

Oriental Liver Fluke Infestation Presenting More Than 50 Years After Immigration

Dear Editor,

Opisthorchis sinensis (previously known as *Clonorchis sinensis*) is an Oriental liver fluke. This trematode can be found worldwide but its prevalence is highest in East Asia such as China, Taiwan, Japan and Korea. Clinical presentation ranges from asymptomatic carriage to severe infestation resulting in liver failure. We report a case of a Chinese immigrant who presented with intermittent fever and tea-coloured urine. In view of the absence of a definitive diagnosis of cholangiocarcinoma and supportive circumstantial evidence, a possible diagnosis of *Opisthorchiasis* was made by a multi-disciplinary team. This is the longest infestation period recorded, the previous being 50 years reported by Seah.¹

Case Report

A 70-year-old Chinese female was admitted to the hospital with complains of intermittent fever for the past 1 year. She also reported of tea-coloured urine during these febrile episodes. There was no history of abdominal pain. The only significant history was an episode of jaundice 30 years prior to this admission that resolved spontaneously. She was born in southern China and had moved to Singapore in her teens. There is no other history of travel outside Singapore since arrival. On examination, she was afebrile and haemodynamically stable. There was no icterus or any stigmata of chronic liver disease. On abdominal examination, there was a firm but non-tender hepatomegaly. The laboratory data included the following: conjugated bilirubin 7 $\mu\text{mol/L}$, unconjugated bilirubin 9 $\mu\text{mol/L}$, aspartate aminotransferase 108 U/L, alanine aminotransferase 68 U/L, alkaline phosphatase 251 U/L and white cell count of $2.97 \times 10^9/\text{L}$. Faecal examination did not reveal any egg, cyst or parasite.

She underwent further imaging to elucidate the cause of her symptoms and hepatomegaly. Ultrasound of the abdomen revealed an 11.3 x 9.4 x 8.3 cm cystic mass at the liver hilum projecting into the right lobe. Echogenic material was seen in the region of the gallbladder neck. Computed tomography (CT) scan showed extensive dilatation of the entire biliary tract with dilatation of the peripheral biliary radicles in both lobes of the liver. The common bile duct was also dilated to a diameter of 6.2 cm (Fig. 1). Although endoscopic cholangiography would help in establishing the diagnosis, it was felt that it might introduce infection into the biliary system causing life-threatening cholangitis in an otherwise stable patient. A magnetic resonance imaging

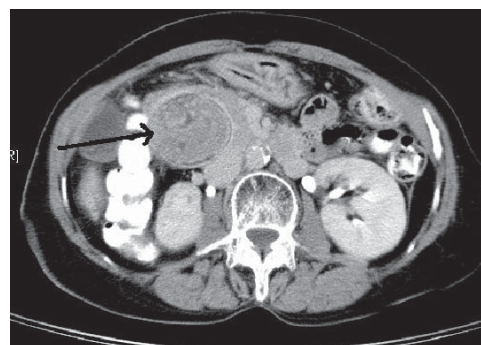


Fig. 1. CT scan showing a giant common bile duct with curvilinear opacity and echogenic sludge.

(MRI) scan was done instead; the findings are consistent with that of the CT scan. A possible diagnosis of *Opisthorchiasis* was made and she was offered anti-helminthic treatment. She remained well despite refusing medication and was discharged home well. Her repeat blood investigations revealed normal full blood count and liver function tests. She was followed-up at the surgical outpatient clinic and a second faecal examination was also negative. Two years later, the patient remains well with no recurrence of symptoms.

Discussion

Opisthorchis sinensis is endemic in China, Taiwan, Japan and Korea, infecting over 19 million people.² This parasite is a flat, narrow worm measuring 10 to 20 mm long, 3 to 5 mm wide and 1 mm thick. It inhabits the biliary tract of humans (definitive host). The eggs laid are swept down the common bile duct to the duodenum and are excreted in the faeces. These are ingested by appropriate fresh water snails (first intermediate host) and undergo metamorphosis before being released as cercariae. These cercariae penetrate the musculature of suitable fresh water fish (second intermediate host) and become metacercariae. Ingestion of raw or poorly cooked, contaminated fish results in the completion of its life cycle. The metacercariae excyst in the duodenum, pass into the common bile duct and migrate to the smaller biliary radicles and develop into adult flukes. These liver flukes may then persist for 50 years or more (as in our patient) and there is no tissue invasive phase.

