A Fluke Diagnosis

A 27-year-old man presented with a 1-month history of epigastric pain, weight loss and night sweats following a hiking trip to Bolivia. He was pyrexial at 37.8ºC, with a pulse rate of 90 beats/min and blood pressure of 128/83 mmHg. He was mildly tender over the epigastrium. Laboratory investigations showed a mildly elevated white blood cell count of 11.82 x 10^9/L with an eosinophilia of 4.82 x 10^9/L (normal range 0.00 to 0.72 x 10^9/L), erythrocyte sedimentation rate of 36 mm/hr and normal liver function test. His stool culture was negative for ova, cysts or trophozoa. He was investigated with an intravenous contrast enhanced computed tomography (CT) (Fig. 1) and later magnetic resonance imaging (MRI) of the liver (Fig. 2).

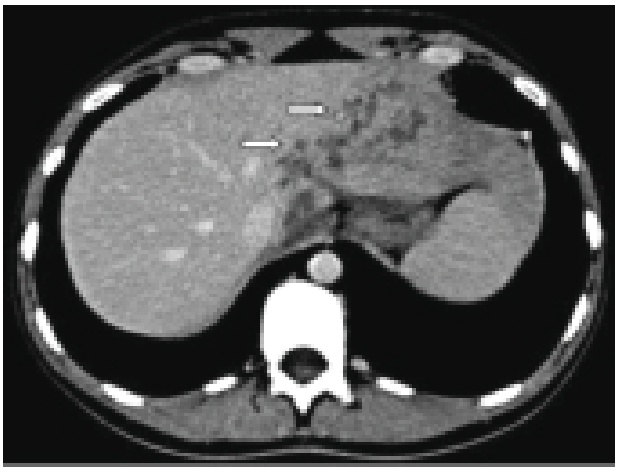

Fig. 1. Intravenous contrast enhanced axial CT scan image shows multiple, tortuous, hypodense tracks in the left and caudate lobes of the liver (arrows) extending from the liver capsule, centrally towards the porta hepatis.

What is the most likely diagnosis for this patient?

A. Acute bacterial cholangitis
B. Recurrent pyogenic cholangitis
C. Clonorchiasis
D. Toxocariasis (visceral lava migrans)
E. Fascioliasis

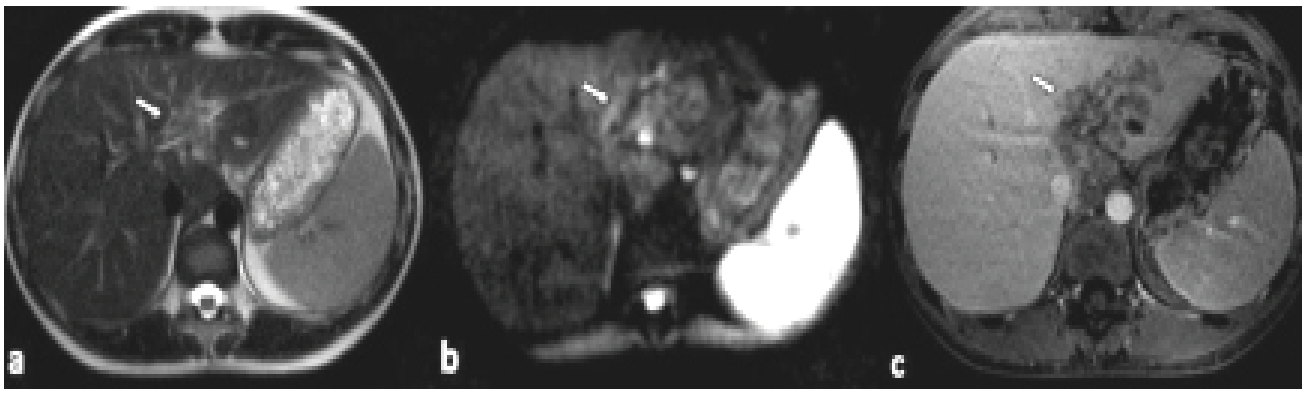

Fig. 2. Axial MRI (a) T2W sequence shows focal hyperintensities in the liver adjoining the porta hepatis (arrow); (b) DWI sequence shows restricted diffusion at the portahepatis (arrow) extending to the left and caudate lobes, more extensive than abnormality seen on the T2W sequence; (c) Contrast enhanced T1W sequence shows small round to ovoid hypointense, non-enhancing nodules in the caudate and left lobes of the liver (arrow) extending from the liver capsule, centrally towards the porta hepatis, corresponding to the region of restricted diffusion. There is no biliary tree dilatation.

Answer: E

Discussion

The patient went on to have a fine needle aspiration of the liver which showed normal hepatocytes with neutrophil and eosinophil infiltration. No parasites, granulomas, necrotic material or malignant cells were seen. Serology test for fasciola antibody IgG was positive and he was treated with a single dose of triclabendazole with good symptomatic relief.

