Fascioliasis mimicking malignancy in humans

Fasciolosis remediando cáncer en humanos

Luis A. Marcos¹,², Angélica Terashima¹

1. Medical Director, Infection Prevention Department, Forrest General Hospital, Hattiesburg, MS, USA
2. Laboratorio de Parásitología, Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Lima, Perú.

Abstract

Fascioliasis has become a re-emergent infectious disease in the Andean Region. Microscopic pathological findings have been mostly described in animals but not in humans. We describe histopathological findings of three liver and one cutaneous biopsy (neck) from human cases with Fasciola hepatica infection that were initially diagnosed as possible cancer, mass, metastases or tumour. The pathological patterns included liver fibrosis, eosinophilic necrosis with multiple hepatic abscesses, track-like lesions with eosinophils that corresponds to the migration of the juvenile parasite through the liver, and immature parasite in the peritoneum mimicking peritoneal carcinomatosis. The present study adds more information in the human histopathology in fascioliasis during the acute infection of F. hepatica.

Key words: Fasciola hepatica | Histology | Pathology | Biopsy | Peru (Source: BIREME: DeCs).

Resumen

Fasciolosis se ha convertido en una enfermedad infecciosa re-emergente en la región Andina. Los hallazgos patológicos por microscopía han sido en su mayoría descritos en animales pero no en humanos. Describimos los hallazgos patológicos de tres biopsias de hígado y una biopsia de cuello de casos humanos por la infección de F. hepatica quienes fueron inicialmente diagnosticados con un posible cáncer, masa, metástasis o tumor. Los patrones histológicos encontrados en estos casos incluyen fibrosis del hígado, necrosis eosinofílica con múltiples abscesos hepáticos, lesiones tipo rastro con eosinófilos que corresponden a la migración del parasito juvenil a través del hígado, presencia del parasito inmaduro en el peritoneo remediando una carcinomatosis peritoneal. El presente estudio agrega mas información en la patología humana de fasciolosis y sugerimos reconocer estos patrones histológicos para sospechar en la infección por F. hepatica especialmente en los estadios iniciales de la enfermedad.

Palabras clave: Fasciola hepatica | Histología | Patología | Biopsia | Perú. (Fuente: BIREME: DeCs).
Introduction

Fascioliasis is a parasitic disease caused by two flukes, *Fasciola hepatica* (*F. hepatica*) or *F. gigantica*. Cases of human fascioliasis can be present in all continents, and it affects approximately 17 million people around the world. The Andean Region of South America seems to be one of the more affected regions worldwide. In Peru, 1,684 cases have been reported between 1963 and 2004. Recent data indicated that another 1,000 human cases with fascioliasis may have been reported after 2004 (Terashima, personal communication). Prevalence rates in the range between 8 to 72% in Peru, and up to 60% in Bolivia have been reported. For all these reasons, fascioliasis is a major concern in public health in South America.

*F. hepatica* infection has two clinical phases, acute and chronic. The acute phase, up to 4 months of duration, is characterized by the migration of larvae from the duodenum through the intestinal wall, peritoneal cavity, across Glisson's capsule entering the liver parenchyma and reaching the biliary ducts. *Fasciola* may produce subcapsular hemorrhages, hepatic degeneration, eosinophils infiltration, lymphocytes and macrophages, fibrosis, venous thrombosis, appearance of necrotic cords with giant cells and granulation tissue and granuloma-containing parasite egg. In humans, subcapsular hemorrhages, multiple hepatic abscesses, hepatic necrosis, liver calcifications and severe anemia have been reported.

The chronic phase occurs months to up to 13.5 years after infection. In theory, it begins when adult parasites deposit eggs in the biliary ducts. The chronic infection may present with biliary obstruction, gallstones, bacterobilia or hepatic dysfunction. In addition, *F. hepatica* infection may be associated with bile duct hyperplasia and possible cirrhosis of the liver. Furthermore, the number of parasites seems to be critical in the hepatic damage and consequent liver fibrosis. In an animal study in Peru, 50% of livers infected by *F. hepatica* from cattle collected in a slaughterhouse had liver cirrhosis by histological examination.

We hypothesize that besides the well-known histopathological characteristics described in animals, we can include novel histological clues in human fascioliasis along with a clinical picture which might increase the suspicion on fascioliasis in the clinical practice especially when a diagnosis of malignancy is entertained.

Material and Methods

Patients. Between 2000 to 2005, 4 cases, 3 with a liver biopsy and 1 with an extrahepatic biopsy (before a confirmed diagnosis of *F. hepatica* infection) were identified at the Hospital Nacional Cayetano Heredia and Instituto Especializado de Salud del Nino in Lima, Peru.

Confirmed case. A liver biopsy in a patient with acute fascioliasis (fever, hepatomegaly, eosinophilia, CT-determined liver lesions) confirmed by a positive serological test (Fas2 ELISA or Western blot) and finding of the parasite in the tissue; or with chronic fascioliasis confirmed by detecting eggs in stools and detecting the parasite or eggs in the biopsy.

