Case Report: First Molecular Diagnosis of Liver Abscesses Due to *Fasciola hepatica* Acute Infection Imported from Vietnam

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Abstract. We report a case of *Fasciola hepatica* liver abscesses in a 67-year-old female returning from a trip to Vietnam. She has been suffering from a fever, right abdominal pain for 4 days, and major eosinophilia. Radiologic investigations showed multiple hypodense confluent abscesses in the right lobe of the liver, complicated by occlusive thrombosis of the right branch of the portal vein. The serological investigation of helminth-elicited eosinophilia showed only a positive serology for *F. hepatica*. Despite repeated negative stool examinations for any intestinal pathogen, the diagnosis was established by the detection of *F. hepatica* DNA in stool and pus aspirate samples.

Hepatic fascioliasis are zoonoses, caused mainly by the trematode *Fasciola hepatica* and *Fasciola gigantica*, also called liver flukes.¹ These parasites infect the main bile ducts and gallbladder of animals and humans.¹ Both species follow a two-host life cycle, where definitive hosts are humans or other mammals (mainly livestock), and intermediate hosts are freshwater gastropod snails of the family Lymnaeidae.¹ The WHO estimates that the global burden of the disease consists of 2.4 million people infected in more than 70 countries worldwide.² In Southeast Asia, it appears in the top 10 of the most prevalent neglected tropical infections.³ *Fasciola hepatica* infection mainly occurs after the consumption of freshwater wild plants, mainly watercress, contaminated with encysted metacercariae rejected by *Lymnaea trunculata*.¹ After ingestion, the metacercariae leave the cyst in the duodenum, cross the intestinal barrier, and pass through the liver (hepatic phase) before migrating into the bile ducts (biliary phase). The typical symptoms of the acute form, while the juvenile parasites migrate from the intestine to the liver, include fever, hypereosinophilia, right upper quadrant pain, and immune allergic reactions.³ Here, we report an atypical imported case of *F. hepatica* from Vietnam presenting as hypereosinophilic liver abscesses.

THE CASE

A 67-year-old female patient living in Southeastern France was hospitalized in June 2018 in the department of infectious diseases at the University Hospital (IHU-Méditerranée Infection) of Marseille, France, with a 4-day history of abdominal pain and a 6-kg weight loss caused by asthenia and anorexia. The patient was born in Vietnam and returns to her native country to visit her family every 3 years for about 3 months; symptoms began on the last trip. She was not taking any medication and did not abuse alcohol. Her medical history was not significant, except for a spontaneous and resolved hepatitis B infection. At clinical presentation, she had a low-grade fever (38°C). Physical examination showed a right upper

quadrant pain. She presented both palpable bilateral cervical adenopathy and left inguinal adenopathy.

Initial blood test showed an elevated white cell count of 19,000/μL with 68% of eosinophil, a subnormal C-reactive protein 17 mg/L, and mildly elevated liver enzymes: alkaline phosphatase 315 U/L (< 105), gamma-glutamyl transferase 174 U/L (< 40), alanine aminotransferase 123 U/L (< 30), and aspartate aminotransferase 75 U/L (< 25).

In addition, the patient presented a polyclonal hypergammaglobulinemia with an increased total IgE level (14 times greater than the normal level). Both computed tomography (CT) and T2-weighted magnetic resonance imaging scans showed multiple hypodense confluent abscesses in the right lobe of the liver; the largest of which measured 40 mm in diameter (Figure 1A). These lesions were complicated by an occlusive thrombosis of the right branch of the portal vein. Malaria (thin and thick blood films and polymerase chain reaction [PCR]) and dengue fever (serology, nonstructural protein 1 antigen, and PCR) tests were negative. Repetitive microscopic examination of stool specimens, looking for vegetative and cystic forms of protozoa, larvae, or helminth eggs, remained negative, despite the presence of Charcot-Leyden crystals. The serological investigation of helminth-elicited eosinophilia showed only a positive serology for *F. hepatica* (ELISA and western blot). Then, for better clarification of the diagnosis, the patient underwent a CT scan-guided puncture of the liver abscesses. The microscopic examination of the pus aspirate revealed Charcot-Leyden crystals. According to the molecular method previously described by Cabada et al.,⁴ identification of *F. hepatica* was finally confirmed by PCR and sequencing targeting the *F. hepatica* internal transcribed spacer 1 region of the rRNA gene (GenBank AJ243016) on both stools and pus aspirate samples. The diagnosis of *Fasciola* liver abscesses was retained.

