Fasciola hepatica-induced acute pancreatitis: Report of two cases and review of the literature

Facsiola hepatica'ya bağlı akut pankreatit

Orhan SEZGİN[1], Engin ALTINTAŞ[1], Anıl TOMBAK[2], Enver ÜÇBİLEK[1]

Departments of [1]Gastroenterology, [2]Internal Medicine, Mersin University, School of Medicine, Mersin

Fasciola hepatica is a zoonotic liver fluke that can cause disease in humans. F. hepatica is known to cause bile duct inflammation and biliary obstruction, but is rarely reported as responsible for producing acute pancreatitis. We report two patients complaining of acute pancreatitis. Endoscopic retrograde cholangiopancreatography showed distinct features, and sphincterotomy allowed extraction of multiple parasites. A high index of suspicion, specific ultrasonographic findings and eosinophilia are very helpful in the diagnosis of the disease.

Key words: Fasciola hepatica, acute pancreatitis

Fasciola hepatica insanlarda hastalık yapabilen zoonotik bir hastalıktır. Fasciola hepatica safra kanallarında inflamasyon ve tıkanıklığa yol açabilen fakat akut pankreatit sebebi olarak nadiren bildirilmiş bir hastalıktır. Biz akut pankreatiti olan iki hasta sunacağız. Endoskopik retrograd kolanjiopankreatografi tipik özelliklerini gösterirken, sfinkterotomi pek çok parazitin çıkarılmasına olanak sağladı. Öncelikle hastalıktan şüphelenmek ve özgün ultrasonografi bulguları ve eozinofili hastalığın tanısında çok yardımcıdır.

Anahtar kelimeler: Fasciola hepatica, akut pankreatit

INTRODUCTION

Acute pancreatitis is a severe and life-threatening disease. It is a frequent cause of acute medical abdominal emergencies. The major causes of acute pancreatitis include gallstone disease, alcohol ingestion, metabolic disorder such as hypertriglyceridemia and hypercalcemia, drug intake, various interventions including endoscopic retrograde cholangiopancreatography (ERCP), and surgery (1, 2). Parasitic diseases causing acute pancreatitis are extremely rare. In clinical practice, acute pancreatitis is an extremely rare finding in the course of *Fasciola hepatica (F. hepatica)* infestation (3-7). We present two patients with acute pancreatitis due to *F. hepatica*.

CASE REPORTS

Case 1

A 51-year-old female was admitted to our hospital due to a sudden onset of nausea and upper abdominal pain in May 2005. She cited no history of drug abuse or alcohol ingestion, gallstone disease, abdominal trauma or surgery. Physical examination revealed severe tenderness in the epigastrium with hypoactive bowel sound and fever (38°C). Laboratory data on admission showed elevated serum levels of pancreatic enzymes, i.e., amylase (1046 IU/L; reference range: 35-133 IU/L) and lipase (1538 IU/L; reference range: 7-38 IU/L). White blood cell count was 7,750 mm^{-3} (reference range: 3,200-8,500 mm^{-3}), and eosinophil rate was 9.7% (reference range: 0.5%-5%). Alkaline phosphatase was 148 IU/L (reference range: 98-279 IU/L), and bilirubin was 1.3 mg/dl (reference range: 0-1 mg/dl). Serum values were as follows: alanine aminotransferase (ALT) 325 IU/L (reference range: 16-31 IU/L), aspartate aminotransferase (AST) 612 IU/L (reference range: 16-31 IU/L), and lactate dehydrogenase (LDH) 904 IU/L (reference range: 200-480 IU/L); calcium was within reference ranges.

