HYPEREOSINOPHILIA AND LIVER MASS IN AN IMMIGRANT

CHARLES M. NOYER, CHRISTINA M. COYLE, CRAIG WERNER, JEAN DUPOUY-CAMET, HERBERT B. TANOWITZ, AND MURRAY WITTNER

Departments of Medicine and Pathology, Albert Einstein College of Medicine, Bronx, New York; Laboratoire de Parasitologie-Mycologie, Troupe Hospitalier Cochin, Paris, France

Abstract. Human infection with the sheep liver fluke Fasciola hepatica is a global zoonosis that usually parallels the prevalence of infection in sheep and other ruminants. The disease is endemic in South and Central America, Puerto Rico, the Caribbean region, many parts of Africa, Asia, the Middle East, Australia, and China. There have been a number of focal outbreaks reported from Europe, including southern France and the Mediterranean region. Since acute fascioliasis has rarely been reported in the United States, physicians in this country frequently overlook the diagnosis. Therefore, we report a case of acute human fascioliasis and review the pathogenesis, diagnosis, and treatment of this disease in a recently arrived immigrant.

CASE REPORT

A 26-year-old woman from the Dominican Republic was well on arrival in the United States in late February 1997. One month later she presented to a local hospital complaining of several hours of severe, sharp, right upper quadrant pain radiating to the right shoulder, with fever and chills. She denied a history of gallstones, jaundice, use of nonsteroidal anti-inflammatory drugs or oral contraceptives, urinary changes, or recent trauma. On admission to the hospital her temperature was normal, and she had mild right upper quadrant tenderness without hepatosplenomegaly or masses. A test result for β-human chorionic gonadotropin was negative, and she had peripheral eosinophilia (27%). An abdominal computed tomography (CT) scan with intravenous contrast demonstrated a 6.0 × 5.0 × 4.0 cm complicated, heterogeneous, necrotic mass in the right lobe of the liver, which extended from the dome to the inferior border, and laterally to the capsule. The mass contained internal septations with surrounding parenchymal hemorrhage (Figure 1A). An IgG-enzyme immunoassay result for antibodies to Echinococcus granulosus was low positive.

The patient was then transferred to our institution for further management. She denied exposure to farm animals, dogs, or fresh water, but she had frequently eaten uncooked “berro” or watercress (Nasturtium officinale). Other family members were well. She had a temperature of 36.9°C, clear lungs, and no liver tenderness or hepatosplenomegaly. One week later her white blood cell was 16,800/mm³ with 5,200/mm³ eosinophils (27%). She had an alkaline phosphatase level of 523 U/liter, a bilirubin level of 0.5 mg/dL. Review of the latter one. Indirect immunofluorescence (IIF) tests for antibodies to Fasciola hepatica performed on serum obtained one and two weeks after the negative FAST-ELISA result revealed increasing titers of 1:80 and 1:160, respectively (1:20 borderline positive; Laboratoire de Parasitologie-Mycologie, Groupe Hospitalier Cochin, Paris, France). The result of an immunoelectrophoresis test was also positive, showing three bands on the first serum and four bands on the latter one.

The patient was treated with a single dose (10 mg/kg, 700 mg) of triclabendazole (Fasinex®; Novartis, Basel, Switzerland). A CT scan 12 weeks later (Figure 1B) showed almost complete resolution of the lesion. Subsequent stool examinations remained negative for F. hepatica eggs up to 16 weeks after presentation. Her symptoms have not recurred and the eosinophilia and the other laboratory test results have returned to normal levels. One year later her eosinophil count was 200/mm³ and she remained well.

DISCUSSION

Acute fascioliasis is infrequently recognized in the United States because there are few diagnostic tests available and it is too early in the infection to find the characteristic eggs in the stool. In the present case, hypereosinophilia and a large necrotic hepatic lesion in a patient who frequently consumed fresh watercress were the major reasons to suspect the diagnosis. The history of ingestion of uncooked freshwater plants, especially watercress, is almost always obtained. On occasion, infection can occur by drinking untreated fresh water containing the infective larvae. Urticaria, which is frequently seen in acute fascioliasis, was not evident in this patient.

