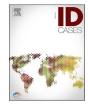


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Case report The Liver's hidden foe: A case study on Human Fasciolasis

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<i>Keywords:</i> Human fascioliasis Fasciolahepatica Liver fluke Ethiopia	Human fascioliasis, caused by Fasciola hepatica and Fasciolagigantica, is a neglected tropical disease of increasing public health significance. Reported cases are rare, with only one serologically confirmed instance in Ethiopia to date. We present the case of a male patient in his late twenties, without identified risk factors, who presented with bilateral upper quadrant pain persisting for a year and a history of repeated treatment for H. pylori gastritis. Initial ultrasound findings prompted further investigation with abdominal CT, contrast-enhanced MRI, and MRCP, leading to a diagnostic shift confirmed by a positive enzyme-linked assay for Fasciola hepatica. This case highlights the diagnostic challenges and the critical role of radiological imaging—ultrasound, CT, and MRIin identifying key features such as biliary dilation and parenchymal abnormalities, crucial for early detection and effective management of human fascioliasis.

1. Introduction

Fascioliasis is a parasitic hepatobiliary zoonosis found worldwide, caused by liver flukes known as Fasciola hepatica and F. gigantica. These parasites undergo a complex life cycle that includes an intermediate snail host, transmission via carrier organisms like aquatic plants, and infection of final mammalian hosts such as cattle, sheep, and humans. Fascioliasis has been observed on every inhabited continent, yet the variety of hosts varies depending on geographical location as well as socioeconomic and developmental factors.[1,2].

Until recently, human cases of fascioliasis were sporadic, but now they are increasingly documented in Europe, the Americas, and Oceania (where only F. hepatica is transmitted) this is due to the increase in international travel rates, as well as in Africa and Asia (where both F. hepatica and F. gigantica occur). According to the WHO, it is estimated that at least 2.4 million people are infected across over 75 countries globally, with millions more at risk. Fascioliasis is present on every continent, and where cases are reported in animals, human infections are also likely present. [3,4]. The global rise in fascioliasis diagnoses can be attributed to greater accessibility and utilization of ultrasound and CT scans, increased recognition of imaging's crucial role in diagnosis, and advancements in specific serological testing methods and cross-sectional imaging can be very helpful in the diagnosis of fascioliasis as well as to differentiate it from other liver diseases with a very similar clinical picture. [4,5].

2. Case presentation

A man in his late twenties presented to the outpatient clinic with intermittent burning pain in the upper abdomen, both right and left quadrants, over the past year. He also reported nausea, loss of appetite, fatigue, intermittent fever, and a weight loss of 7 kg. He had received multiple treatments for H. pylori gastritis in a clinic in his home town and underwent two upper GI endoscopies and the first one had a duodenal ulcer while the second one after the treatment of H.pylori with triple therapy (Omeprazole, Amoxicillin and Clarithromycin) was a healed doudenal ulcer. Physical examination revealed normal vital signs and no abnormalities. Initial diagnosis included gastritis and

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Abbreviations: CDC, Centers for Disease Prevention and Control; CT, Computed Tomography; ELISA, Enzyme-linked immunosorbent assay; ESR, Erythrocyte Sedmentation Rate; FDA, Food and Drug Adminstration; HbsAg, Hepatitis B surfcae Antigen; HCV, Hepatitis C Virus,HIV, Human Immunodeficiency Virus; hsCRP, High sensitivity C-Reactice Protein,IgG, Immunoglobuling G; INR, International Normalized Ratio; MRI, Magnetic Resonance Imaging; MRCP, Magnetic Resonance Cholagiopancreatography; PT, Prothrombin Time; PTT, Partial Thromboplastin Time; WHO, World Health Organization.

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consideration of a liver abscess, prompting blood work up, stool examination, and an abdominal ultrasound as shown in (Fig. 1) which recommended to have a contrast-enhanced abdominal CT scan (Fig. 2). Incidental liver lesions on the abdominal ultrasound and CT scan prompted further investigation, including abdominal MRI with contrast and MRCP (Fig. 3) as well as serological tests for Fasciola hepatica and Toxocara.

The complete blood count, serum creatinine, ESR, and hsCRP levels were all within normal limits according to our laboratory standards. Urinalysis and stool examination did not show any abnormalities. Tests for HIV antibody, HBsAg, HCV antibody, and stool occult blood were negative. The stool antigen test for H. pylori was positive. .

The liver function tests showed a mildly elevated transaminases with elevated direct bilirubin and prolonged prothrombin time.