Abdominal ultrasonography showed bile duct dilation and hyperechoic materials filling the common

Address for correspondence: Orhan SEZGİN
Mersin Üniversitesi Tıp Fakültesi
Gastroenteroloji Bilim Dalı Mersin, Turkey
Phone: + 90 324 337 43 00-1140
E-mail : sezginorhan@ttmail.com, orhansezgin@mersin.edu.tr

Manuscript received: 25.10.2008 **Accepted:** 01.04.2010

doi: 10.4318/tjg.2010.0081

bile duct (CBD) (Figure 1) and diffuse enlargement of the pancreas. A cholangiogram depicted dilation and numerous motile curvilinear filling defect images in the CBD, and irregularities at the bile duct wall (Figure 2). An endoscopic sphincterotomy was done with extraction of multiple Fasciola flukes (Figure 3). The following day, post ERCP ultrasound showed prominent bile duct wall thickness after the clearance of the flukes from the CBD (Figure 4a,b). Treatment with triclabendazole as a single oral dose of 10 mg/kg was ordered. Follow-up demonstrated normal laboratory values and no evidence of the disease for three years thereafter.

Case 2

A 70-year-old male was admitted to our hospital due to nausea, upper abdominal pain and jaundice for three days in May 2007. He did not cite any history of drug abuse or alcohol ingestion, gallstone disease, abdominal trauma or surgery. He had a history of watercress consumption. On physical examination, severe tenderness in the epigastrium with jaundice was noted. Laboratory data on admission showed elevated serum levels of pancreatic enzymes, i.e., amylase 621 IU/L and lipase 1978 IU/L. White blood cell count was 12,600 mm^{-3}, eosinophil rate was 26%, alkaline phosphatase was 205 IU/L, and bilirubin was 10 mg/dl. Serum values of ALT and AST were 107 IU/L and 44 IU/L, respectively; LDH and calcium were within their reference ranges.

Abdominal ultrasonography showed bile duct dilation and gallbladder wall thickening (5.2 mm). There were numerous hyperechogenic, non-shadowing materials at the fundus of the gallbladder (Figure 5) and diffuse enlargement of the pancreas. A cholangiogram depicted dilatation and numerous motile curvilinear filling defect images in the CBD and irregularities at the bile duct wall. An endoscopic sphincterotomy was done with extraction of multiple Fasciola flukes. Treatment with triclabendazole as a single oral dose of 10 mg/kg was ordered. Follow-up demonstrated normal laboratory values and no evidence of the disease for one year thereafter.

DISCUSSION

Fascioliasis is a rare zoonotic disease, caused by *F. hepatica,* a liver fluke. *F. hepatica* infests sheep, cattle and other herbivorous animals; humans are only accidental hosts (8). Infection results from in-

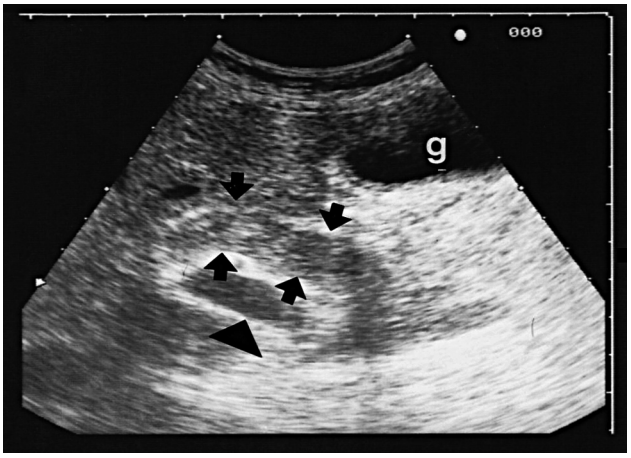

Figure 1. Abdominal ultrasonogram showing dilated common bile duct (arrows) filled by hyperechogenic fasciola flukes. Arrowhead: portal vein, g: gallbladder.