The patient was administered 15 mg rivaroxaban twice daily (for portal occlusive thrombosis) and triclabendazole 600 mg for 2 days, followed by a subsequent resolution of symptoms and a quick decrease in the eosinophilia level to 2G/L. At the follow-up visit 3 months after discharge from the hospital, the patient was doing well, the abscesses lesions in the liver were reduced in number, and the size on CT scan and the portal thrombosis had almost disappeared (Figure 1B).

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FIGURE 1. Hepatic abscesses due to *Fasciola hepatica* before (A) and 3 months after treatment (B). (A) Computed tomography scan and magnetic resonance imaging T1 sequence. (B) Magnetic resonance imaging T1 three months after treatment. This figure appears in color at www.ajtmh.org.

DISCUSSION

This present case of hepatic fascioliasis is atypical because of the presence of multiple liver abscesses combined with portal thrombosis confirmed by a molecular diagnosis. A systematical literature search was conducted in the database MEDLINE using the following key words: liver/abscess/fasciola/human. We found 14 case reports concerning 36 patients describing liver abscesses due to *F. hepatica* during the acute phase (Table 1).^{5–18} Abscess formation occurs during the migration step, when *F. hepatica* penetrates the Glisson's capsule and passes through the liver parenchyma to finally reach the bile ducts.¹⁹ In the 14 case reports, male adults were the most represented. Clinical presentation was not specific, with mostly pain in the right upper quadrant (36/36, 100%) and fever (28/36, 77.7%). Patients had eosinophilia (26/28, 92.8%) and anemia (19/25, 76%). Also, CT scan results were not specific to a *F. hepatica* origin: images were compatible with hypodense collections similar to pyogenic or amebic liver abscesses. Only one case describes an occlusive thrombosis of portal hepatic vein combined with a liver abscess.¹⁴

Specific and sensitive microbiological tools are crucial to improve the diagnosis of fascioliasis. In 29/36 patients, *F. hepatica* serology was positive. Positive results by ELISA need to be confirmed by western blotting to avoid cross-reactivity with other helminthiasis. In six previous cases, the adult fluke was seen during endoscopic retrograde cholangiography.^{5–8,10,13} In our present case, *F. hepatica* DNA detection by qPCR allowed the final diagnosis to be made and the positive serological results to be consolidated. To the best of our knowledge, qPCR was not used in

previous cases. Stool investigations are not helpful during the hepatic phase of the infection because the eggs do not appear in the stools until 3–4 months after ingestion of contaminated food or drink. However, in our patient, *F. hepatica* qPCR was also positive in a stool sample, probably because of the detection of DNA released by the parasite from the bile ducts.

Few cases have been reported in travelers returning from Asia. According to the WHO, areas of high transmission of fasciolosis are the highlands of South America, the Nile valley, the Caspian Sea basin, as well as East Asia and Southeast Asia.² In Europe, imported cases have been reported in travelers, soldiers, and immigrants.¹ In previous cases, patients were mainly from or had traveled to endemic areas, such as Cuba and Morocco, the Middle East, South Asia, and East Asia.^{1–3,6} In our case report, the patient had traveled to Vietnam. In this country, fascioliasis appears to be highly endemic, with more than 20,000 human cases in 2011 due to *F. gigantica*, *F. hepatica*, and hybrid forms of these two species.²⁰ The central-highland rural region is considered hyperendemic with 10,000 reported cases between 2006 and 2009.²⁰ Our patient stayed in the central area of Tuy Hoa, in the province of Phu Yen (Figure 2).

