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Original Article

Evaluation of patients diagnosed with fascioliasis: A six-year experience at a university hospital in Turkey

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Abstract

Introduction: In this study, clinical, laboratory, radiological, and serological examinations of fascioliasis patients were analyzed, and data with a significant impact on differential diagnosis were evaluated.

Methodology: Clinical, radiological, and laboratory findings and treatment responses of a total of 22 fascioliasis patients, treated between October 2009 and September 2014, were evaluated. Nineteen patients were diagnosed with fascioliasis at the invasive phase and three patients at the chronic phase. Patients were followed up for clinical, laboratory, and radiology findings for a period of three months to one year after treatment.

Results: The most frequent complaints in both groups were abdominal pain, and the most common physical examination finding was epigastric tenderness. In the performed examination, an eosinophil elevation in whole blood count was detected in 19 patients (100%) in the hepatic phase, and in 2 patients (66.6%) in the biliary phase. The results of the *Fasciola hepatica* indirect hemagglutination assay (IHA) test ordered in the diagnosis were positive in all patients. Treatment with 10 mg/kg/day triclabendazole for two consecutive days was effective.

Live parasites were extracted from patients in the biliary phase with endoscopic retrograde cholangiopancreatography. In the follow-ups, remission in IHA titer and clinical and radiological improvement was achieved in all patients.

Conclusions: If hypereosinophilia is detected by peripheral smear in patients who are admitted with complaints such as abdominal pain, weakness, nausea, myalgia, and weight loss, radiological evaluation and serological tests should be performed and fascioliasis should be considered in the differential diagnosis.

Key words: *Fasciola hepatica*; fascioliasis; triclabendazole.

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Introduction

The causal agent of fascioliasis disease is *Fasciola hepatica*, which causes infection by settling in the liver and bile ducts. *Fasciola hepatica* is commonly seen in domestic animals such as sheep, goats, and cattle, and is sporadically encountered in humans having vectors or intermediate hosts [1]. It was determined that the disease was endemic in humans in various geographical regions, and its prevalence has varied between low and very high [2,3]. An estimated 2.4 to 17 million people are infected in more than 51 countries [4]; 91 million are at risk worldwide [5]. This disease in humans shows an increasing importance, which is due to its recent widespread emergence related to climate and global changes and also its pathogenicity in the invasive, biliary, and advanced chronic phases in the human endemic areas, mainly of developing countries [6].

Diagnosis of fascioliasis is difficult in non-endemic regions and may be delayed since it may be confused with other diseases of the liver or bile ducts. Diagnosis of *Fasciola hepatica* infection traditionally depends on the detection of eggs in stool specimens. However, this method is complex and not reliable [1,7]. Computerized tomography findings are used in the diagnosis of fascioliasis in patients in the acute (invasive) phase, and ultrasonography findings are used in patients in the biliary phase [6,8]. The diagnosis has to be confirmed, which depends on serological findings and parasite tests [8]. Triclabendazole and bithionol are effective agents for the treatment of fascioliasis [9].

In this study, clinical, laboratory, radiological, and serological examinations in fascioliasis patients were analyzed and data with a significant impact on differential diagnosis were evaluated.

Methodology

This study was designed in Gaziantep University Medical Faculty Hospital, Clinic of Infectious Diseases and Microbiology, Gaziantep, Turkey. Gaziantep is a province in the southeastern Anatolia region of Turkey, with an urban and rural human population of 1,846,769 in 2014. The Medical Faculty Hospital is a reference hospital that renders service to outpatients and inpatients with an 800-bed capacity in Gaziantep; the Clinic of Infectious Diseases and Microbiology is a 12-bed clinic at the hospital.

Twenty-two patients diagnosed with fascioliasis were followed up and treated between October 2009 and September 2014. The demographic and clinical findings, diagnostic criteria, and treatment and outcome of invasive and biliary phase patients were analyzed retrospectively.

Patients were diagnosed with fascioliasis, which was suspected on the basis of the clinical picture, on the anamnestic recall of consuming contaminated watercress, on the detection of eosinophilia (blood eosinophil count > 500–1000 per μL of blood), and on typical findings at ultrasound or computed abdominal tomography (CAT) [10]. Confirmation relied on positive specific *Fasciola hepatica* indirect hemagglutination assay (IHA) and/or the presence of *Fasciola hepatica* eggs in stool, duodenal aspirates, or bile specimens.

