

# Fasciola hepatica infection: Clinical and computerized tomographic findings of ten patients

Fasciola hepatica infeksiyonu: On hastanın klinik ve bilgisayarlı tomografi bulguları

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**Background/aims:** *Fasciola hepatica* is the cause of liver infection, fascioliasis. Although rare, it is still a problem even in developed countries. In this study, the clinical and computerized tomographic findings of 10 patients diagnosed with fascioliasis are summarized. **Methods:** The medical records of the patients with fascioliasis were retrospectively examined. Clinical, laboratory findings and computerized tomographic results were recorded. **Results:** Abdominal pain, fever, eosinophilia and abnormal liver function tests were the most commonly encountered symptoms and signs. One patient was human immunodeficiency virus -positive with active tuberculosis. Serologic test for *Fasciola hepatica* was positive in all patients. Nodular masses without prominent enhancement, and branching low-attenuated tubular lesions were the most commonly seen tomographic findings and were supportive for the diagnosis. All except the HIV-positive patient received bithionol therapy; six patients responded well, two lost contact with the clinic and one patient who was unresponsive to bithionol therapy received triclabendazole. During follow-up of the six patients who responded, all the clinical and radiological findings regressed. **Conclusion:** In any patient with peripheral eosinophilia, abdominal pain and elevated liver enzymes, especially when CT reveals tubular and nodular hypodense lesions particularly in subcapsular area, *F. hepatica* infection should be considered. Either triclabendazole or bithionol can be used effectively for the treatment.

**Key words:** *Fasciola hepatica*, liver infection, HIV, tuberculosis, computerized tomography

## INTRODUCTION

The liver fluke *Fasciola hepatica* (*F. hepatica*) that causes fascioliasis is a rare cause of hepatobiliary system infections. It is a trematode that infects sheep, goats and cattle. Human beings are accidental hosts. After ingestion of infective form me-

**Amaç:** *Fasciola hepatica* hepatobiliyer sistemde fasioliasis olarak adlandırılan infeksiyonun sebebidir. Bu infeksiyon nadir görülmekle birlikte, halen gelişmiş ülkelerde bile rastlanmaktadır. Bu çalışmada fasioliasis tanısı alan toplam on hastanın klinik ve bilgisayarlı tomografi bulguları özetlenmiştir. **Yöntem:** *Fasciola hepatica* tanısı almış on tane hastanın kayıtları geriye dönük olarak incelenmiştir. Hastaların klinik, laboratuvar bulguları ve bilgisayarlı tomografi sonuçları kaydedilmiştir. **Bulgular:** Karın ağrısı, ateş, eozinofili ile birlikte karaciğer fonksiyon testlerinde bozulma en sık rastlanan belirti ve bulgularıdır. Hastalardan biri Human Immunodeficiency Virus pozitif ve aktif tüberküloz nedeniyle takip edilmekteydi. *Fasciola hepatica* serolojik testi tüm hastalarda pozitif. Nodüler belirgin kontrast tutmayan kütleler ve dallanan yapıda tübüler düşük dansiteli alanlar bilgisayarlı tomografide en sık gözlenen bulgularıdır. HIV pozitif hasta hariç tüm hastalara bithionol tedavisi uygulandı ancak iki hasta takip edilemedi, altısı tedaviye iyi yanıt verirken bir hastanın tedavisi yanıtızlık nedeniyle triklobendazole değiştirildi. Takip edilen altı hastanın klinik ve radyolojik bulgularının hepsinde düzelme gözlemlendi. **Sonuç:** Karın ağrısı, eozinofili ve karaciğer fonksiyon testlerinde bozulma olan hastalarda eğer bilgisayarlı tomografide karaciğerde tübüler ve nodüler hipodens lezyonlar tespit edilirse ve özellikle de subkapsüler alanda görülürse aklı mutlaka *Fasciola hepatica* infeksiyonu gelmelidir. Bithionol ve triklobendazole tedavi için kullanılabilir.