Mature flukes inhabit the biliary tree where they deposit unembryonated eggs. These immature eggs pass down the bile ducts into the duodenum and eventually to the environment with the feces. After 9–15 days, miracidia hatch and penetrate various species of lymnaeid snails, the first intermediate hosts. After 4–7 weeks, they leave the snail as free-swimming cercariae and either encyst on various aquatic plants or sink to the bottom, in either case, developing into metacercariae. Humans are infected by drinking contaminated fresh or field water, or by consuming uncooked aquatic plants, especially watercress (berro), algae (algas), tortora, and kjosco. Metacercariae excyst in and then penetrate through the duodenal wall. Migrating in the peritoneum, the
In the present case, the patient initially was referred to our Tropical Medicine Clinic for treatment of hydatid cyst disease when the serologic test result was interpreted at another institution as consistent with echinococcosis. The results of additional laboratory studies for fascioliasis, including the FAST-ELISA on serum obtained at admission, were negative. However, serum obtained one and two weeks later were strongly positive (IIF and immunoelectrophoresis). Recently, immunodiagnosis of human fascioliasis using cysteine proteinases (Fas1 and Fas2) as antigens was shown to be highly specific and sensitive. Circulating Fasciola antigen has been detected in both serum and urine samples in patients by testing with monoclonal antibodies. The specificity of this assay was 100% and sensitivities were 98% and 97% for serum and urine, respectively. An ELISA and micro-ELISA were used to detect antibodies to Fasciola in humans using excretory-secretory antigen. The sensitivity of each method was 100%; the specificity was 100% for the ELISA and 97% for the micro-ELISA. These new diagnostic tests are promising advances in the reliable diagnosis of fascioliasis; however, they are currently not readily available.

Recently, triclabendazole (6-chloro-5-(2,3-dichlorophenoxy)-2-methyl thiobenimidazole) has successfully (cure rate = 80−100%) eradicated acute and chronic fascioliasis in humans and various herbivores. Praziquantel and bithionol (no longer available in the United States) are frequently ineffective. The mechanism of action of triclabendazole has not been established. However, similar to other anthelmintic benzimidazole compounds, i.e., albendazole and mebendazole, it binds to tubulin. It is unclear if this is its major site of action. In this regard, it has been suggested that triclabendazole may inhibit protein synthesis in Fasciola. It is well tolerated and easily administered in one or two doses. Patients may develop mild right upper quadrant pain within 24−48 hours after administration, which is probably due to death of the fluke within the liver or bile ducts. Pharmacologic studies in humans suggest that significantly higher absorption of triclabendazole can be achieved if administered postprandially. Recently, a new fascicidal agent derived from the stem of the Commiphora molmol tree proved effective in the treatment of Fasciola-infected humans; there were no reported adverse reactions to this agent.

Individuals who have not been cured by oral drug therapy
have been treated successfully with endoscopic retrograde cholangiopancreatography and flushing of the biliary system with povidone iodide. In this regard, there have been several reports of triclabendazole-resistant *Fasciola hepatica* in ruminants. Although not studied, it is possible that treatment failures in humans may have been due to resistance to triclabendazole.

Acute fascioliasis should be suspected in immigrant patients with marked eosinophilia, liver abscess, and a history of ingestion of uncooked watercress or other aquatic plants. Triclabendazole appears to be the primary drug for treatment of acute and chronic fascioliasis.

Authors’ addresses: Charles M. Noyer, Christina M. Coyle, and Craig Werner, Department of Medicine, Albert Einstein College of Medicine, 1600 Morris Park Avenue, Bronx, NY 10461. Jean Dupouy-Camet, Laboratoire de Parasitologie-Mycologie, Troupe Hospitalier Cochon, 75679 Paris Cedex 14, France. Herbert B. Tanowitz and Murray Wittner, Department of Pathology, Albert Einstein College of Medicine, 1600 Morris Park Avenue, Bronx, NY 10461.

Reprint requests: Murray Wittner, Department of Pathology, Albert Einstein College of Medicine, 1600 Morris Park Avenue, Bronx, NY 10461, Telephone: (718-430-2059, Fax: 718-430-8543, E-mail: wittner@aecom.yu.edu.

REFERENCES