Korean J Gastroenterol Vol. 77 No. 1, 39-44
https://doi.org/10.4166/kjg.2020.152
pISSN 1598-9992 eISSN 2233-6869

CASE REPORT

트리클라벤다졸로 치료한 간질에 의한 간농양

박현준[1,2], 최길순[1], 정민정[3], 이상욱[1,2]
고신대학교 의과대학 내과학교실[1], 장기려 기념 간 연구소[2], 병리학교실[3]

Fasciola Hepatica Induced Hepatic Abscess Treated with Triclabendazole

Hyun Joon Park[1,2], Gil-Soon Choi[1], Minjung Jung[3] and Sang Uk Lee[1,2]
Department of Internal Medicine[1], Chang Kee-Ryo Memorial Liver Institute[2], and Department of Pathology[3], Kosin University College of Medicine, Busan, Korea

Fascioliasis is a zoonotic disease caused by *Fasciola hepatica* that infects mainly cattle, sheep, and goats. Humans can be infected by water or aquatic plants contaminated with metacercariae. The authors encountered two cases of *F. hepatica* infection. One patient reported abdominal discomfort with marked eosinophilia. The other patient had chest discomfort with marked eosinophilia. The abdominal CT images revealed hypodense lesions in the liver. The ultrasonography-guided liver biopsy findings in both patients were indicative of parasitic infections. Serological tests confirmed the definite diagnoses. Both patients were treated with a single dose of triclabendazole, which is the treatment of choice for fascioliasis. These findings suggest that a diagnosis of fascioliasis, particularly in the acute phase, should be considered in patients with abdominal pain, marked eosinophilia, and hypodense hepatic lesions on CT. **(Korean J Gastroenterol 2021;77:39-44)**

Key Words: *Fasciola hepatica*; Fascioliasis; Liver abscess; Triclabendazole

INTRODUCTION

Fasciola hepatica infections previously occur mainly in Western Europe, Central and South America, and the Middle East, but they are now widespread across all continents.[1,2] Several cases of human *F. hepatica* infection have been reported in Korea.[3-5] Fascioliasis is a zoonotic disease caused by *F. hepatica*, a flat, leaf-shaped liver fluke that usually infects cattle, sheep, and goats. The clinical signs and symptoms of fascioliasis usually include fever, abdominal pain, hepatomegaly, and abnormal liver function test results with peripheral eosinophilia.[6,7] In non-endemic regions, the diagnosis of an *F. hepatica* infection is usually delayed because it is uncommon, and its symptoms are similar to those of other infectious diseases. Therefore, the diagnosis of an *F. hepatica* infection should be considered to reduce complications in patients with fever, abdominal pain, hepatomegaly, and eosinophilia.

The authors recently encountered two cases of *F. hepatica* infection that were diagnosed serologically and treated successfully. This paper recognizes neglected diseases and increases the knowledge of fascioliasis.

Received October 29, 2020. **Revised** December 3, 2020. **Accepted** December 5, 2020.

교신저자: 이상욱, 49267, 부산시 서구 감천로 262, 고신대학교 의과대학 고신대학교복음병원 내과
Correspondence to: Sang Uk Lee, Department of Internal Medicine, Kosin University Gospel Hospital, Kosin University College of Medicine, 262 Gamcheon-ro, Seo-gu, Busan 49267, Korea. Tel: +82-51-990-6205, Fax: +82-51-990-3049, E-mail: tacronimus@naver.com, **ORCID:** https://orcid.org/0000-0002-1165-7011

Financial support: None. Conflict of interest: None.