**Anahtar kelimeler:** "*Fasciola hepatica*", karaciğer, HIV, tüberküloz, bilgisayarlı tomografi

tacercaria, they excyst in the intestine, perforate the intestinal wall, enter the peritoneum and then pass through the liver capsule to enter the biliary tree (1, 2). Fascioliasis can be detected throughout the world, with a significant number of patients

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from Eastern Europe, Iran, Northern Africa and South America (3). *F. hepatica* infection has two different stages, in which signs and symptoms are quite different. The hepatic phase of the illness occurs when the organism perforates the liver and begins to migrate through the liver parenchyma toward the biliary radicles. It takes 1-3 months after ingestion of metacercariae. Urticaria, pruritis, fever, pain in the right hypochondrium, hepatomegaly, hypergammaglobulinemia and marked eosinophilia are the classical signs and symptoms of this stage. Mild hepatitis, severe subcapsular hemorrhage and frank hepatic necrosis can also be detected. The biliary stage usually presents with intermittent right upper quadrant pain with or without cholangitis or cholestasis (4-9). Stool studies, serology, radiographic techniques or biopsy can all be used for the diagnosis. Triclabendazole and bithionol are effective agents for the therapy of fascioliasis. We summarize herein the findings of 10 patients who were diagnosed with fascioliasis.

## MATERIALS AND METHODS

Medical records of the patients who admitted to Hacettepe University Department of Internal Medicine during the last seven years and who were diagnosed as *F. hepatica* infection were investigated. Their clinical and tomographical findings were retrospectively analyzed, and the diagnostic tools and treatment modalities were also noted. Serological tests were performed using the manual enzyme-linked immunosorbent assay (ELISA) for excretory-secretory (ES) antigen of the parasite as described elsewhere (9). Bithionol and triclabendazole were the two medications used for treatment.

## RESULTS

*F. hepatica* infection was detected in 10 patients [6 male, 4 female; mean age 40.3 (17-53)]. Six patients had abdominal pain, and five had fever up to 39°C; chills (n:1), weakness (n:2), pruritis and dyspnea (n:1), muscle pain (n:1), and night sweats and weight loss (n:1) accompanied presenting symptoms in some patients. One patient was human immunodeficiency virus (HIV)-positive; he had active tuberculosis but was not taking his anti-tuberculosis drugs regularly. One was symptomless; he was evaluated because of the presence of *F. hepatica* infection in his brother (Table 1).

**Table 1.** Symptoms of the patients

Symptom	Number of patients
Abdominal pain	6
Fever	5
Chills	1
Weakness	2
Muscle pain	1
Pruritis and dyspnea	1
Night sweats and weight loss	1

Eight patients had abnormal liver function tests. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were high in two; alkaline phosphatase (ALP) and gamma glutamyl transpeptidase (GGT) were high in four; and ALT, AST, ALP and GGT were all high in two patients. Only one patient had elevated bilirubin levels. All patients except one had eosinophilia (Table 2).

**Table 2.** Laboratory findings of the patients

Laboratory findings	Mean (Minimum maximum)
ALT	72.13 (8-256)
AST	117.87 (24-669)
ALP	294.8 (73-810)
GGT	83 (24-243)
Bilirubin	0.96 (0.21-4.72)
Eosinophilia	30.87 (3-55)

ALT: Alanine aminotransferase (U/L: Normal: 5-40), AST: Aspartate aminotransferase (U/L: Normal: 8-33), ALP: Alkaline phosphatase (U/L: Normal: 35-129), GGT: Gamma glutamyl transpeptidase (U/L: Normal: 5-40), Bilirubin (mg/dl: Normal: 0.1-1.2), Eosinophil (percentage in peripheral smear)

Abdominal ultrasonography (US) was available in all patients; only five were performed in our clinic, including one from our institution, and three were reported as normal. Minimal irregularity in liver parenchyma, hepatomegaly, and increase in periportal echogenicity were reported. A solid, heterogeneous lesion was present in one patient.

Computerized tomography (CT) was performed in all patients and demonstrated low-attenuated nodular masses, either conglomerated like microabscess (n=9) (Figures 1, 2) or an isolated lesion with irregular margin (n= 3), of different size with or without rim enhancement and without demonstration of a prominent contrast uptake after administration of intravenous (i.v.) contrast. Subcapsular tubular branching hypodense lesions were seen in five patients (Figures 3, 4). Subcapsular hypodense area surrounded by enhanced rim of parenchyma was seen in one patient (Figure 3) (Table 3). One patient had a mass measuring

**Table 3.** Computerized tomographic findings of *F. hepatica* infection in 10 patients

	Liver		Spleen
	Central	Peripheral	
Nodular solitary lesion with hazy margins	2	1	
Nodular multiple lesions like microabscess	4	5	1
Tubular branching lesion	5		
Subcapsular low density area surrounded by enhanced rim of parenchyma		1	

46x33 mm with irregular margins and suspicious solid appearance in the anterior segment of the right liver lobe which was hypodense before administration of i.v. contrast and heterogeneous after.