The diagnosis of *Fasciola hepatica* infection with hepatic phase was based on the presence of characteristic findings on the CAT and the exclusion of all other known diseases that cause hepatic lesions on tomographic examination. Diagnosis of the biliary phase of the disease was established by seeing live parasites during endoscopic retrograde cholangiopancreotography (ERCP).

Patients were treated with 10–12 mg/kg/day triclabendazole for two consecutive days. Patients were followed up for clinical, laboratory, and radiology findings for a period of three months to one year after the treatment.

This study was performed in accordance with World Medical Association Helsinki Declaration (2000). Approval of the local ethics board was obtained.

Results

The average age of the 22 patients included in the study was 43 ± 14.82 years, and the female/male ratio was 15/7. Of all the patients, 81.8% were from rural areas and 18.1% were from urban areas. All patients had histories of eating watercress without first washing or cooking it. Fifteen (68.18%) patients were female, and all of them were housewives. When all patients were diagnosed with fascioliasis, IHA test finding was determined (≥ 1/620) by positivity for *Fasciola hepatica* antibody. None of the patients had parasite eggs in their stool examinations. Since clinical and laboratory findings consistent with biliary obstruction were not present, ERCP was not performed in 19 patients. However, in 3 (15.7%) other patients, diagnosis was established by the finding of a live parasite during ERCP; these patients were considered to be in the biliary phase. No pathological finding except for eosinophilic series increase consistent with peripheric smear was detected in the results of the bone marrow aspiration. Symptoms and physical

Table 1. Symptoms and physical examination findings of patients.

	Invasive/acute phase (n = 19), (%)	Biliary/chronic phase (n = 3)
Sex		
Male	7	-
Female	12	3
Age (years ± SD)	42±15.60	51 ± 13.02
Average time for the onset of symptoms	21 ± 18.3 weeks	48 ± 12.4 weeks
Abdominal pain	19 (100)	3 (100)
Pain in the upper right quadrant	13 (86.66)	3 (100)
Nausea	11 (73.33)	3 (100)
Fever	7 (53.84)	1 (33.3)
Myalgia	6 (46.15)	0 (0)
Arthralgia	6 (46.15)	1 (33.3)
Weight loss	6 (46.15)	1 (33.3)
Itching	5 (38.46)	2 (66.6)
Biliary colic	3 (23.07)	3 (100)
Coughing	1 (7.69)	0 (0)
Residence		
Rural area	15 (78.9)	3 (100)
Urban area	4 (21.0)	0 (0)

examination findings of the diagnosed patients are shown in Table 1, and laboratory findings are shown in Table 2.

Patients with invasive phase fascioliasis

Nineteen patients were diagnosed with fascioliasis in the hepatic phase. The mean age of these patients was 42 ± 15.6 years. The most common symptom was abdominal pain (100%) and pain in the upper right quadrant (86.6%). Eosinophilia was the most common laboratory finding (100%). In the ultrasonography of the patients, hepatomegaly (100%), minimal irregularity in the liver parenchyma (78.9%), parenchymal heterogeneity, and nonspecific lesions with irregular contours and mixed echogenity in the subcapsular area in the vicinity of bile ducts (52.6%) were detected. On CAT scan, the main abnormalities were multiple nodular lesions such as micro-abscesses in 17 (89.4%) patients, tubular branching lesions in 10 (52.6%), multiple small hypodense lesions without distinct margins with subcapsular localizations in 6 (31.5%), and lymph node enlargement in the portal area in 3 (15.7%) patients (Figures 1–3).

Patients with biliary phase fascioliasis

Three patients were diagnosed with fascioliasis in the biliary phase. The mean age of these patients was 51 ± 13.02 years. The most common symptom was localized, intermittent abdominal pain lasting for a long time that felt like colic, especially in the right side (100%). One patient was admitted to the hospital with findings of prominent acute cholecystitis. On physical examination, epigastric tenderness and tenderness with palpation at the upper right quadrant were found in all patients.

Figure 1. Microabscess foci showing branching and multiple solid masses in the vicinity of intrahepatic bile ducts.