The serological tests confirmed the diagnosis of the Fasciola hepatica and oral triclabendazole as well as quadruple therapy (Pantoprazole, Metronidazole, Amoxicillin and Clarithromycin) for the H.pylori was prescribed.

3. Discussion

Fasciola hepatica and Fasciolagigantica are large liver flukes with a complex life cycle involving mammalian hosts and intermediate freshwater snails, typically of the genus Lymnaea. Eggs released in feces hatch into miracidia upon contact with water, infecting snails. Within snails, miracidia develop into sporocysts, rediae, and cercariae, which encyst as metacercariae on vegetation. Human infection occurs through ingestion of contaminated plants. Metacercariae excyst in the duodenum, migrating through liver parenchyma to mature into adult flukes in bile ducts. These parasites primarily infect domestic and wild ruminants but can also cause fascioliasis in humans.

3.1. Diagnostic challenge

3.1.1. Clinical presentation

Fascioliasis encompasses two distinct clinical and diagnostic phases: an acute phase characterized by larval migration through the liver parenchyma, and a chronic phase where mature flukes reside in the bile ducts, laying eggs. In the chronic phase, eggs are intermittently shed in stool due to bile duct drainage, making stool studies unreliable for detecting low parasite burdens or acute infections without egg production. The clinical presentation of human fascioliasis can mimic several other differential diagnoses, often complicating accurate diagnosis unless a high index of suspicion is maintained. Typical symptoms include epigastric pain, right upper quadrant pain, intermittent fever, nausea, vomiting, anorexia, weight loss, urticarial itching, peripheral eosinophilia and intermittent diarrhea [6,7]. These nonspecific manifestations can lead clinicians astray, particularly when the infection manifests extra-hepatically, potentially presenting with symptoms such as a dry cough [8], Severe wheezing[9], or even acute necrotizing pancreatitis[10]⁻ There are reports in the literature that human fasciolasis may mimik sepsis[11] ⁻ cerebral aneurysm[12], colon tumor [13] and periotoneal carcinomatosis[14].

Human toxocariasis, a soil-transmitted zoonosis, was considered in the differential diagnosis due to the patient's clinical presentation. Toxocariasis typically presents as visceral larva migrans or ocular larva migrans, though many cases are asymptomatic. Visceral larva migrans, common in preschool children, involves larvae migrating to tissues such as the liver, lungs, and skeletal muscle, causing nonspecific symptoms like fever, myalgia, weight loss, cough, rashes, and hepatosplenomegaly, often with hypereosinophilia. Central nervous system involvement (neurotoxocariasis) is rare and can lead to eosinophilic meningoencephalitis. Risk factors include geophagia, poor hygiene, consumption of raw vegetables from contaminated gardens, and exposure to undewormed puppies; less commonly, infection can occur from eating raw meat of paratenic hosts like chickens or lambs. Our patient had no such risk factors, and serologic tests for Toxocara were negative. [15–18].

In our case presentation, the patient displayed several of these symptoms; however, a persistently positive H. pylori test initially diverted attention from considering alternative diagnoses for approximately a year. Furthermore, the absence of identifiable risk factors like consumption of contaminated or under cooked vegetables, consumption of raw or under cooked meat especially raw liver consumption further complicated the diagnostic process in this particular case. This highlights the importance of maintaining a broad differential diagnosis approach and conducting thorough investigations, when faced with such clinical complexities especially where clinical manifestations may overlap with other conditions or where risk factors are not readily apparent.Top of FormBottom of Form.

3.1.2. Serological studies

Serological studies across various research efforts have presented varying figures for sensitivity and specificity. For instance, a Peruvian study reported a sensitivity of 100 % and a specificity of 95.6 %[19]. A study from Spain reported the respective sensitivity and specificity of

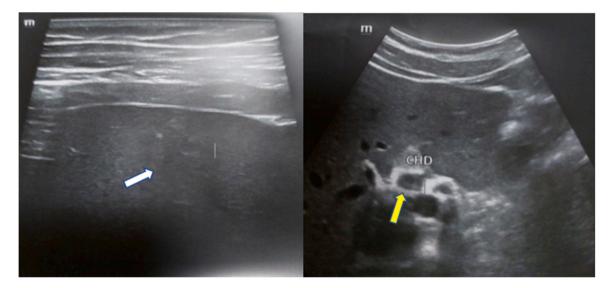


Fig. 1. Ultrasound images the liver of a patient with Fasciola hepatica. The images show peripheral ill-defined heterogeneous echogenicity in the right hepatic lobe (white thick arrow) and common hepatic duct wall thickening (yellow arrow).