The outcome of our case was favorable after drainage and treatment with two doses of triclabendazole, which is presently the recommended treatment.

As a conclusion, for patients returning from Southeast Asia, especially central Vietnam, presenting liver abscesses and eosinophilia, clinicians should evoke the diagnosis of *F. hepatica* infection. In this context, diagnostic methods should include molecular tools such as PCR on the liquid aspirated from the abscess or stool sample.

FIGURE 2. Map of Vietnam: city of stay of the patient (Tuy Hoa) and known regions of hyperendemicity for fascioliasis. Areas of high prevalence of fascioliasis (500 to 20,000 cases between 2000 and 2012, adapted from Bui et al. 2015). This figure appears in color at www.ajtmh.org.

Received September 9, 2019. Accepted for publication September 25, 2019.

Published online November 4, 2019.

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REFERENCES

1. Ashrafi K, Bargues MD, O'Neill S, Mas-Coma S, 2014. Fascioliasis: a worldwide parasitic disease of importance in travel medicine. *Travel Med Infect Dis* 12: 636–649.
2. World Health Organization. *Foodborne Trematode Infections* [Internet]. Available at: http://www.who.int/foodborne_trematode_infections/fascioliasis/en/. Accessed July 27, 2018.
3. Hotez PJ, Bottazzi ME, Strych U, Chang LY, Lim YA, Goodenow MM, AbuBakar S, 2015. Neglected tropical diseases among the

TABLE 1
Previous cases of liver abscesses due to *Fasciola hepatica*

Ref (n*)	Age (years)	Gender	Country	Imported	Pain	Fever	Eosinophilia	Serology	Ova in stools/abscess	Adult flukes	Treatment
5 (1)	64	F	Iran	No	Yes	No	-	ND	-	Yes (ERCp)	ND
6 (1)	40	F	India	No	Yes	Yes	++	ND	ND	Yes (ERCp)	Bithionol
7 (1)	65	F	Cuba and Morocco	Yes	Yes	ND	++	+	ND	Yes (ERCp)	Praziquantel and nitazoxanide for 7 days
8 (16)	3, 5–11	F/M	Egypt	No	Yes	16/16	++	+(16)	+(7)	Yes (ERCp)	Single dose of triclabendazole
9 (8)	17–56	F/M	Iraqi Kurdistan	No	ND	Yes (4)	ND	+(6)	-	No	Albendazole 3-day course/(1) triclabendazole
10 (1)	67	M	India	No	Yes	Yes	+	ND	ND	Yes (ERCp)	Single dose of triclabendazole
11 (1)	39	M	Hong Kong, Pakistan, and India	Yes	Yes	Yes	++	-	-/+	No	Single dose of triclabendazole
12 (1)	56	M	Korean	No	Yes	Yes	++	+	-	No	Praziquantel and nitazoxanide for 7 days
13 (1)	7	F	India	No	Yes	Yes	-	ND	-	Yes (ERCp)	Triclabendazole 10 mg/kg/day once
14 (1)	76	F	Turkey	Yes	Yes	Yes	++	+	-	No	Triclabendazole 10 mg/kg/day once
15 (1)	50	F	Iran	No	Yes	No	++	+	ND	No	Single dose of triclabendazole
16 (1)	38	F	Turkey	No	Yes	No	++	+	ND	No	Triclabendazole 10 mg/kg/day once
17 (1)	34	M	Ethiopia	Yes	Yes	Yes	++	+	-	No	Triclabendazole 10 mg/kg/day for 2 days
18 (1)	58	F	China	No	Yes	Yes	++	+	ND	No	Triclabendazole 10 mg/kg/day for 2 days

ERCp = endoscopic retrograde cholangiography; ND = not described; M = male; F = female.

* Number of patients reported.