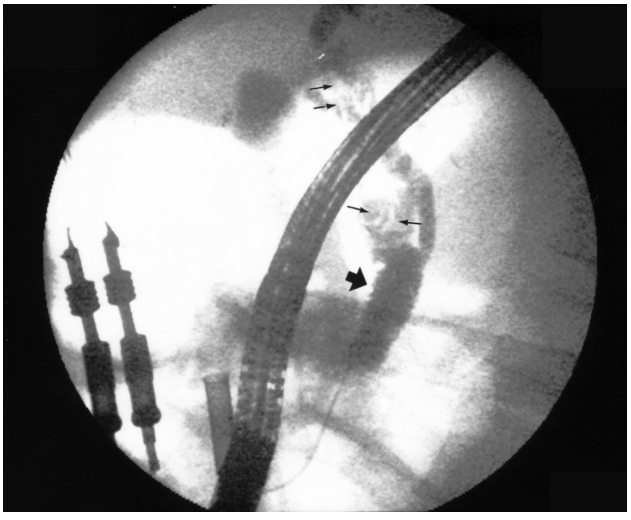

Figure 2. Cholangiogram showing bile duct dilation, curvilinear filling defects (thin arrows), and irregularities on the bile duct wall (thick arrow).

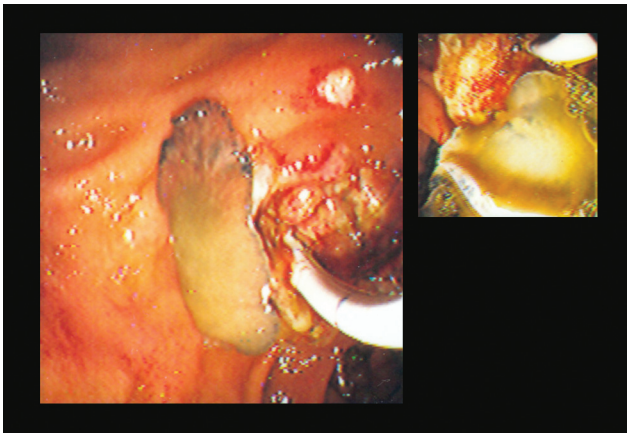

Figure 3. After sphincterotomy, *Fasciola hepatica* was extracted by balloon catheter.

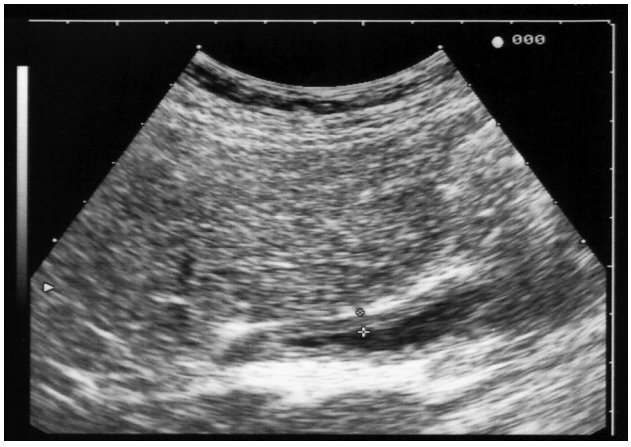

Figure 4a. Post endoscopic retrograde cholangio pankreatography longitudinal ultrasonogram showing prominent thickness on the common bile duct wall (asterisk).

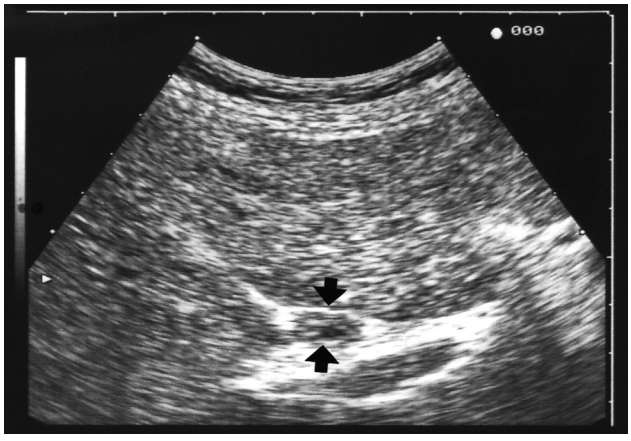

Figure 4b. Transverse sonogram of the common bile duct showing thickened wall (arrows).