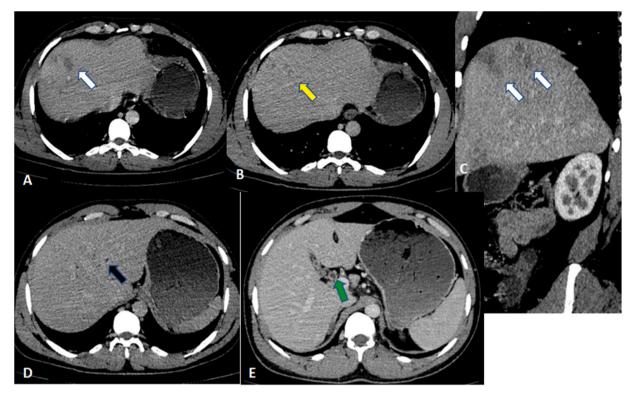


Fig. 2. Multiphasic abdominal CT images at the liver level: Post-contrast axial (A, B, D & E) and coronal (C) images of a patient with Fasciola hepatica. The scans show peripheral subcapsular region multifocal, ill-defined, hypoattenuations in the right hepatic lobe (white thick arrows) which showed progressive contrast filling in the delayed phase (yellow arrow). The axial images also display mild intrahepatic biliary duct dilatation (black arrow) and common hepatic duct wall thickening (green arrow).

ELISA were 95.3 % and 95.7 % respectively[20]. The specificity of the indirect hemagglutination test using purified adult Fasciola hepatica antigen F1 is 96.9 % for serological diagnosis of Fasciola hepatica infection.[21].

3.1.3. Role of radiology

Radiologic modalities like ultrasound and computed tomography (CT) play a crucial role in detecting liver abnormalities such as focal lesions, periportal fibrosis, and thickening of the gallbladder wall, which are characteristic manifestations of fascioliasis. These imaging methods enable the visualization of adult parasites within the bile ducts, assisting in the differentiation of fascioliasis from other liver disorders.[22].

In the early phase, ultrasound commonly reveals focal hypoechoic lesions in the liver, with less frequent diffuse involvement. Typically, ultrasound shows hypoechoic lesions in the liver parenchyma with irregular margins. After approximately eight weeks, ductal ectasia and thickening of the bile duct walls may appear, as evidenced by our case where the common bile duct showed thickening on ultrasound. Occasionally, ultrasound can detect mobile flukes within dilated bile ducts and the gallbladder. Biliary dilation and thickening of bile duct walls may suggest chronic inflammation and fibrosis. ⁽⁵⁾[23].

CT scans reveal areas of decreased attenuation in the liver, indicating regions of necrosis and fibrosis. Biliary dilation is apparent, often with calcifications along the bile ducts in chronic instances. CT findings associated with hepatic fascioliasis include numerous small, clustered hypodense lesions that typically exhibit peripheral enhancement. In advanced cases, CT may show subcapsular hepatic lesions with reduced attenuation, as observed in our patient. As the disease progresses and involves the biliary system, CT demonstrates dilated bile ducts with tracking along the periportal areas. Worms may occasionally be visualized within the bile ducts. Liver MRI can reveal lesions characterized by low signal on T1-weighted imaging (T1WI) and high signal on T2-weighted imaging (T2WI), extending from the liver capsule into

deeper liver tissues which were seen in our case. Additionally, T2weighted imaging and magnetic resonance cholangiopancreatography (MRCP) may show mild dilation of the bile ducts with filling defects appearing as low-signal areas. Nodules that are hyperintense on T2weighted imaging and hypointense on T1-weighted imaging may display peripheral enhancement. Other findings may include intrahepatic and extrahepatic biliary dilation, enhancement of the liver capsule, liver heterogeneity, and mixed T2 hyperintensity [4,5,23,24].

Based on the imaging findings, potential differential diagnoses for our patients include liver abscess, focal steatosis, liver hemangioma, and cholangiocarcinoma.Liver abscess typically presents as hypoattenuating lesions with peripheral rim enhancement on contrast-enhanced CT. These abscesses may have a fluid-filled center and are often accompanied by surrounding inflammatory changes or edema. While liver abscesses can cause biliary duct dilation if they compress or obstruct the ducts, they are not typically associated with biliary duct wall thickening. In contrast, Fasciola hepatica infection manifests as ill-defined, subcapsular hypoattenuations, often with associated biliary duct wall thickening due to the migration of the flukes and resultant inflammation [25].