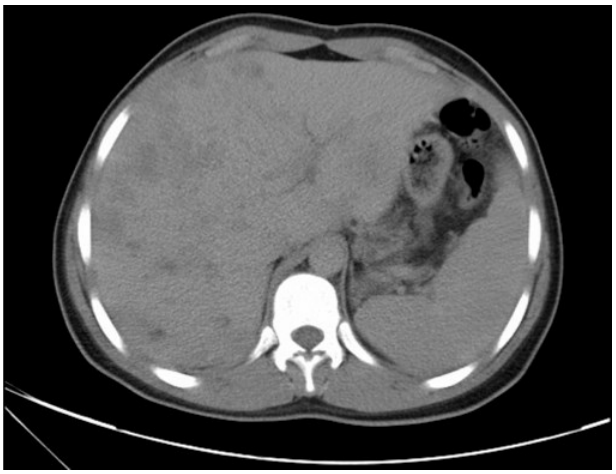

Figure 2. Irregular hypodense lesion giving the impression of mass with subcapsular localization in the liver.

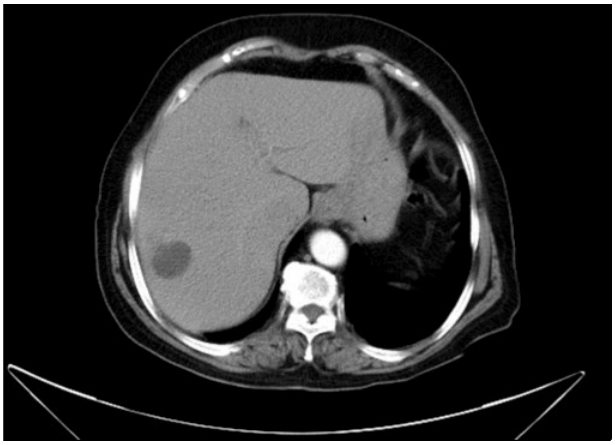

Table 2. Laboratory findings of patients.

Variables	Invasive phase (mean ± SD)	Biliary phase (mean ± SD)
Hb (g/dL)	14.5 ± 1.48	10.8 ± 2.1
WBC (n/mm3)	18.75 ± 10.25	7.07 ± 0.70
Eosinophil (% of total WBC count)	53.6 ± 13.77	20.3 ± 11.21
Platelet (n/mm^3)	282 ± 56	279 ± 82
ESR (mm/h)	41 ± 16.96	80 ± 29.43
ALT (U/dL)	55.5 ± 35.86	152 ± 32.45
AST (U/dL)	35 ± 20.76	184 ± 60
ALP (U/dL)	236 ± 123.16	269 ± 141
GGT (U/dL)	56 ± 19.94	135 ± 13.92
Total bilirubin (U/dL)	0.62 ± 0.28	4.78 ± 2.13
Serum IgE level	566.5 ± 128.53	1,040 ± 86.46

WBC: white blood cell; ESR: erythrocyte sedimentation rate; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; GGT: γ glutamyl transferase.

In the laboratory examinations, leucocyte and thrombocyte counts of the patients were normal in whole blood count. Eosinophilia count was high in two patients (31.21% and 21.4%) and normal in one patient (2.4%). Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), γ glutamyl transferase (GGT), and total bilirubin values were high in all patients. In the abdominal ultrasonography (USG) of the patients in the biliary phase, the gallbladder wall was found to be thicker than normal in three (100%) patients; dilatation in intrahepatic bile ducts and irregularity in the choledoch distal end and in the bile duct in the part opening to the duodenum was found in three (100%) patients; and echogenity with linear extension into the lumen were determined as parasites in all patients. CAT scans showed no abnormalities in two (66.6%) patients, and subcapsular low-density areas were surrounded by a rim of parenchyma in one (33.3%) patient. ERCP demonstrated a radiolucent, roughly crescent-shaped shadow in the common bile duct in all patients. After standard sphincterotomy, live *Fasciola hepatica* were removed using a balloon catheter from the extrahepatic bile ducts.

There were no side effects attributed to triclabendazol. Clinical and laboratory improvement was seen in 86% of the patients, and improvement in CAT findings was seen in 60% of the patients during the controls performed three months after the treatment. Six months later, clinical and laboratory improvement was seen in all patients, and improvement in imaging findings was seen in 80%.