gestion of metacercariae on uncooked and unwashed vegetables (e.g., watercress and sorrel). After oral ingestion, the larvae ex-cyst and pass through the intestinal wall into the peritoneum. They find their way through the liver to the bile ducts, where they reside as adult worms. The adult *F. hepatica* fluke is a flat, brownish colored, leaf-shaped organism measuring 2.5x1 cm (9, 10, 15). In humans, maturation and excretion of the eggs take about 3-4 months.

Most of the cases in humans have been reported from South America, Africa, Australia, Mediterranean countries, and China (11, 12). These countries have significant sheep and livestock industries. In general, the geographic prevalence of the human disease is parallel to that of endemic animal illness. Although raising livestock is a common practice in Turkey, human fascioliasis is quite rare. In a study performed by us previously, we determined that the rate of seroprevalence for *F. hepatica* was 0.8% in Mersin province (13), which was a hypo-endemic level.

The disease mainly involves the hepatobiliary system and manifests in two stages: the hepatic stage and biliary stage (9, 14, 15). The clinical manifestations of fascioliasis differ according to the stage of the disease. During the first or migration stage, in which hepatic invasion occurs, fever, right upper quadrant pain, hepatomegaly, and eosinophilia occur. During the second stage, the parasite resides in the biliary tract and is responsible for a variety of symptoms. Affected individuals usually complain of intermittent episodes of biliary colic, which may or may not be associated with fever and chills, symptoms usually found with cholangitis. When symptoms are mild or not present at all and eosinophilia is not present, the diagnosis of parasite infestation is difficult to confirm. Occasionally, bile duct obstruction and/or cholangitis do develop. As we showed previously, eosinophilia was the most significant laboratory finding (15). Our two cases had increased eosinophil count related to fasciola infestation. However, the clinical presentation of pancreatitis has only been reported five times (3-7). In conducting a comprehensive review of the literature, we found only two reports in which persons were diagnosed with acute pancreatitis and treated by ERCP (5, 6). Our patients presented with biliary obstruction and acute pancreatitis.

The adult parasite resides in the bile ducts and, by virtue of its suckers, adheres to the duct wall and remains stationary in the bile ducts. It is thought that, when the eggs of the parasite are discharged

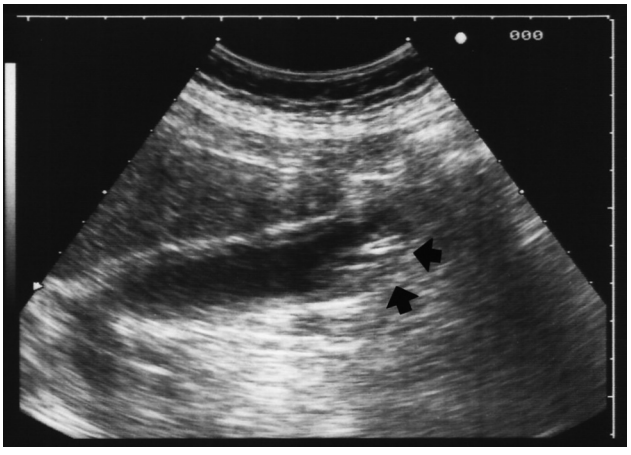

Figure 5. Abdominal ultrasonogram of Case 2 showing hyperechogenic, non-shadowing material at the gallbladder fundus (arrows).

into the bile ducts, they travel through the ampulla, obstructing the pancreatic duct causing pancreatitis (3). Another hypothesis that has been proposed is that pancreatitis results from the passage of dead adult worms, which lodge in the ampulla causing obstruction to the pancreatic duct (3).