CASE REPORT

1. Case 1

A 39-year-old woman was admitted with dyspepsia and epigastric discomfort. She had traveled to several countries, including Canada, Turkey, and Malaysia. Her diet consisted of variable products, such as beef, chicken, lamb, horses, fruit, fish, and vegetables. She was diagnosed with diabetes mellitus 3 years earlier and underwent a left thyroid lobectomy for thyroid cancer 2 years ago. She had suffered from epigastric discomfort and febrile sense for more than 2 months. Abdominal ultrasonography revealed a liver abscess at a local clinic, and she was referred to the Kosin University Gospel Hospital. The physical examination was unremarkable except for mild tenderness in the right upper abdomen. The laboratory tests revealed a hemoglobin level of 12.2 g/dL and a white blood cell (WBC) count of 12,600/mm^3 with eosinophilia (45%). Except for ALP (126 U/L; normal, <100 U/L), the other biochemical test results were within the normal limits. She underwent three-phase liver CT to evaluate the liver lesion. Multiple clustered hypodense lesions with mild intrahepatic bile duct dilatation were visible in the right hepatic lobe (Fig. 1A). Ultrasonography-guided liver biopsy performed for a pathological assessment revealed acute hepatitis with increased eosinophil infiltration, but no parasitic organisms were identified (Fig. 2). A stool examination for parasites or eggs was negative. The serologic tests of *Toxocariasis* and *Clonorchis sinensis* by enzyme-linked immunosorbent assay (ELISA) were negative but positive for *F. hepatica*. The patient was treated with triclabendazole at a single dose of 10 mg/kg orally through the Korea Orphan & Essential Drug Center (KOEDC). Approximately 4 months after discharge, the patient's WBC count was 6,120/mm^3 without eosinophilia (4.9%), and the findings of hepatic infestation improved on the CT scan (Fig. 1B).

2. Case 2

A 65-year-old woman who underwent a thyroid lobectomy for thyroid cancer 10 years earlier was admitted with chest discomfort. She had lived in rural areas with a habit of eating watercress. One month before presentation, she visited a local clinic with chest discomfort and was diagnosed with asthma. Her clinical symptoms did not improve with corticosteroid use. The physical examination findings were un-

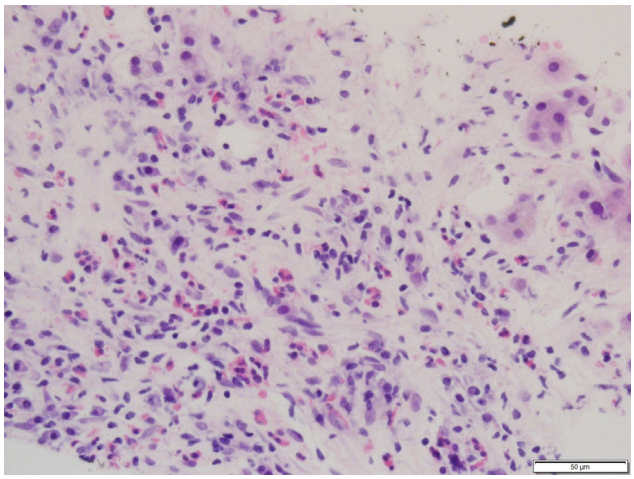

Fig. 2. Microscopic findings of the case one patient. Portal inflammation by eosinophils, lymphocytes, plasma cells, and macrophages extends to the hepatic lobules (H&E, ×200).

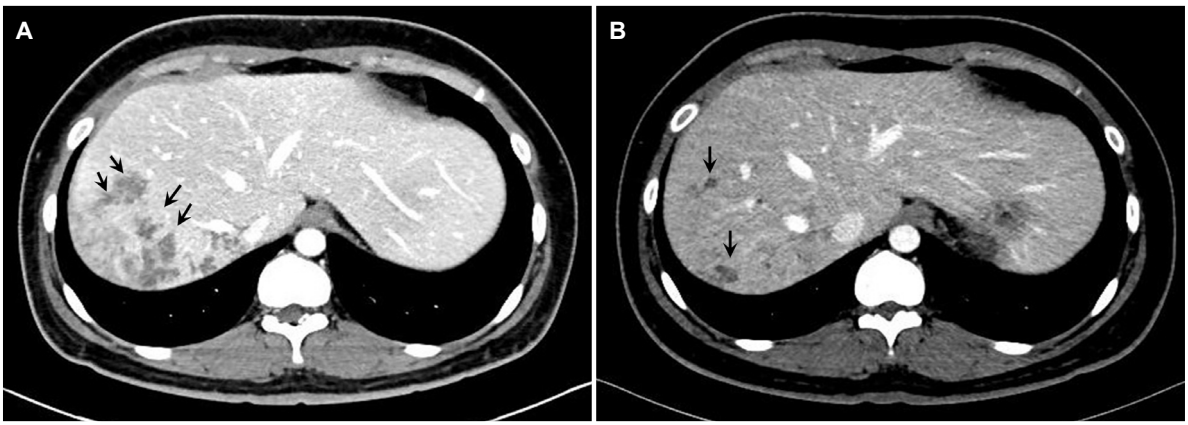

Fig. 1. Axial computed tomography scan images of the case one patient. (A) Multiple clustered hypodense lesions (black arrows) were observed (on the admission day). (B) Few hypodense lesions (black arrows) were observed (Four months from discharge).