Neither ova nor parasites were detected. Serologic test for *F. hepatica* was the most commonly used method for diagnosis and revealed positive results in all patients.

Liver biopsy was performed in three patients (2 had biopsies before the results of serology were obtained in order to clarify the etiology of abnormal liver function tests; 1 had biopsy in order to rule out a malignancy accompanying fascioliasis due to presence of a heterogeneous solid lesion in CT). All the biopsy results were consistent with inflammation characterized by the presence of necrotic debris and inflammatory cells.

Endoscopic retrograde cholangiopancreatography (ERCP) was performed for two patients (Patients 2 and 10) due to elevation of ALP levels. Both ERCPs were done before the positive serology results were obtained. There was no abnormality in the biliary tract of either patient.

**Figure 1.** CT revealed enlarged liver totally involved with microabscesses arranged in a tract-like fashion (arrow)**Figure 2.** CT showed low-density masses with hazy margins located in the center and right lobe of the liver (arrow) and multiple tubular low-attenuated lesions extending to the subcapsular region at the periphery of left hepatic lobe (arrow)**Figure 3.** CT showed subcapsular low-density areas surrounded by enhanced rim of parenchyma (arrow) associated with multiple hypodense street-like arranged areas in right hepatic lobe (arrow)**Figure 4.** CT demonstrated nodular (arrow) and tubular (arrow) intrahepatic and peripherally branching lesions, which demonstrate diminished attenuation

Discrimination of the phases of the disease was retrospectively done utilizing symptom durations, CT and US findings (10). Seven patients were at hepatic and three at biliary stage.

Bithionol was administered to nine patients at a dose of 30-50 mg/kg/day for two weeks. The patient with HIV infection did not receive therapy. Six patients responded well to bithionol therapy. Two patients lost contact with the clinic. Of the six patients, only three had negative control serology results. Clinical improvement along with the regression of pathological findings in control CTs were accepted as response to the treatment. The mean follow-up of the five patients was 12.3 (6-24) months. One patient did not respond to bithionol so triclabendazole was started. His therapy was completed recently and he is still being followed up in our clinic.

## DISCUSSION

We retrospectively analyzed the clinical and laboratory findings of 10 patients with fascioliasis. Abdominal pain and fever along with abnormal liver function tests and eosinophilia were the most commonly encountered symptoms and signs. Positive serology results were supported by CT findings. Most patients responded to therapy with bithionol.

For the diagnosis of *F. hepatica*, there are several methods which can be useful at different stages of the disease. Stool studies for ova and parasites can be used but it is unrevealing during the first phase. Demonstration of either ova or parasites was not possible in our patients. ELISA is the most widely used method for the diagnosis. It is rapid, sensitive and quantitative (11, 12). This was the most commonly used method in our clinic and it revealed positive results in all patients regardless of the stage. The serology was not applied until biopsy and ERCPs were done in two patients; diagnosis was delayed in these two patients.

Radiographic techniques such as CT and US are not only useful for confirmation of diagnosis but also helpful in the follow-up to evaluate the efficacy of medical therapy. Although it is non-invasive and inexpensive, US may not be diagnostic in the hepatic phase secondary to heterogeneity of the liver because of the poorly defined nodules; it is more useful in the biliary stage of the disease (13). Adult flukes promote hyperplasia and hypertrophy of the duct epithelium resulting in thickening of the duct walls and periductal fibro-

sis (14, 15). US reveals irregular thickening of the common bile duct wall and biliary dilation (16-18). Mobile vermiform structures without acoustic shadowing within the gall bladder and in the bile ducts can be visible; they represent the worms and this appearance can be confused with stones (17, 18). Abdominal US was normal in three patients. Considering that US is an operator-dependent radiographic technique and that half of the US procedures were done outside our clinic, US was not a reliable visualization method for our series. Nevertheless, this should not be accepted as a limitation for use of US as a first step in the algorithm of patients with abdominal pathologies.