Focal steatosis is characterized by hypoattenuating areas on noncontrast CT and hyperintense regions on T1-weighted MRI. These hypoattenuating areas are usually segmental or lobar and show no specific enhancement pattern on post-contrast images. Unlike Fasciola hepatica infection, focal steatosis does not involve biliary duct wall thickening. The hypoattenuations in focal steatosis are diffuse and lack defined borders, whereas Fasciola hepatica presents with subcapsular hypoattenuations and biliary duct wall thickening, indicative of parasitic migration and inflammation [26,27].

Liver hemangiomas are benign vascular tumors that appear hyperechoic on ultrasound and show peripheral nodular enhancement on arterial phase CT or MRI, with centripetal fill-in on delayed phases. Hemangiomas are well-defined and exhibit a homogenous enhancement

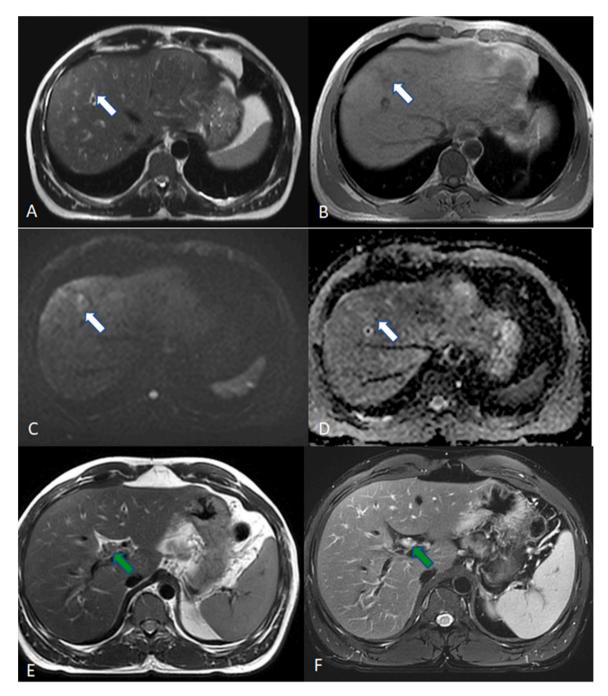


Fig. 3. Abdominal MRI images: Axial T2WI (A & E), T1WI (B), DWI (C), Apparent Diffusion Coefficient (D), and fat suppressed T2WI (F) of a patient with Fasciola hepatica. The scans show peripheral subcapsular region ill-defined lesions in the right hepatic lobe which are slightly hyperintense on T2WI and hypointense on T1WI with facilitated diffusion (white thick arrows). Common hepatic duct has wall thickening and internal signal loss (green arrow).

pattern. There is no involvement or thickening of the biliary ducts in hemangiomas. In contrast, Fasciola hepatica infection presents with illdefined, subcapsular hypoattenuations and biliary duct wall thickening due to the inflammatory response and direct involvement of the biliary ducts by the parasite [28].

Cholangiocarcinoma is a malignancy of the bile ducts that presents as an irregular, hypovascular mass with intrahepatic biliary ductal dilation and prominent ductal wall thickening, often with strictures. This condition is typically more centrally located within the bile ducts and has a mass-like appearance. Elevated CA 19–9 levels are often seen. In contrast, Fasciola hepatica infection causes biliary duct wall thickening without forming a mass, associated with subcapsular geographic hypoattenuations and eosinophilia [29]. As demonstrated in our case, the integration of multiple modalities of radiologic imaging significantly enhances the diagnostic accuracy of Fasciola hepatica infection. By employing techniques such as ultrasound, computed tomography (CT), magnetic resonance imaging (MRI) with contrast enhancement, and magnetic resonance cholangiopancreatography (MRCP), clinicians can effectively delineate characteristic features of the disease within the hepatic and biliary systems. This comprehensive approach not only aids in confirming the diagnosis but also plays a pivotal role in excluding other potential differential diagnoses, thereby guiding the diagnostic pathway toward an accurate identification of fascioliasis. Such precision in imaging not only improves clinical decision-making but also underscores the importance of thorough radiological evaluation in the management of complex

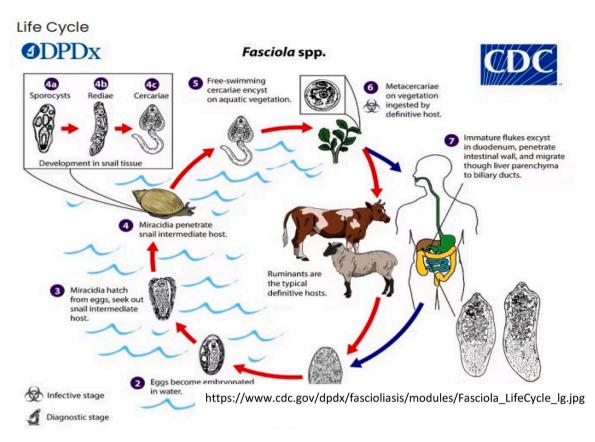


Fig. 4. Life cycle of fasciola.