remarkable except for skin rashes on the chest and abdomen. The laboratory tests revealed a hemoglobin level of 13.1 g/dL, a WBC count of 5,500/mm^3 with eosinophilia (36.8%), and an ALP level of 104 U/L (normal, <100 U/L). The other biochemical test results were within the normal limits. The patient underwent chest and abdominal CT to determine the cause of the peripheral eosinophilia. Several ill-defined low-density lesions were noted in the right hepatic lobe (Fig. 3A). An ultrasonography-guided liver biopsy revealed inflammation with necrosis and increased eosinophil infiltration, but no viable parasitic organisms (Fig. 4). A serologic test by ELISA was positive for *F. hepatica*, but the serologic tests of *Toxocariasis* and *Clonorchis sinensis* were negative. A stool examination for parasites or eggs was negative. The patient was treated with triclabendazole at a single dose of 10 mg/kg orally through the KOEDC. Approximately 2 months after discharge, the patient's WBC count was 6,720/mm^3 without eosinophilia (4.0%), and the hepatic lesions were improved on a CT scan (Fig. 3B).

DISCUSSION

Human fascioliasis is usually caused by the ingestion of aquatic plants, such as watercress, or by drinking water contaminated with metacercariae. The disease can also be contracted by eating the uncooked liver of infected animals.[2] Human fascioliasis has a clinical course consisting of an acute hepatic phase and a chronic biliary phase.[2,6] The hepatic phase generally begins 4-12 weeks after metacercariae ingestion. After humans acquire the parasite, the infected

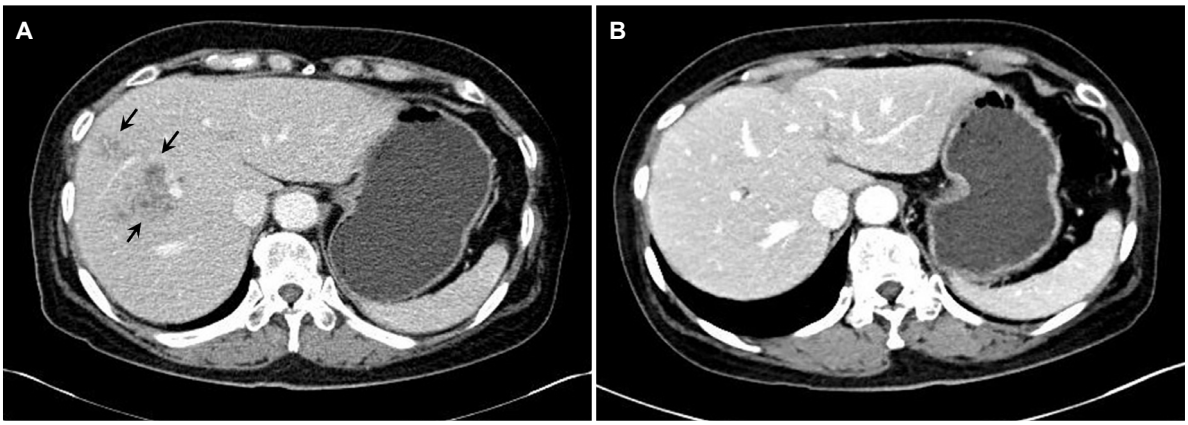

Fig. 3. Axial computed tomography scan images of the case two patient. (A) On the admission day, several ill-defined linear low densities (black arrows) were noted. (B) No active hepatic lesions were noted 2 months after discharge.

