



# The clinical characteristics of fascioliasis in pediatric patients

Çocukluk çağı fasioliyaz olgularımızın klinik özellikleri

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## The known about this topic

Fascioliasis is a trematode flatworm infection caused by *Fasciola hepatica* and *F. gigantica*. *Fasciola hepatica* is mesoendemic in Turkey.

## Contribution of the study

Our study showed that the patients' dietary habits, eosinophilia, and markedly elevated IgE levels may be significant predictors for the physicians to suspect fascioliasis.

## Abstract

Fascioliasis is a trematode flatworm infection caused by *Fasciola hepatica* and *F. gigantica*. *Fasciola hepatica* is mesoendemic in Turkey. Six cases of pediatric fascioliasis are presented here. All patients had histories of consumption of various raw vegetables. Four of our patients were at the hepatic phase, and two were at the biliary phase. Except for one patient, all patients had eosinophilia. In three patients, total IgE levels were markedly increased. In these patients, there was an eosinophilic leukomoid reaction accompanied by a high total IgE level. Except for one of our patients, all patients had positive indirect hemagglutination tests. This patient was diagnosed as having fascioliasis with a compatible clinical picture. Except one, all of our patients were completely treated with a single-treatment regimen of triclabendazole; one patient needed re-administration. Only in patient 1, liver enzymes increased after triclabendazole administration because he had taken the medication for longer than prescribed by mistake. The elevation of liver enzymes was not observed in the other patients who received the correct dose. All patients recovered completely with triclabendazole treatment. The patients' dietary habits, eosinophilia, and markedly elevated IgE levels may be significant predictors for physicians to suspect fascioliasis.

**Keywords:** Child, eosinophilia, *Fasciola hepatica*, triclabendazole

## Öz

Fasioliyaz *Fasciola hepatica* ve *F. gigantica*'nın neden olduğu bir trematod enfeksiyonudur. *Fasciola hepatica* Türkiye'de mezoendemiktir. Burada altı çocuk fasioliyaz hastası sunuldu. Dört olgu hepatik fazda, iki olgu biliyer fazdaydı. Tüm hastalarda çeşitli çiğ sebzelerin tüketimi öyküsü vardı. Bir hasta dışında tüm hastalarda eozinofili saptandı. Üç hastada total IgE düzeyi belirgin şekilde yüksek bulundu. Bu hastalarda total IgE düzeyi yüksekliğine eşlik eden eozinofilik lökomoid reaksiyon vardı. Bir hasta dışında tüm hastalarda indirekt hemagglütinasyon testi pozitif, bu testin negatif bulunduğu hastaya fasioliyaz tanısı uyumlu klinik bulgular ile konuldu. Bir hasta dışında tüm hastalar tek kür triklabendazol tedavisi ile iyileşti. Bir hastada ikinci kür triklabendazol tedavisi gerekti. Triklabendazol tedavisini önerilenden uzun kullanan bir hastada karaciğer enzimlerinde yükselme gözlemlendi. Bu hasta dışında hiçbir hastada triklabendazole bağlı karaciğer enzimlerinde yükselme saptanmadı. Tüm hastalarımız triklabendazol tedavisi ile tam olarak iyileşti. Sonuç olarak hastaların beslenme alışkanlıkları, eozinofili ve belirgin olarak yükselmiş IgE düzeyleri fasioliyazdan şüphelendirici önemli belirteçlerdir.

**Anahtar sözcükler:** Çocuk, eozinofili, *Fasciola hepatica*, triklabendazol

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## Introduction

Fascioliasis is a trematode flatworm infection caused by *Fasciola hepatica* and less commonly by *F. gigantica*. In-

fections have been reported from all continents, except Antarctica. In Van Province in Turkey, the seroprevalence of fascioliasis was previously reported as 5.6%, comparable to that reported in other regions of Turkey (1). Fasci-

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oliasis, like other trematode infections, may present with few or no symptoms. There are a few reported pediatric fascioliasis cases in the literature. Herein, we report our pediatric fascioliasis cases.

**Cases**

We review pediatric patients with confirmed fascioliasis in Yuzuncu Yil University Medical Faculty in Van Province, located in the Eastern region of Turkey. Six pediatric patients were diagnosed as having fascioliasis between March 1<sup>st</sup>, 2014, and April 30<sup>th</sup>, 2016. Fascioliasis was diagnosed a) if eggs were detected in the stool with the patients’ clinical symptoms and signs being compatible with fascioliasis, and/or b) using *Fasciola* spp. indirect hemagglutination test (IHA) (titer: 1/160) with the patients’ clinical symptoms and signs being compatible with fascioliasis. Patients were treated with triclabendazole (10 mg/kg per day for one or two days). All patients were scheduled for a follow-up visit after treatment completion; the first scheduled visit was one week after treatment, and subsequent follow-up visits were scheduled monthly thereafter. Complete blood count and liver enzyme tests were performed during each follow-up visit. Demographic data, epidemiologic history, physical examination findings, laboratory test results, duration of follow-up, and treatment outcomes were recorded in all patients included in the study. Informed consent was obtained from all patients.