- Association of Southeast Asian Nations (ASEAN): overview and update. *PLoS Negl Trop Dis* 9: e3575.
- Cabada MM, Malaga JL, Castellanos-Gonzalez A, Bagwell KA, Naeger PA, Rogers HK, Maharsi S, Mbaka M, White AC Jr., 2017. Recombinase polymerase amplification compared to real-time polymerase chain reaction test for the detection of *Fasciola hepatica* in human stool. *Am J Trop Med Hyg* 96: 341–346.
 - Behzad C, Lahmi F, Iranshahi M, Mohammad Alizadeh AH, 2014. Finding of biliary fascioliasis by endoscopic ultrasonography in a patient with eosinophilic liver abscess. *Case Rep Gastroenterol* 8: 310–318.
 - Das K, Sakuja P, Aggarwal A, Puri AS, Tatke M, 2007. Non-resolving liver abscess with *Echinococcus* cross-reactivity in a non-endemic region. *Indian J Gastroenterol* 26: 92–93.
 - Dronamraju SS, Jaques BC, Schmid M, Samuel JR, Charnley RM, 2014. Fascioliasis: a rare cause of liver abscess. *Postgrad Med J* 90: 179–180.
 - El-Shabrawi M, El-Karaksy H, Okasha S, El-Hennawy A, 1997. Human fascioliasis: clinical features and diagnostic difficulties in Egyptian children. *J Trop Pediatr* 43: 162–166.
 - Hassan HA, Majid RA, Rashid NG, Nuradeen BE, Abdulkarim QH, Hawramy TA, Rashid RM, Farris AB, Guarner J, Hughson MD, 2013. Eosinophilic granulomatous gastrointestinal and hepatic abscesses attributable to basidiobolomycosis and fascioliasis: a simultaneous emergence in Iraqi Kurdistan. *BMC Infect Dis* 13: 91.
 - Jha AK, Goenka MK, Goenka U, Chakrabarti A, 2013. Hepatobiliary fascioliasis in non-endemic zones: a surprise diagnosis. *Arab J Gastroenterol* 14: 29–30.
 - Kang ML, Teo CH, Wansaicheong GK, Giron DM, Wilder-Smith A, 2008. *Fasciola hepatica* in a New Zealander traveler. *J Travel Med* 15: 196–199.
 - Kim JB, Kim DJ, Huh S, Cho SY, 1995. A human case of invasive fascioliasis associated with liver abscess. *Korean J Parasitol* 33: 395–398.
 - Menon P, Sinha AK, Rao KL, Khurana S, Lal S, Thapa BR, 2015. Biliary *Fasciola gigantica* infestation in a nonendemic area—an intraoperative surprise. *J Pediatr Surg* 50: 1983–1986.
 - Mueller J, Dagenbach S, Riecken B, Klinger C, 2017. Ambiguous hepatic mass and fever after stay in Turkey. *Internist (Berl)* 58: 503–506.
 - Riazi H, 2001. Large liver abscess: unusual presentation of fascioliasis: case report and literature review. *Saudi J Gastroenterol* 7: 113–115.
 - Sapmaz F, Kalkan IH, Guliter S, Nazlıoğlu A, 2013. A clinical presentation of a very rare infection: parenchymal *Fasciola hepatica*. *Turkiye Parazitolo Derg* 37: 305–306.
 - Teichmann D, Grobusch MP, Göbels K, Müller HP, Koehler W, Suttrop N, 2000. Acute fascioliasis with multiple liver abscesses. *Scand J Infect Dis* 32: 558–560.
 - Wang JK, Ma WJ, Lu Q, Zheng EL, Yang Q, Hu HJ, Liu F, Li QS, Li FY, 2017. First case report of retroperitoneal metastasis of fascioliasis after surgery. *Medicine (Baltimore)* 96: e9258.
 - Dusak A, Onur MR, Cicek M, Firat U, Ren T, Dogra VS, 2012. Radiological imaging features of *Fasciola hepatica* infection—a pictorial review. *J Clin Imaging Sci* 2: 2.
 - Bui Thi D, Pham ND, Saegerman C, Losson B, 2016. Current status of fasciolosis in Vietnam: an update and perspectives. *J Helminthol* 90: 511–522.