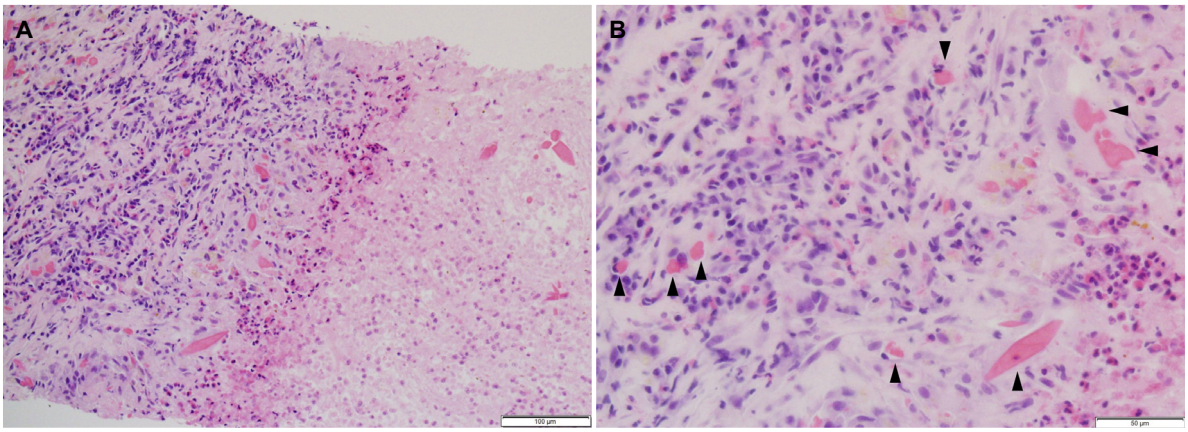

Fig. 4. Microscopic findings of the case two patient. (A) Inflammation of eosinophils, lymphocytes, plasma cells, and macrophages was noted at the border of the necrotic area (H&E, ×200). (B) Multiple Charcot-Leyden crystals (arrowheads) were noted in the center and periphery of the necrotic area (H&E, ×400).

Table 1. Previous Case Reports of *Fasciola Hepatica* Infections

	Case 1[17]	Case 2[18]	Case 3[19]	Case 4[20]	Case 5[8]	Case 6[8]	Case 7[8]	Case 8[8]
Age (years)/sex	23/F	38/F	45/F	58/F	53/M	56/M	23/M	54/F
Watercress ingestion	–	+	+	–	+	+	+	–
Symptom duration before admission	7 days	2 months	4 months	2 months	10 days	14 days	45 days	2 days
Clinical symptoms								
Abdominal pain	+	+	–	+	+	+	+	+
Fever	+	–	+	+	+	–	+	–
Cutaneous reactions	Skin rash	–	–	–	–	–	Generalized pruritus	Facial papular rash
Others	Wheezing, dry cough	–	–	Weight loss	–	–	–	–
Laboratory test results								
White blood cell count (/mm^3)	21,800	8,100	13,120	Unknown	34,200	14,800	14,700	15,300
Eosinophil count (/mm^3)	9,900	4,050	3,280	Eosinophilia	15,100	9,910	4,940	6,130
Liver CT findings	Multiple distinctive hypo-attenuating linear and nodular lesions	Multiple hepatic subcapsular hypodense lesions	Unknown	Irregular low-density lesions with obscure boundaries in the subcapsular portion	Several hypodense lesions with irregular borders in posterior segment of right lobe, thrombosis of right portal vein branch	Confluent hypodense liver lesions in segments 4, 5, and 8	Mild hepatomegaly, several hypodense lesions with irregular borders, tunnel-like irregular lesions	Hypodense lesions with diffuse limits in segments 6 and 7, dilated bile ducts
Stool examination result	Negative	Not performed	Ova	Negative	Unknown	Unknown	Unknown	Unknown
Serological test (*F. hepatica* antibody) result	Positive	Positive	Unknown	Positive	Positive	Positive	Positive	Positive
Biopsy result	Not performed	Not performed	Not performed	Numerus eosinophilic cells, lymphocytes and Charcot-Leyden crystals	Not performed	Not performed	Not performed	Not performed
Treatment of choice	Triclabendazole 10 mg/kg/day for 2 days	Triclabendazole 10 mg/kg/day for 2 days	Nitazoxanide 500 mg twice daily for 7 days	Triclabendazole 10 mg/kg/day for 2 days	Triclabendazole 10 mg/kg/day for 1 day	Triclabendazole 10 mg/kg/day for 1 day	Triclabendazole 10 mg/kg/day for 1 day	Triclabendazole 10 mg/kg/day for 1 day