Discussion

Fascioliasis is a parasitic disease seen not only in developing countries, but in developed countries as well. This zoonotic infection is frequently observed in Africa, Western Europe, and Latin America [11,12]. The seroprevalence of the disease in the eastern part of our country was reported to be 2.78%, irrespective of age, level of education, and socio-economic status [13]. In Turkey, previous enzyme-linked immunosorbent assay (ELISA) (anti-body detection) studies on the seroprevalence of fascioliasis have determined a prevalence of 3.01% in Antalya province [12,14]; 2.4% in Isparta center; 9.3% in a village in Isparta province [12,15]; 0.55% in patients with no family history of fascioliasis and 1.93% in patients with a family history of fascioliasis in Mersin province [16]; and 2.78% of 540 randomly selected healthy people in Elazığ province [13]. In a recent study conducted in Van province, 89 of 1,600 patients were found to be seropositive by ELISA [12].

Figure 3. Hypodense lesion giving the impression of mass with parenchymal localization in the liver.

The reservoir of infection is herbivorous animals such as sheep and cattle. Humans are infected when they eat aquatic plants with metacercaria without first washing and cooking them. In our study, 15 (68.1%) patients were female and all of them were housewives. These findings lead to the conclusion that it is possible that women have a more frequent history of contact with watercress compared to men.

The disease has two clinical phases presenting different symptoms and findings. The *Fasciola hepatica* worm reaches the peritoneum cavity first and then the liver capsule before reaching the duodenum. The worm perforates the liver capsule and enters into the bile ducts. After reaching the bile ducts, the helminth develops and transforms into a mature worm within three months [11]. Fever, abdominal pain, gastrointestinal disturbances, urticaria, and respiratory symptoms are among the major symptoms [6]. In their study, Ulger *et al*. reported that 95% of patients had abdominal pain, and 79% of them had eosinophilia [17]. The symptoms and clinical and radiological findings of our patients were similar to those of previously published studies. The most frequently seen complaints in our patients in the invasive phase were abdominal pain, upper right quadrant pain, weakness, and nausea. Epigastric tenderness, tenderness in the upper right quadrant, and urticarial lesions were detected on physical examination. Intermittent fever complaint was recorded in the history of 9 (47.36%) of the 19 patients in the invasive phase, but in the physical examination performed in the follow-up, fever was detected only in 7 (53.8%) patients.

In the chronic phase, cholangitis and cholecystitis were the results of inflammation, epithelial hyperplasia,

and thickening and dilatation of the bile ducts and gallbladder walls [6]. In patients admitted in the biliary phase, abdominal pain, pain in the upper right quadrant, biliary colic, jaundice associated with the obstruction of bile ducts by the adult parasite, and inflammatory response were the most common complaints [18]. In this phase, serum ALP, GGT, and total bilirubin values were elevated, consistent with cholestasis [19]. In patients admitted in the biliary phase, complaint of pain in the form of colic (especially localized on the right side), and ALP, GGT, and bilirubin elevation were detected; these findings supported cholestasis. Eosinophil count was high in two patients (66.66%) and normal in one (33.3%) patient. Hepatic fascioliasis manifests as clusters of microabscesses arranged in a characteristic tract-like fashion, usually in the subcapsular regions in CAT, and shows slow evolution of the lesion on follow-up examinations [20,21]. In their study, Kabaalioğlu *et el*. reported that 90% of patients had liver lesions, and 79% had multiple lesions [22]. In patients in the biliary phase, gallbladder wall thickening and dilatation in extrahepatic bile ducts related to chronic inflammation may be seen [1]. ERCP is the first choice for patients in the chronic phase. ERCP and sphincterotomy are used to extract parasites from the biliary tree [23]. In the literature, it was reported that patients in the biliary phase may admit to the hospital due to acute pancreatitis as well [18]. In our three patients who had a diagnosis of biliary phase fascioliasis, parasites were seen and extracted with ERCP after USG; abdominal CAT was not performed. Acute cholecystitis findings were evaluated in one patient. Acute pancreatitis findings were not observed. Specificity of the IHA test in the serological diagnosis of *Fasciola hepatica* infection has been reported to be 96.9% [24]. Clinical suspicion of *Fasciola hepatica* infection and detection of radiological findings also contribute to the diagnosis. We detected clinical symptoms and findings specific to the disease and eosinophilia and characteristic CAT findings in peripheric smears in all patients in the invasive phase. We diagnosed the disease with high IHA titer. Diagnosis of the patients in the biliary phase was established by clinical and laboratory findings consistent with biliary obstruction, and also by detecting and extracting *Fasciola hepatica* in ERCP.