There were six pediatric patients with fascioliasis (age range, 4–16 years; mean age, 10.16 years). The patients’ clinical, laboratory, and imaging findings are summarized in Tables 1 and 2. Some important matters not mentioned in the tables are reported here.

Patient 1 had taken triclabendazole for longer than prescribed by mistake. He should have taken it for two days but he continued the medication for four days. Four days after treatment completion, liver enzyme levels increased and bilirubin was normal. During follow-up, liver enzyme levels gradually normalized.

Patient 2 was diagnosed as having biliary fascioliasis and was administered triclabendazole. After one week, the patient presented to our hospital with severe abdominal pain. A physical examination revealed Murphy’s sign, consistent with the diagnosis of acute cholecystitis. Abdominal ultrasonography (US) showed a hydropic gall bladder and dilated intra- and extrahepatic bile ducts, whereas before treatment, his abdominal US showed a distended gall bladder with very dense content but no hydrops and no intra- or extrahepatic bile duct dilatation. The patient was hospitalized

**Table 1. Pediatric fascioliasis patients’ clinical characteristics, test results, treatment, and its adverse effects (Van, 2014-16)**

Patient	Age/sex	Symptoms	Dietary history	Fasciola IHA <sup>a</sup>	Stool examination	Abdominal imaging findings	Chest X-ray	Treatment (dosage/duration)
1	11/M	Abdominal pain	Raw plant	Negative	Negative	Choledoch duct wall thickening and mobile parasites in gallbladder	Normal	Triclabendazole 10 mg/day, 4 days
2	16/M	Abdominal pain	Raw plant	1/2560	Positive	Distention in the gallbladder, dense content in gallbladder	Normal	Triclabendazole 10 mg/day, 1 day
3	16/M	Arthralgia	Raw plant	1/320	Negative	Hepatosplenomegaly	Loeffler’s syndrome	Triclabendazole 10 mg/day, 2 days
4	9/F	Abdominal pain	Raw plant	1/320	Negative	Multiple geographically hypoechoic areas in the liver. The largest one is 34 mm in diameter. Lymphadenopathy in the portal hilus, bile duct dilated, oval lesion (8x4 mm in gallbladder lumen)	Normal	Triclabendazole 10 mg/day, 2 days
5	5/M	Abdominal pain	Raw plant	1/640	Negative	Hepatomegaly, liver parenchyma heterogeneity	Normal	Triclabendazole 10 mg/day, 1 day
6	4/M	Abdominal pain, fever, poor appetite	Water-cress	1/640	Negative	Geographically hypoechoic areas in the liver	Loeffler’s syndrome	Triclabendazole 10 mg/day, 2 days

<sup>a</sup>Cut-off: 1/160

**Table 2. Laboratory findings of the pediatric patients with fascioliasis (Van, 2014-16)**

Patient	At admission						One month after treatment						
	Hgb	WBC	AEC	PLT	AST/ALT	T. bil	Total IgE	CRP	ESR	WBC	MEC	AST/ALT	Total IgE
1	12	6800	680	258.000	96/65	0.29		54	25	5900	2.360	30/15	254
2	14	12.100	0	175.000	249/184	2.1	17	3.4	5	7300	1.200	18/8	
3	10.5	57.600	44.300	438.000	32/15	0.5	2800	3.3	32	9700	970	23/11	1.170
4	11.8	12.600	4280	334.000	25/15	0.26	380	8.1	25	9900	990	26/11	228
5	12.7	38.000	19.760	417.000	40/33	0.46	2540	22.5		11.100	555	28/13	755
6	11.9	40.300	6045	362.000	25/16	0.4	1110	35	14	12.900		37/30	

Normal values: Hgb (Hemoglobin): 11–18 g/dL, WBC (White blood cell count): 4–11×10<sup>3</sup>/mL, AEC (Absolute eosinophil count): 0–500/mL, PLT (Platelet count): 150–400×10<sup>3</sup>/mL, AST/ALT (Aspartate aminotransferase/alanine aminotransferase): 0–37 U/L /0–41 U/L, T. bil (Total bilirubin): (0.2–1.2 mg/dL), CRP (C-reactive protein): 0–5 mg/L, ESR (Erythrocyte sedimentation rate): 0–20 mm/hour



**Figure 1.** A thoracic computed tomography (CT) showed multiple, peripherally localized nodular lesions, with surrounding ground-glass opacity or halo in the superior lobes of both lungs, indicating Löeffler's syndrome

and hydrated for three days. His abdominal pain gradually resolved completely. Ten days later, a follow-up abdominal US was performed, and the findings were normal.