Confirmation of the diagnosis of *F. hepatica* is usually based on microscopic identification of the characteristic eggs in the feces or bile. In our previous study, we determined the *F. hepatica* ova in the stool of only one patient out of nine (15). Because man is an accidental host for this parasite, the number of flukes reaching the biliary tree is usually small, and some of them never achieve sexual maturity. In consequence, the number of eggs in the feces is small, and fewer than 35% of the cases of chronic fascioliasis are diagnosed by parasitic stool tests (16). Serological tests may be helpful, but these are not reliable in many countries (17). The method most widely used is the enzyme-linked immunosorbent assay. The assay detects antibodies to the excretory-secretory antigen products from adult *F. hepatica* (18).

Abdominal ultrasonography and ERCP may be useful in defining characteristic findings of the *F. hepatica* parasite within the bile ducts. The characteristic ERCP findings are linear, or filamentous, curved or angled, motile filling defects located in the bile duct and irregularities on the inner surface of the bile ducts (15). Ultrasonography especially provides useful information (19). Hepatic lesions produced by migration of the trematodes are hypoechoic nodules and cystic lesions on ultrasound. In the biliary stage, ultrasound seems to be more useful, and may show biliary dilation and especially bile duct wall thickening, suggesting biliary fascioliasis. Adult flukes, either due to a direct irritating effect or perhaps to the induction of a high proline concentration in the bile, promote hyperplasia and hypertrophy of the duct epithelium and enveloping periductal fibrosis, resulting in thickening of the duct walls (20). A significant sonographic finding for fascioliasis is that dilated bile ducts are filled with nonshadowing material isoechoic to the liver. This feature is related to the fasciola flukes absolutely filling the bile ducts (15). It disappeared after extraction of the fasciolae. In fascioliasis, flukes in the gallbladder as mobile or non-mobile vermiform structures without acoustic shadowing may also be demonstrated by ultrasound (15). Although there was no conclusive evidence, we thought that the second case might have had flukes within the gallbladder.

While several drugs can be used during the hepatic stage, ERCP is particularly effective in the biliary stage. Parasite removal during ERCP is one therapeutic option in patients with acute biliary obstruction due to *F. hepatica* (15, 21).

Although emetine, bithionol and praziquantel have been used for treatment of this parasite in the past (22), triclabendazole is currently the drug of choice, and it is safe and effective as a single oral dose of 10 mg/kg. It is highly efficient against both mature and immature worms and has been successfully administered to patients with fascioliasis (15, 23, 24). The only side effects are due to disintegrating dead parasites. However, it is not yet approved for this indication worldwide (except in Egypt), although it is recommended by the World Health Organization (25). Therefore, triclabendazole was administered on the basis of compassionate drug use.

In conclusion, fascioliasis should be considered in the differential diagnosis of abdominal pain, especially if associated with eosinophilia. Pancreatitis is an extremely rare complication that can be associated with biliary involvement. A high index of suspicion and specific sonogram findings are very helpful in the diagnosis. However, serological studies and ERCP can confirm the diagnosis.

REFERENCES

1. Bourke JB. Incidence and mortality of acute pancreatitis. Br Med J 1977; 2: 1668-9.
2. Seligson U, Cho J-W, Ihre T, Lundh G. Clinical course and autopsy findings in acute and chronic pancreatitis. Acta Chir Scand 1982; 148: 269-74.
3. Maroy B, Moullot P, Daloubeix H, Mathey JC. Acute pancreatitis complicating biliary distomatosis caused by Fasciola hepatica in a patient with a choledochal diverticulum. Ann Gastroenterol Hepatol (Paris) 1987; 23: 67-70.
4. Hauser SC, Bynum TE. Abnormalities on ERCP in a case of human fascioliasis. Gastrointest Endosc 1984; 30: 80-2.
5. Veerappan A, Siegel JH, Podany J, et al. Fasciola hepatica pancreatitis: endoscopic extraction of live parasites. Gastrointest Endosc 1991; 37: 473-5.
6. Echenique-Elizondo M, Amondarain J, Liron de Robles C. Fascioliasis: an exceptional cause of acute pancreatitis. J Pancreas 2005; 6: 36-9.
7. Parsak CK, Koltaş IS, Sakman G, et al. Surgery in Fasciola hepatica pancreatitis: report of a case and review of literature. Z Gastroenterol 2007; 45: 313-6.
8. Price T, Tuazon C, Simon G. Fascioliasis: case reports and review. Clin Infect Dis 1993; 17: 426-30.