In previous studies, *Echinococcus granulosus* and *Fasciola hepatica* infection and the cross-reaction between them were reported [25,26]. Kaya *et al*. also reported in their study that 59% of the patients diagnosed with fascioliasis tested positive for *Echinococcus granulosus* antibodies in an indirect immunofluorescence antibody test [27]. They concluded that this might be due to the fact that helminths possess some antigens that are responsible for serological cross-reactions. *Echinococcus* indirect immunofluorescence antibody test was requested for all our patients, and only two of them (9.09%) had positive results.

Triclabendazole or bithionol are used in the treatment of fascioliasis. They are effective for both adult and immature worms [9,18,28,29]. Prevention mainly concerns measures to avoid individual infection by considering the different human infection sources [23].

Triclabendazole at a dose of 10 mg/kg body weight reportedly is effective in about 80%–90% of patients and is well tolerated. The most common drug-related side effects are nausea, vomiting, and abdominal pain [30]. All patients in the invasive phase recovered with triclabendazole treatment. Parasites were extracted with ERCP from patients in the biliary phase; in addition, triclabendazole was administered. No side effects were observed in both groups. Though clinical and laboratory recovery were seen in all patients within a couple of weeks, radiological full recovery took longer (6 ± 3.5 months). Limitations of this study include its retrospective nature and small number of patients.

Conclusions

In cases of detection of hypereosinophilia in peripheric smears of patients admitting with complaints of abdominal pain, weakness, nausea, myalgia, and weight loss, radiological evaluation and serological tests should be performed and fascioliasis should be considered in the differential diagnosis at first. In addition, when patients have cholestasis findings on admission to the hospital, biliary phase fascioliasis should be considered. Treatment with 10 mg/kg/day triclabendazole for two consecutive days is effective.

References

1. Lim JH, Mairiang E, Ahn GH (2007) Biliary parasitic diseases including clonorchiasis, opisthorchiasis and fascioliasis. Abdom Imaging 33: 157-165.
2. Parkinson M, O'Neill SM, Dalton JP (2007) Endemic human fasciolosis in the Bolivian Altiplano. Epidemiol Infect 135: 669-674.
3. Mas-Coma MS, Esteban JG, Bargues MD (1999) Epidemiology of human fascioliasis: a review and proposed new classification. Bull World Health Organ 77: 340-346.
4. Mas-Coma S, Valero MA, Bargues MD (2009) Chapter 2. Fasciola, lymnaeids and human fascioliasis, with a global overwiew on disease transmission, epidemiology, evolutionary genetics, molecularepidemiology and control. Adv Parasitol 69: 41-146.