The pathogenesis of *Opisthorchiasis* is related to chronic irritation and injury to the ductal epithelium by the mechanical activities of the suckers and by body movements, by the production of toxic metabolic products, by the immune reaction of the host and by secondary bacterial

infection.³ Early stages of proliferation and desquamation of epithelium is followed by progressive dilatation of the bile ducts with ductal fibrosis and cavitation.¹ The cavity/cyst wall is formed by the distended bile duct with marked epithelial adenomatous hyperplasia.³ There is little fibrosis in the portal tracts (c.f schistosomiasis) and portal hypertension does not occur.

The majority of infected people have low fluke count and are usually asymptomatic. Clinical manifestation depends on the number of parasites present, duration of infestation and the frequency of re-infestation. Early symptoms include indigestion, diarrhoea and bloatedness. Fever and hepatomegaly may be present as in our case. Jaundice will be present in the event of biliary obstruction. Patients may also present with complications such as biliary calculi, acute cholangitis, recurrent pyogenic cholangitis, acute pancreatitis and also cholangiocarcinoma.

The diagnosis can be established by the detection of characteristic eggs in the stools and in duodenal aspirate or bile. However, this was not detected in our patient. This may be due to low fluke count or that the adult flukes had been killed by secondary bacterial infection.⁴ There may be associated leukocytosis with eosinophilia, which is absent in our patient. Our patient had mild leukopenia which is likely non-specific and could suggest the presence of infection. New methods for diagnosis based on the detection of parasite DNA and antigens in faeces by dot-blot hybridisation techniques are now being developed.³ They are very expensive and our patient could not afford them. Imaging modalities, such as ultrasound, form an important tool in the investigation process. Ultrasound is useful in the detection of bile duct dilatation and periductal thickening of the biliary tree. A diffuse dilatation of the peripheral intrahepatic bile ducts with disproportionately less extrahepatic biliary dilatation should raise the suspicion for Opisthorchiasis.⁵ Stones or biliary sludge in Opisthorchiasis are isoechoic to the liver and do not shadow and hence can be missed by ultrasonography. M-mode sonograms sometimes pick up linear echoes moving quickly in the peripheral bile ducts. A CT scan helps to demonstrate the ductal dilatation and any associated abscesses, stone or sludge. The case was discussed at a hospital multi-disciplinary meeting and a probable diagnosis of Opisthorchis infestation was made based on the circumstantial supportive evidence. The epidemiology of the origin of the patient suggests that it could be Opisthorchis infestation. An important differential to exclude would be cholangiocarcinoma. MRI is a useful tool to detect subtle cases of cholangiocarcinoma and MRI failed to reveal features suggestive of cholangiocarcinoma in our patient. Hepatic angiography may be useful if liver

resection is planned, as cholangiocarcinoma is relatively avascular (c.f hepatocellular carcinoma).

Antimony sodium tartrate, chloroquine, mebendazole, albendazole, bithional and dehydroemetine have been used with varying success rates. Hexachloroparaxyol showed promising results but causes neurotoxicity and nephrotoxicity, and has been withdrawn. Praziquantel (75 mg/kg) in 3 divided doses is the usual treatment of choice with nearly 100% cure rates. Biliary drainage and surgery might be necessary if cholangitis supervenes. Our patient remained well on follow-up despite not being on anti-helminthic medication. This may represent an incidental period of quiescence rather than actual cure. We will continue to monitor her condition.

Conclusion

This case highlights the fact that infected patients may seek medical attention many years later and Opisthorchiasis should be suspected in patients with diffuse peripheral biliary dilatation in appropriate clinical settings even after many years of migration from endemic areas.

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