9. Mahmoud AAF. Trematodes (schistosomiasis) and other flukes. In: Mandell GL, Bennett JE, Dolin R, eds. Principles and practice of infectious diseases. 4th ed. New York: Churchill Livingstone, 1995; 2538-44.
10. Arjona R, Riancho J, Aguado J, et al. Fascioliasis in developed countries: a review of classic and aberrant forms of the disease. Medicine (Baltimore) 1995; 74: 13-23.
11. Harinasuta T, Bunnag D. Liver, lung and intestinal trematodiasis. In: Warren KS, Mahmoud AF, eds. Tropical and geographical diseases. 2nd ed. New York, NY: McGraw-Hill, 1990; 473-89.
12. Chen MG, Mott KE. Progress in assessment of morbidity due to Fasciola hepatica infection: a review of recent literature. Trop Dis Bull 1990; 87: R1-38.
13. Özturhan H, Emekdaş G, Sezgin O, et al. Seroepidemiology of Fasciola hepatica in Mersin province and surrounding towns and the role of family history of the fascioliasis in the transmission of the parasite. Turk J Gastroenterol 2009; 20(3): 198-203.
14. Carpenter HA. Bacterial and parasitic cholangitis. Mayo Clin Proc 1998; 73: 473-8.
15. Sezgin O, Altıntaş E, Dişibeyaz S, et al. Hepatobiliary fascioliasis: clinical and radiologic features and endoscopic management. J Clin Gastroenterol 2004; 38: 285-91.
16. Bell DR. A new method for counting Schistosoma mansoni eggs in the faeces with special reference to therapeutic trials. Bull World Health Organ 1968; 29: 525.
17. Harris NL, McNeely WF, Shepard JAO, et al. Case records of the Massachusetts General Hospital. Weekly Clinicopathological Exercises. N Engl J Med 2002; 346: 1232-9.
18. Espino AM, Dumenigo BE, Fernandez R, et al. Immunodiagnosis of human fascioliasis by enzyme-linked immunosorbent assay using excretory-secretory products. Am J Trop Med Hyg 1987; 37: 605-8.
19. VanBeers B, Pringot J, Geubel A, et al. Hepatobiliary fascioliasis: non-invasive imaging findings. Radiology 1990; 174: 809-10.
20. Isseroff H, Sawma JT, Reino D. Fascioliasis- role of proline in bile duct hyperplasia. Science 1977; 198: 1157-9.
21. Aubert A, Meduri B, Prat F, et al. Fascioliasis of the common bile duct: endoscopic ultrasonographic diagnosis and endoscopic sphincterotomy. Gastroenterol Clin Biol 2001; 25: 703-6.
22. Lluch JF, Presa F, Elcuaz R, et al. Visualization of motile leaf-like forms using endoscopic retrograde cholangiopancreatography. Enferm Infecc Microbiol Clin 1997; 15: 491-2.
23. Markwalder K, Koller M, Goebel N, Wolff K. Fasciola hepatica infection: successful therapy using triclabendazole. Schweiz Med Wochenschr 1988; 118: 1048-52.
24. El-Karaksy H, Hassanein B, Okasha S, et al. Human fascioliasis in Egyptian children: successful treatment with triclabendazole. J Trop Pediatr 1999; 45: 135-8.
25. Triclabendazole and fascioliasis: a new drug to combat an age-old disease. Fact Sheet No. 191. Geneva, Switzerland: World Health Organization, April 1998.