Patient 3 presented with arthralgia. He had a 10-day history of shoulder, knee, and back pain. He denied having

a cough, sputum or dyspnea. He had severe eosinophilia. A chest X-ray showed perihilar and pericardial interstitial infiltration in both lungs. Thoracic computed tomography (CT) imaging showed multiple, peripherally localized nodular lesions, with surrounding ground-glass opacity or halo in the superior lobes of both lungs, indicating Löeffler's syndrome (Fig. 1).

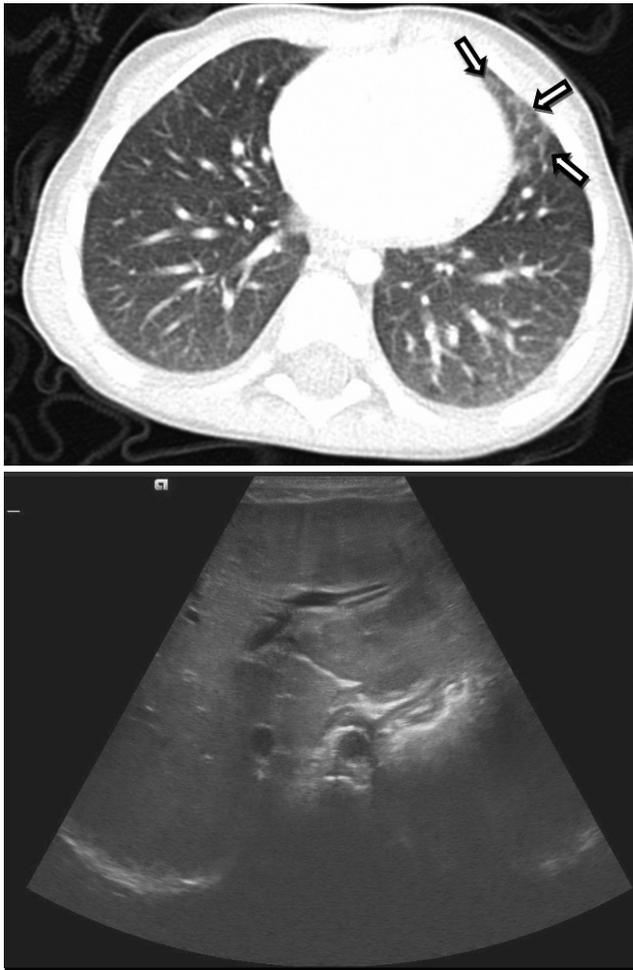
Patient 4 was referred to our hospital with a preliminary diagnosis of an abdominal mass. Ultrasonography (US) indicated a higher possibility of *F. hepatica* than of mass lesions. The patient underwent liver biopsy, and a pathologic examination of the specimen revealed severe mixed inflammatory infiltrates of eosinophils and lymphocytes and necrotic foci surrounded by histiocytes. Triclabendazole was administered for two days. Follow-up US performed three months later revealed that the hepatic mass lesion had become significantly smaller but remained in residual quantities. After the second triclabendazole treatment, the residual lesion completely disappeared.

Patient 5 presented with abdominal pain for one week. He was diagnosed as having hepatic fascioliasis and was administered triclabendazole.

Patient 6 presented with abdominal pain, poor appetite, and fever. The patient's abdominal pain was very disturbing and woke him up at night. He had hepatic fascioliasis accompanied by Löeffler's syndrome (Fig. 2).

## Discussion

*Fasciola* genus includes species of liver flukes that live inside the bile ducts of sheep, cattle, buffalo, goat, donkey, horse, and rabbit, and *Fasciola* spp. eggs get scattered to the environment by these animals' stools. Fascioliasis is transmitted to humans through the consumption of raw plants contaminated with metacercariae. Typically, un-



**Figure 2. Loeffler's syndrome**

cooked aquatic plants are reportedly responsible for fascioliasis transmission, particularly watercress. However, several terrestrial plants have also been reported to cause transmission of fascioliasis. Other reported foods are lettuce, alfalfa, spinach, spearmint, arugula, leek, and several other green leafy plants that typically grow near infected animals (2). These plants grow near the water channels or need frequent irrigation before they can be sold; thus, they can be contaminated by the metacercariae-carrying water used for irrigation. Drinking contaminated fresh water from streams is another risk factor (2). Van is a province where livestock is very common, particularly sheep and cattle. Here, people traditionally collect various herbs from the paddies in the spring and eat them. Owing to animal husbandry and the consumption of organic plants being common in Van Province, there is a prevalent risk for fascioliasis transmission to humans. One of our patients had a history of watercress consumption, other patients reported that they consumed various raw vegetables.