Fascioliasis is caused by *Fasciola Hepatica*, a liver fluke which is a parasitic flatworm of the class trematoda. It infects sheep, goats and cattle. Humans are an accidental host through the consumption of contaminated freshwater plants and other aquatic products eaten raw or insufficiently cooked. Once ingested, the parasite passes through the stomach into the duodenum where it burrows through the intestinal lining into the peritoneal cavity. It finds the liver capsule after a period of days and then begins feeding.[1,2]

Fascioliasis occurs in 2 stages. The first stage, approximately 1 to 3 months after ingestion of the parasite, is the hepatic stage. The fluke digests hepatocytes as it migrates from the liver capsule towards the biliary radicals, leading to clusters of peripheral small sterile necrotic cavities and abscesses. They have a typical serpentine arrangement that persists for many months or even years. Mild hepatitis and subcapsular haemorrhage has also been reported.[1,2] While some patients are asymptomatic during this stage, others may develop fever, urticaria, right upper quadrant pain, hepatomegaly, hypergammaglobulinaemia and marked eosinophilia.[1,2]

After a few months in the liver, the parasites become established in the biliary ducts starting its biliary stage that can last for decades. The flukes mature and start releasing eggs into the biliary tree which are excreted in the faeces. At first, they reside in smaller biliary branches, but as they grow, they move toward the central and extrahepatic biliary tree and gallbladder. They cause biliary inflammation, bile duct wall thickening, and intra and extrahepatic biliary dilatation. At this stage, patients may develop intermittent right upper quadrant pain with or without cholangitis, cholestasis and eosinophilia.[1,2]

Ultrasound may not be diagnostic in the hepatic phase due to heterogeneity of the liver caused by the poorly defined nodules. However in the biliary stage of the disease, adult flukes promote hyperplasia and hypertrophy of the bile ducts resulting in duct wall thickening and periductal fibrosis seen as irregular thickening of the common bile duct wall and biliary dilatation. Gallbladder wall thickening is also seen. Mobile vermiform structures without acoustic shadowing within the gallbladder and in the bile ducts represent the worms.[1,2] On CT, in the hepatic phase, multiple serpentine, branching, hypoattenuating subcapsular lesions pointing toward the central liver are seen representing the tracks of the parasites. Multiple clustered hypoattenuating nodules are also seen representing the necrotic cavities and abscesses (tunnels and caves sign).[2] Liver capsule thickening, subcapsular haemorrhage and abscess like lesions up to 10 cm in diameter have also been reported.[1,2] MRI reveals similar findings to CT associated with isointense or hypointense lesions on T1W and isointense or hyperintense lesions with surrounding hyperintensity on T2W sequences.[1]

While stool studies for ova and parasites can be used, it can be unrevealing during the hepatic phase.[1]

Enzyme-linked immunosorbent assay (ELISA) is the most widely used method of diagnosing fascioliasis and detects antibodies against antigen products from adult *Fasciola Hepatica*.[1] A study by Aksoy et al[1] reports a 100% sensitivity for serological detection of fascioliasis. All patients in this study had characteristic findings on CT. A study by Maguire et al[3] also reports that ELISA is more than 90% sensitive in detecting antibodies to the excretory-secretory antigen products from whole worms, but states that the specificity may be less owing to cross-reactivity with other helminthes. While several articles report characteristic appearances on imaging, in patients with a serological diagnosis of fascioliasis, no sensitivity or specificity values for imaging in the diagnosis of fascioliasis has been documented.[1,4]

In acute bacterial cholangitis, the bile ducts are dilatation with diffuse and concentric wall thickening and enhancement. Parenchymal changes such as wedge-shaped or peribiliary areas of T2W hyperintensity and contrast enhancement are seen. Complications such as rim enhancing liver abscesses and portal vein thrombosis may also be seen.[2]

Recurrent pyogenic cholangitis is a progressive biliary disease characterised by recurrent episodes of bacterial cholangitis. Persistent inflammation and subsequent bile duct fibrosis leads to bile stasis and intrahepatic pigmented stone formation. Imaging is characterised by strictures of the peripheral ducts, with decreased branching and abrupt tapering (arrowhead appearance) associated with disproportionate dilatation of the central and extrahepatic bile ducts. The periportal space is thickened owing to periductal inflammation and fibrosis. Liver abscesses and portal vein thrombosis may also be seen. Long-lasting intrahepatic duct obstruction or portal vein thrombosis may result in lobar or segmental atrophy, typically affecting the left lobe or right posterior segments.[2]

In this case, the blood eosinophilia and recent travel to South America suggests a parasitic infestation.

Clonorchiasis, caused by the *trematode C* sinensis, is a small parasite which obstructs peripheral bile ducts with characteristic sparing of the extrahepatic ducts. Peripheral small bile ducts show evidence of chronic inflammation, dilatation and wall thickening. In some patients, there is diffuse uniform dilatation of the entire peripheral biliary

tree.[2] In toxicariasis, caused more commonly by *Toxocara canis*, the dog ascarid, there are multiple, ill-defined, oval low-attenuating intraparenchymal nodules, which are best seen or only seen on the portovenous phase and are either not seen or faintly seen on the arterial and equilibrium phases of dynamic contrast imaging. On follow-up imaging, the lesions may improve or sometimes change location, reflecting migration of larva in the liver, supporting the phenomenon of visceral larva migrans.[5] These imaging features were not demonstrated in the present case.

While fascioliasis can be detected throughout the world, a significant number of patients are from Eastern Europe, Iran, Northern Africa and South America.[1] In our patient, the travel history and blood eosinophilia suggests a parasitic infestation, however the "tunnels and caves" seen on CT and MRI point quite characteristically to a fluke!

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