Periportal lymphadenopathy may accompany the infection; this finding was first reported by Kabaloğlu and colleagues (13). Multiple, small, indistinct, hypodense lesions ranging from 2 to 10 mm in diameter, microabscesses arranged in a tunnel-like, branching pattern and frequent subcapsular locations of the lesions are the most commonly seen abnormalities on CT scan of these patients. Frequently, liver capsular thickening, subcapsular hemorrhage and abscess-like lesions up to 7 to 10 cm in diameter may also be present (19, 20). In some patients, CT scan of the abdomen may be normal and no abnormal finding is seen in diagnostic exams (9). Subcapsular low-attenuated lesion surrounded by thick rim of enhanced parenchyma is a different and unpublished imaging feature of *F. hepatica* infection (Figure 3). Magnetic resonance (MR) reveals similar findings with CT associated with iso- or hypointense lesions on T1-weighted and isointense or hyperintense lesions with surrounding hyperintensity on T2-weighted images. MR imaging demonstrates various suggestive changes associated with traumatic hepatitis caused by the migration of the worm in the liver (13, 21). None of our patients underwent MR imaging because CT was suggestive and supportive for the diagnosis of fascioliasis. In our series, most of the patients were in hepatic stage which made CT more valuable in diagnosis.

Diagnosis may be delayed because of the wide spectrum of the differential diagnosis and low incidence of the *F. hepatica* infection. Similar abnormal US and CT findings may represent viral hepatitis, liver abscess, malignancy, cholecystitis, sclerosing cholangitis and AIDS-related cholangitis, ruptured hydatid cyst and parasites such as ascariasis and clonorchiasis (22-25). Though diverse, all patients had abnormalities on abdominal to-

mography similar to those previously reported. Except for the first patient, the diagnosis of *F. hepatica* infection was considered at first sight for the remainder of the patients. Patient 1 had one isolated lesion so biopsy was performed in order to differentiate the lesion, but it was consistent with inflammation.

Though liver biopsy is not usually indicated, classical findings of the biopsy specimens include necrotic debris, track-like destruction of parenchyma, polymorphonuclear leukocyte (PMNL) infiltration with abundant eosinophils, Charcot-Leyden crystals, granulomas with or without eggs, fibrosis and bile duct proliferation (26). Inflammation with PMNL was demonstrated in the biopsy specimen of our three patients. Demonstration of granulomas or eggs was not possible. Invasive techniques such as percutaneous cholangiography and ERCP show abnormalities especially in the biliary stage, but they are prerequisite for diagnosis (27, 28). ERCP was performed in two of our patients in the hepatic phase but neither of the patients had abnormality in the biliary tract.

Although the Centers for Disease Control and Prevention recommends triclabendazole as the first-line agent for the treatment of *F. hepatica*, bithionol is an alternative drug for *F. hepatica*. We used bithionol because it was readily available in our clinic compared to triclabendazole. It is reported to be highly effective but frequent side effects such as nausea, vomiting, pruritus, urticaria, abdominal colic and rash are the disadvantages (29-34). One of our patients refused therapy, but nine received bithionol as therapy. Six of them responded both

clinically and radiologically; two patients unfortunately lost contact with the clinic. One patient did not respond to bithionol therapy so triclabendazole was administered. His therapy has just been completed and he is being followed by our clinic.

The patient with HIV infection was being followed for tuberculosis. Individuals with HIV-induced immune suppression appear to be particularly susceptible to *Mycobacterium tuberculosis* infection even at moderate stages of viral infection. This patient was compliant neither with his tuberculosis nor antiretroviral therapy. CT was performed due to increase in abdominal pain and fascioliasis was incidentally discovered. Serology confirmed the diagnosis. To our knowledge, this is the first patient to have these three infections concomitantly.

The possible delay in diagnosing a patient with fascioliasis is due to the lack of appropriate consideration of this possibility, especially in western countries (35). Contaminated water and water plants are the potential sources of *F. hepatica* infection. Although today's world has become more civilized, parasitic infections are still a threat. Serological tests for parasites are less frequently used compared to stool examinations. If a patient presents with abdominal pain and fever, and if elevated liver enzymes along with eosinophilia accompany hypodense lesions with irregular margins at tomography, serology for *F. hepatica* will not be an effort in vain even in the presence of just a single symptom or sign. It must be immediately done before more invasive approaches in order to distinguish fascioliasis from other causes.

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