metacercariae reach the duodenum, penetrate the intestinal wall, enter the abdominal cavity, penetrate the liver capsule, and invade the liver parenchyma. After approximately 6 weeks, the trematode invades the bile duct system.[6] In the hepatic phase, the clinical symptoms include fever, abdominal pain, nausea, vomiting, urticaria, diarrhea, anemia, and hepatomegaly. The laboratory tests usually reveal peripheral eosinophilia and abnormal liver function test results.[6,8] Typical enhanced CT findings in the acute phase include multiple, round, or oval clustered hypodense lesions with peripheral enhancement.[9] On the other hand, fascioliasis is difficult to differentiate from other causes of liver abscesses, such as pyogenic or amoebic infections. In addition, physicians usually consider *Toxocariasis* or *Clonorchis sinensis* first in patients with peripheral eosinophilia and eosinophilic abscess of the liver. A diagnosis of fascioliasis is usually determined by the detection of eggs in the stool or duodenal aspirates. In the acute phase, however, eggs may not be visible in the stool or aspirates.[10] A liver biopsy is not usually performed, but the typical pathological findings of *F. hepatica* include granulomatous inflammation with or without eggs, diffuse eosinophilic infiltration, migration track, Charcot-Leyden crystals, necrotic debris, and fibrosis.[11] Therefore, serologic tests, including ELISA, are required to diagnose fascioliasis in the acute phase. According to an endemic area study in Peru, ELISA revealed a sensitivity, specificity, and negative predictive value of 92.4%, 83.6%, and 97.2%, respectively.[12] In Korea, a serologic test by ELISA is available to refer to specialized agencies, and it takes approximately 10 days for the test result to be notified. The ELISA test for *F. hepatica* is based on the antibody response method, and the test result is expressed as a numerical value.[12] The ELISA test is not perfect for distinguishing between overt and resolved infections; therefore, careful interpretation is required in clinical practice.[12]

In the chronic biliary phase, patients usually present with epigastric or right upper quadrant pain, jaundice, intermittent fever, but approximately 50% of patients have no symptoms.[7] The laboratory tests show an elevation of total bilirubin, ALP, and GGT levels due to cholestasis. In particular, GGT begins to increase at 9 weeks after infection and increases significantly at 18 weeks. On the other hand, peripheral eosinophilia may not be observed in approximately 50% of patients because it could not be used for screening in endemic areas.[13] In the biliary phase, a diagnosis is based on a stool examination, serologic tests including ELISA, CT, and ERCP.[6,14] The detection of eggs in the stool, as well as in the duodenal and biliary aspirates is usually available at 10 weeks after infection.[2] The CT findings of the biliary phase reveal bile duct dilatation, irregular wall thickening, and low attenuation in the periportal areas. In some cases, multiple calcifications in the liver parenchyma may be observed.[9] ERCP may be helpful in a diagnosis if the biliary phase of the *F. hepatica* infection is suspected. Flukes can be seen as a filling defect in the bile duct, and they can also be extracted by ERCP.[13,14]

The two patients had atypical symptoms, such as dyspepsia, epigastric or chest discomfort, and a febrile sense with marked peripheral eosinophilia. The CT images revealed multiple clustered hypodense lesions and several ill-defined linear low densities in the liver. Infections with *Toxocariasis* or *Clonorchis sinensis* were first considered, but no eggs were revealed by stool examinations. Therefore, it was suspected that the patients were in the acute phase of the *F. hepatica* infection. The pathology findings of the liver biopsies supported the diagnosis of a parasitic infection, but *F. hepatica* could not be differentiated from other parasites. Ultimately, both patients were diagnosed definitively according to the serologic test results.

Praziquantel, the drug of choice for various trematodes, is ineffective on fascioliasis[15]; rather, a single dose of triclabendazole (10 mg/kg) is recommended. Bithionol (30-50 mg/kg for 15 days) can also be effective.[7,16] Only eight well-organized cases of human fascioliasis were reviewed; all but one were treated with triclabendazole (Table 1). In that case, nitazoxanide was prescribed because triclabendazole is unavailable in Nepal. In Korea, triclabendazole can be obtained only through the KOEDC, and it takes approximately 3-5 days to receive triclabendazole after submitting the required documents. In the present two patients, triclabendazole was administered successfully, and no adverse reactions or recurrence occurred.