Table 1 Liver function tests

	Result	Normal Range
SGOT/ALT	46 IU/L	0-37IU/L
SGPT/AST	73 IU/L	0 -40 IU/L
ALP	74 IU/L	30 –120 IU/L
Direct Bilirubin	2.15 mg/dL	0 –0.25 mg/dL
PT	18 s	10 –14 s
PTT	34.7 s	25 –35 s
INR	1.5	-
Serum Albumin	4.3 g/dL	3.4 −5.4 g/dL
Serum Total Protein	6.4 g/dL	6.6 -8.8 g/dL

Table 2

Serology studies for Fasciola hepatica and Toxocara.

	Result	Unit	Reference range
Fasicola Hepatica Indirect Hemagglutination Assay	1:320	titer	< 1:160
Fasciola hepatica IgG	35.8	U/ ml	< 9.0
Toxocaracanis abs (IgG)	0.98	U	< 9.0

parasitic infections affecting the liver.

3.2. Treatment

Triclabendazole, endorsed by the WHO for treating fascioliasis and FDA-approved since February 13, 2019 for patients aged 6 years and older, effectively targets both immature and adult parasites, making it suitable for both acute and chronic phases of the disease. It boasts high cure rates, with generally mild and temporary adverse reactions post-

treatment. The recommended dose is 10 mg/kg body weight administered as a single dose in clinical practice like our case and preventive chemotherapy. In cases of treatment failure, clinicians may escalate the dosage to 20 mg/kg body weight given in two divided doses spaced 12–24 h apart. Despite Triclabendazole's limited accessibility, reports indicated successful treatment with metronidazole and High dose mebendazole as an alternative [3,30–32].

3.3. Follow-up

After therapy, it's important to monitor several aspects including the reduction of eosinophilia, absence of eggs in stool samples, and a decline in serology titers as well as clinical improvement. Repeating tests that were positive initially within three to six months is advisable. Additionally, observing resolution of biliary tract abnormalities on ultrasound can provide valuable insights post-therapy. The enzyme-linked immunosorbent assay (ELISA) proved highly reliable for both diagnosis and monitoring during treatment [33,34].

Following a diagnosis of fascioliasis in a patient, it is important to screen family members for the infection using serological tests since eggs are often absent early in the infection course. Asymptomatic individuals should also be treated to mitigate the risk of potential future complications associated with the disease. Research conducted in Peru revealed that adults diagnosed with fascioliasis were four times more likely to reside with a child who was also infected with Fasciola. The study also highlighted that factors such as poverty and dietary habits were significantly associated with an increased risk of Fasciola infection. Specifically, adults who were infected with fascioliasis had a markedly higher likelihood of cohabiting with children who carried the parasite. This underscores the importance of broadening the scope of screening and treatment within families to manage and prevent the spread of fascioliasis effectively [31,35].

4. Conclusion

Fasciola hepatica remains a significant global public health concern, impacting both human health and livestock productivity. Human fascioliasis is under-diagnosed in many parts of Africa; therefore, radiologists can play a pivotal role in its diagnosis. Advances in imaging and diagnostic techniques, such as our case, have improved disease detection and management. Continued research into the epidemiology, pathogenesis, healthcare-oriented diagnostic algorithms, and treatment of Fasciola hepatica is crucial for developing effective control measures and reducing the disease burden worldwide. In conclusion, radiologic imaging under appropriate clinical scenario serves as an indispensable tool in the diagnosis of human fascioliasis, offering crucial insights. Its role in clinical practice continues to evolve, contributing significantly to the accurate management and surveillance of this parasitic disease.

Ethics approval

A single case report is exempt from institutional ethical approval.

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CRediT authorship contribution statement

Solomon Afework: Writing – review & editing, Investigation. **Teshale Bisrat:** Investigation, Data curation. **Yegzeru Belete:** Writing – review & editing, Writing – original draft, Visualization, Supervision. **Abdulkerim Girma:** Writing – original draft, Investigation, Data curation, Conceptualization.

Declaration of Competing Interest

None.

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