Tissue Examination. The paraffin-embedded tissues and slides were collected from the hospitals above mentioned. The tissue samples were examined under light microscope (H&E and Trichrome stains). Permission from both institutions were obtained prior to chart review. Exemption of the requirement for written informed consent was obtained from each institution.

Results

Description of patients enrolled. Four cases (1 male and 3 female) with a mean age of 44.5 years ± 15.9 (range 12 to 63 years) were included. Symptoms persisted on average 7.7 ± 6.7 weeks until presentation (range: 0.5 to 12 weeks). The source of infection was possible watercress in three patients and lettuce in one.
Clinical manifestations were mainly right upper quadrant pain, fever $\geq 38^\circ C$, malaise, anorexia, weight loss $>10$ kg, nausea and vomiting. All cases were suspected to have a biliary malignancy or metastases by imaging or clinically prior biopsy.

Pathological findings. Three cases had a liver biopsy. The fourth case of extra-hepatic Fasciola has been reported elsewhere. The most common findings were the track-like lesion in the liver parenchyma ($n=2/4$), eosinophilic scattered infiltration ($n=2/4$), necrosis and small haemorrhages in the liver ($n=1/4$). No parasite was found in liver biopsies. A juvenile parasite was noted in a peritoneum biopsy mimicking metastases. Laparoscopic or percutaneous CT guided biopsies performed in 3 patients yielded a fluke only in one of them (Figures 1-5).

**Figure 1.** Juvenile parasite migrating in the peritoneal cavity causing destruction and haemorrhages in case (haematoxylin and eosin stain, magnification x100; Bar 500 um). The biopsy in the peritoneum was performed due to clinical suspicion of metastases (Picture obtained with permission from: Marcos LA, Terashima A, Gotuzzo E. Update on hepatobiliary flukes: fascioliasis, opisthorchiasis and clonorchiasis. *Curr Opin Infect Dis.* 2008 Oct;21(5):523-30)*

**Figure 2.** Area of necrosis caused by the juvenile parasite during its migration through the liver parenchyma (track-like lesion), characteristic of acute fascioliasis. There are scattered eosinophils surroundings (haematoxylin and eosin, magnification x100; Bar 500 um).

**Figure 3.** Necrotic abscess with fibrosis (trichrome stain, magnification x100; Bar 500 um).

**Figure 4.** Severe chronic inflammatory process, portal fibrosis and fibrosis moderate to severe (trichrome stain, magnification x100; Bar 500 um).
Discussion

The present study describes the pathological findings of four cases of human fascioliasis either in the liver or as extrahepatic location, showing that, in massive acute infection it may present like metastases in the liver by imaging or clinically.

The human cases reported in the literature with fascioliasis along with histological findings are seldom. For instance, two cases of hepatic fascioliasis due to *F. hepatica* were retrieved from 1969 to 2005 in a Thailand Hospital. The adult parasite was detected in a large cystic lesion in a lobectomized liver specimen in one case, and of deposited eggs in the large liver specimen obtained from open biopsy in another case. Aberrant or ectopic sites of infection -by the immature larvae- are much less common and include subcutaneous tissue (the most common site) or tissues of the intestine walls, lungs, heart, eyes or brain. Ectopic cases are even more uncommon and the diagnosis is made in the histological examination of the tissue. Histological diagnosis has been made in ectopic cases such as the dorsal spine and pancreatitis. Currently, the diagnosis of ectopic cases relies on serological detection or direct observation of eggs or the parasite in the lesion by microscopy.

In human livers, the migration is accompanied by an intense inflammatory reaction with prominent eosinophils as seen in Figure 2. A large serie of 16 human cases with *F. hepatica* infection were reported in 1979, the liver was involved in 13 cases, the gallbladder in 9 cases and the stomach in 2 cases. The lesions containing parasitic remnants or fluke eggs were rarely seen and the most common characteristic lesions seen were surface scarring of the liver, scar tracks and granuloma in the organs.

In our serie, all biopsies were ordered to rule out metastases. The biopsies did not yield any malignant cells or any adult parasites, but they did reveal a juvenile parasite migrating through the peritoneum (Figure 1) and a tunnel-like tract lesion which eventually might be a major criterion for the diagnosis of fascioliasis (Figure 2). This finding are in agreement with other cases reported. The lesions of the liver caused by *F. hepatica* are diverse since most of the times the parasite or eggs are not seen, making the suspicion a challenge for the clinician.
We conclude that the present study adds more information in the human histopathology in fascioliasis during the acute infection.

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Conflict of interest: The authors have no conflicts of interest concerning the work reported in this paper.

References


Correspondence: Luis A. Marcos, MD, MPH. Forrest General Hospital, Hattiesburg, MS. Email: marcoslrz@yahoo.com