proliferation of the epithelial cells, adenomatous formation and fibrous connective tissue infiltration of the wall, H × E stain, × 40.

which were well-differentiated adenocarcinoma and one trabecular hepatocellular carcinoma. One case displayed clusters of tumor cells occluding the large portal vein and one case demonstrated perineural invasion by tumor cells. Two cases of cholangiocarcinoma were associated with hepatic cysts. Leakage of *O. viverrini* eggs to the liver parenchyma with granulomatous formation was found in one case. This patient had been treated with dehydroemetine. One patient had marked dilatation of subcapsular bile ducts which spontaneously ruptured into the peritoneal cavity. This patient died of bile peritonitis and a large number of flukes were recovered from the peritoneal fluid, the liver and the gallbladder.

DISCUSSION

The enlargement of the liver, could be due to other diseases or conditions associated such as malaria, congestive heart failure. However opisthorchiasis was responsible most if not all of them as all patients had enlargement of the liver.

All the patients in this study came from the northeastern part of Thailand. Infection with

O. viverrini starts in the early years of life (Kurathong *et al.*, 1985) and the life-span of the fluke is over 20 years (Harinasuta and Bunnag, 1987). With repeated infection there would be accumulation of flukes with increasing age. Our results support this hypothesis. The number of flukes recovered was much less in children than in adults.

The gross and histological pathology of human opisthorchiasis in adults and in children was similar except changes in the gallbladder and carcinoma were found only in adults. If all of them acquired the infection in the first year of life and the pathological changes of the liver seen in 7–15 year group and 20–68 year group are the same, then the pathology of human opisthorchiasis is well established within 7–15 years, but the changes of the gallbladder take a longer time.

Tansurat in 1971 reported suppurative cholangitis with macro- and micro- abscess formation in the liver in opisthorchis infection. We did not find evidence of it in our series. The hepatic cysts associated with cholangiocarcinoma in 2 patients were similar to previous reports by Viranuvatti and Kasemsant (1955) and Juttijudata *et al.*, (1986).

Carcinoma was found only in adults with a mean age of 51 years. The ratio of adenocarcinoma to hepatocellular carcinoma was 8:2, as previous reported in opisthorchiasis and clonorchiasis by several investigators (Hou, 1956; Chou, 1976; Sonakul *et al.*, 1978, Schwartz, 1980) and substantiated a causal relationship between the cancer and the fluke. However, liver fluke infection is not the sole cause of carcinoma since it was not found in children who had similar pathological changes. Other factors such as nitrosamine (Thamavit, 1978) together with long duration of infection might play an important role in causing malignant changes.

One rare complication seen in our study is the spontaneous rupture of subcapsular dilated bile ducts causing bile peritonitis.

SUMMARY

The pathology of human opisthorchiasis in 22 adults (20 to 68 years) and 7 children (7 to 15 years) at autopsy is described. The changes of the liver in adults and children are similar and are summarized as follows:-

Enlargement of the liver was a common finding. Pericholangitis was observed in most cases. The pathology was confined to the large and medium-sized bile ducts where the flukes inhabited. The small interlobular bile ducts had minimal or unremarkable changes. Dilatation of the bile ducts with hyperplasia, desquamation and proliferation of the bile duct epithelial cells, glandular formation and fibrous connective tissue infiltration of the walls were the most common features. The pathological changes were well established within 7 to 15 years.

Dilatation of the gallbladder, chronic cholecystitis and carcinoma were found only in adults. Eight of ten cases were cholangiocarcinoma and two were hepatocellular carcinoma.

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