5. Keiser J, Utzinger J (2009) Food-borne trematodiases. Clin Microbiol Rev 22: 466.
6. Mas-Coma S, Agramunt VH, Valero MA (2014) Neurological and Ocular Fascioliasis in Humans. In D. Rollinson, editor. Advances in Parasitology, 2014; 84:27-149.
7. Koc Z, Ulusan S, Tokmak N (2009) Hepatobiliary fascioliasis: imaging characteristics with a new finding. Diagn Interv Radiol 15 (4): 247-251.
8. Teichmann D, Grobusch MP, Gobels K, Muller HP, Koehler W, Suttorp N (2000) Acute fascioliasis with multiple liver abscesses. Scand J Infect Dis 32: 558-560.
9. Aksoy DY, Kerimoglu U, Oto A, Erguven S, Arslan S, Unal S, Batman F, Bayraktar Y (2006) Fasciola hepatica infection: clinical and computerized tomographic findings of ten patients. Turk J Gastroenterol 17: 40-45.
10. World Health Organization (2015) Foodborne trematode infections, Fascioliasis diagnosis, treatment and control strategy. Available: http://www.who.int/foodborne_trematode_infections/fasciliasis/fascioliasis_diagnosis/en. Accessed 18 January 2016.
11. El-Shazly AM, Soliman M, Gabr A, Haseeb AN, Morsy AT, Arafa MA, Morsy TA (2001) Clinico-epidemiological study of human fascioliasis in an endemic focus in Dakahlia Governorate, Egypt. J Egypt Soc Parasitol 31: 725-736.
12. Tas CZ, Yılmaz H, Dulger AC, Akdeniz H, Karahocagil MK, Cicek M (2015) Seroprevalence of human fascioliasis in Van province, Turkey. Turk J Gastroenterol 26: 259-262.
13. Kaplan M, Kuk S, Kalkan A, Demirdag K, Ozdarendeli A (2002) Fasciola hepatica seroprevalence in the Elazig region. Mikrobiyol Bul 36: 337-342.
14. Tınar R, Korkmaz M (2003) Fasciolosis. İzmir: 343-358.
15. Kaya S, Demirci M, Demirel R, Aridogan BC, Ozturk M, Korkmaz M (2006) Seroprevalence of fascioliasis and the difference of fascioliasis between rural area and city center in Isparta, Turkey. Saudi Med J 27: 1152-1156.
16. Özturhan H, Emekdaş G, Sezgin O, Korkmaz M, Altıntaş E (2009) 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 20: 198-203.
17. Ulger BV, Kapan M, Boyuk A, Uslukaya O, Oguz A, Bozdag Z, Girgin S (2014) Fasciola hepatica infection at a University Clinic in Turkey. J Infect Dev Ctries 8: 1451-1455. doi:10.3855/jidc.5124.
18. Kaya M, Beştaş R, Cetin S (2011) Clinical presentation and management of *Fasciola hepatica* infection: single-center experience. World J Gastroenterol 17: 4899-4904.
19. Bektas M, Dokmeci A, Cınar KS (2010) Endoscopic management of biliary parasitic diseases. Dig Dis Sci 55: 1472-1478.
20. Han JK, Choi BI, Cho JM (1993) Radiologic findings of human fascioliasis. Abdom Imaging 18: 261-264.
21. Takeyama N, Okumura N, Sakai Y (1986) Computed tomography findings of hepatic lesions in human fascioliasis: report of two cases. Am J Gastroenterol 81: 1078-1081.
22. Kabaalioglu A, Ceken K, Alimoglu E, Saba R, Cubuk M, Arslan G, Apaydın A (2007) Hepatobiliary fascioliazis: sonographic and CT findings in 87 patients during the initial phase and long-term follow-up. Am J Roentgenol 189: 824-828.
23. Ashrafi K, Bargues MD, O'Neill S, Mas-Coma S (2014) Fascioliasis: A worldwide parasitic disease of importance in travel medicine. Travel Med Infect Disease 12: 636-649.
24. 12. Azab M el-S, el Zayat EA (1996) Evaluation of purified antigens in haemagglutination test (IHA) for determination of cross reactivities in diagnosis of fascioliasis and schistosomiasis. J Egypt Soc Parasitol 26: 677-685.
25. 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.
26. Yamano K, Goto A, Nakamura-Uchiyama F, Nawa Y, Hada N, Takeda T (2012) Galbeta1-6Gal, antigenic epitope which accounts for serological cross-reaction in diagnosis of Echinococcus multilocularis infection. Parasitol Res 111: 795-805.
27. Kaya M, Bestaş R, Gırgın S, Çıçek M, Kaplan MA (2012) Increased anti-Echinococcus granulosus antibody positivity in Fasciola hepatica infection. Turk J Gastroenterol 23: 339-343.
28. Mas-Coma S (2005) Epidemiology of fascioliasis in human endemic areas. J Helminthol 79: 207-216.
29. Karabuli TA, Shaikhani MA, Karadaghi SH, Kasnazan KH (2009) Education and imaging. Hepatobiliary and pancreatic: fascioliasis. J Gastroenterol Hepatol 24: 1309.
30. López-Vélez R, Domínguez-Castellano A, Garrón C (1999) Successful treatment of human fascioliasis with triclabendazole. Eur J Clin Microbiol Infect Dis 18: 525-526.

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