In conclusion, the authors encountered two cases of acute-phase *F. hepatica* infection. Physicians should consider fascioliasis, particularly acute hepatic phase infection, in patients presenting with abdominal pain, marked peripheral eosinophilia, and hypodense hepatic lesions on CT. Serologic tests can help diagnose *F. hepatica* infections.

REFERENCES

1. Keiser J, Utzinger J. Food-borne trematodiases. Clin Microbiol Rev 2009;22:466-483.
2. Mas-Coma S, Bargues MD, Valero MA. Fascioliasis and other plant-borne trematode zoonoses. Int J Parasitol 2005;35: 1255-1278.
3. Kim YH, Kang KJ, Kwon JH. Four cases of hepatic fascioliasis mimicking cholangiocarcinoma. Korean J Hepatol 2005;11:169-175.
4. Kang BK, Jung BK, Lee YS, et al. A case of Fasciola hepatica infection mimicking cholangiocarcinoma and ITS-1 sequencing of the worm. Korean J Parasitol 2014;52:193-196.
5. Ha JS, Choi HJ, Moon JH, et al. Endoscopic extraction of biliary fascioliasis diagnosed using intraductal ultrasonography in a patient with acute cholangitis. Clin Endosc 2015;48:579-582.
6. Marcos LA, Terashima A, Gotuzzo E. Update on hepatobiliary flukes: fascioliasis, opisthorchiasis and clonorchiasis. Curr Opin Infect Dis 2008;21:523-530.
7. Aksoy DY, Kerimoğlu U, Oto A, et al. Fasciola hepatica infection: clinical and computerized tomographic findings of ten patients. Turk J Gastroenterol 2006;17:40-45.
8. Fica A, Dabanch J, Farias C, Castro M, Jercic MI, Weitzel T. Acute fascioliasis--clinical and epidemiological features of four patients in Chile. Clin Microbiol Infect 2012;18:91-96.
9. Dusak A, Onur MR, Cicek M, Firat U, Ren T, Dogra VS. Radiological imaging features of fasciola hepatica infection - a pictorial review. J Clin Imaging Sci 2012;2:2.
10. Kaya M, Beştaş R, Cetin S. Clinical presentation and management of Fasciola hepatica infection: single-center experience. World J Gastroenterol 2011;17:4899-4904.
11. Acosta-Ferreira W, Vercelli-Retta J, Falconi LM. Fasciola hepatica human infection. Histopathological study of sixteen cases. Virchows Arch A Pathol Anat Histol 1979;383:319-327.
12. Espinoza JR, Maco V, Marcos L, et al. Evaluation of Fas2-ELISA for the serological detection of Fasciola hepatica infection in humans. Am J Trop Med Hyg 2007;76:977-982.
13. Bektaş M, Dökmeci A, Cinar K, et al. Endoscopic management of biliary parasitic diseases. Dig Dis Sci 2010;55:1472-1478.
14. Gulsen MT, Savas MC, Koruk M, Kadayifci A, Demirci F. Fascioliasis: a report of five cases presenting with common bile duct obstruction. Neth J Med 2006;64:17-19.
15. Patrick DM, Isaac-Renton J. Praziquantel failure in the treatment of Fasciola hepatica. Can J Infect Dis 1992;3:33-36.
16. Keiser J, Engels D, Büscher G, Utzinger J. Triclabendazole for the treatment of fascioliasis and paragonimiasis. Expert Opin Investig Drugs 2005;14:1513-1526.
17. Krsak M, Patel NU, Poeschla EM. Case report: hepatic fascioliasis in a young afghani woman with severe wheezing, high-grade peripheral eosinophilia, and liver lesions: a brief literature review. Am J Trop Med Hyg 2019;100:588-590.
18. Sapmaz F, Kalkan IH, Guliter S, Nazlıoğlu A. A clinical presentation of a very rare infection: parenchymal Fasciola hepatica. Turkiye Parazitol Derg 2013;37:305-306.
19. Sah R, Khadka S, Khadka M, et al. Human fascioliasis by Fasciola hepatica: the first case report in Nepal. BMC Res Notes 2017;10: 439.
20. Wang JK, Ma WJ, Lu Q, et al. First case report of retroperitoneal metastasis of fascioliasis after surgery. Medicine (Baltimore) 2017;96:e9258.