Early diagnosis of fascioliasis is difficult because of the biphasic nature and long latency period of the disease.

Four of our patients were at the hepatic phase, and two were at the biliary phase. Abdominal pain is the most common symptom in the course of fascioliasis; other frequently seen symptoms include fever, appetite loss, weight loss, fatigue, myalgia, and arthralgia (1, 4). Compatible with the currently available literature, the most common presentation and the chief symptom in our patients was abdominal pain. At the biliary phase, eggs can generally be detected in the stool of patients; however, in both our patients at the biliary phase, stool did not contain *Fasciola* spp. eggs. If the infection load is low, fewer eggs are released in the stool. Also, in the biliary phase, eggs can be absent in the stool because the fluke has not adapted to the host and has thus not begun the reproduction cycle at this stage (5).

Parasitic infection is the most common cause of eosinophilia and can also induce an eosinophilic leukemoid reaction. The normal mean peripheral blood eosinophil count is 500 cells/ $\mu$ L, and eosinophilia is defined as mild (500–1500 cells/ $\mu$ L), moderate (1500–5000 cells/ $\mu$ L), and severe (>5000 cells/ $\mu$ L). If the white blood cell (WBC) count is >30.000/ $\text{mm}^3$ , with >30% eosinophils, this situation is defined as an eosinophilic leukemoid reaction, which can lead the patient to undergoing unnecessary bone marrow aspiration (6). Eosinophilia is a common laboratory finding in fascioliasis that occurs most commonly during the migratory phase of the parasites and was reported in 70.8–89.9% of all fascioliasis cases (1, 6). All our patients, except one who had biliary fascioliasis, had eosinophilia, and three had eosinophilic leukemoid reactions. Patients with eosinophilia have to be carefully investigated for fascioliasis because it presents with non-specific symptoms.

Elevation of liver enzymes levels may occur in the course of fascioliasis (4). In two of our cases, liver enzymes were elevated at presentation. Both these cases were of biliary fascioliasis. IgE levels are usually elevated in fascioliasis. It was reported that IgE levels were positively correlated with the egg load and clinical condition (7). Three of our patients with hepatic fascioliasis co-occurring with eosinophilic leukemoid reactions also had significantly increased total IgE levels. Like eosinophilia, a significantly high IgE level without an underlying allergic disease may also make the physician suspect fascioliasis.

The diagnosis of fascioliasis is usually confirmed in serologic tests such as IHA and enzyme-linked immunosorbent assay (ELISA). Except one of our patients (patient 1), all of the other patients had positive IHA. Patient 1 was diagnosed as having fascioliasis with a compatible clinical picture. The predictive values of the serologic tests for

diagnosing fascioliasis are quite high, even though they may give false-positive results due to light infections (8). A pathologic examination is generally not necessary for diagnosis. Pathologic features of hepatic fascioliasis include cellular infiltration comprising eosinophils, macrophages, lymphocytes, and fibrous tissue, and sometimes *F. hepatica* egg granulomas (9). One of our patients underwent a pathologic examination because of the suspicion of a mass in the liver.

Cholangitis and cholecystitis can primarily develop because of the intermittent obstruction of the biliary system and the resulting inflammatory response owing to the *Fasciola* spp. invasion (2). These conditions can also develop after triclabendazole treatment, as in patient 2. Biliary colic is the most common adverse effect of triclabendazole, which is reportedly related to the expulsion of dead or damaged parasites induced by the drug. Liver enzymes increased after triclabendazole administration only in patient 1 because he had taken the medication for longer than prescribed by mistake. Elevated liver enzymes were not observed in the other patients who received the correct dose. Triclabendazole resistance was reported in the literature (10). Except one, all our patients were completely treated with a single-treatment regimen of triclabendazole; one patient needed re-administration. No resistance to triclabendazole was observed.

Fascioliasis may present with non-specific symptoms; however, the most common symptom is abdominal pain. The patients' dietary habits, eosinophilia, and markedly elevated IgE levels may be significant predictors for physicians to suspect fascioliasis.

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