Human Fascioliasis: A Re-emerging Disease in Upper Egypt

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Abstract. In recent years, the number of humans infected with *Fasciola* has risen rapidly. Diagnosis is based mainly on detection of eggs in stool analysis. The rate of infection in Egypt is unknown. In this retrospective study, we describe 23 cases of hepatic fascioliasis, and only 2 of these cases showed eggs in stools. The symptoms of infection, such as pyrexia of unknown origin, epigastric pain, and abdominal distension, were suggestive. Imaging techniques, including abdominal ultrasonography and computed tomography, were very helpful in detecting hepatic changes. An indirect hemagglutination assay proved to be of value for diagnosis. Treatment using a 2-day triclabendazole regimen cured the infection and signs of hepatic involvement disappeared. Combining both imaging techniques and laboratory tests is essential for diagnosis of fascioliasis in the early stage.

INTRODUCTION

Fascioliasis is a food-borne zoonotic disease caused by digenetic trematode of the genus *Fasciola*. The number of human cases increased significantly in the last decade, with an estimated number of the infected population ranging from 2,400,000 to 17,000,000 worldwide.¹ In Egypt, intermediate hybrid forms exist together with *Fasciola hepatica* and *F. gigantica*.² The wide range of egg-size variability makes it difficult to determine species from eggs found in stool analysis.^{3,4} Fascioliasis has been endemic in certain villages in the Nile Delta, but overall prevalence in Egypt is unknown because reports show wide variations in infection rates.⁵

Infection occurs through ingestion of encysted metacercariae that contaminate water or food. The clinical manifestations range from asymptomatic to fever, mild hepatomegaly, or cholangitis, which depend on worm burden. Chronic cases can be discovered accidentally.^{1,6} Unusual clinical manifestations are common as *Fasciola* can be found to be ectopic in the spine, pancreas, kidney, and spleen.^{7,8} Diagnosis depends mainly on finding eggs in stool analysis, but other serological and imaging techniques are also of great value. Computed tomography (CT) can detect microabscesses caused by worms tunneling liver tissues, which is important in follow-up.^{6,9} The drug of choice is triclabendazole at a single dose of 10 mg/kg body weight for 2 days.¹⁰

The clinical presentation of human fascioliasis infection is unusual, ranging from asymptomatic cases to cholangitis, hepatitis, and hepatic focal lesions (HFLs). The real burden of the problem in Egypt is not fully understood. Therefore, herein, we present 23 cases of individuals who were diagnosed with hepatic fascioliasis and were presented at Assiut University Hospital with variable symptoms.

PATIENTS AND METHODS

During the period from March 2012 to December 2013, we were retrospectively able to recruit 23 cases diagnosed to have hepatic fascioliasis among inpatients of the Assiut University Hospitals. Patients were admitted with varying complaints

and all of them were subjected to routine investigations, including complete blood count and peripheral blood film examination, liver and kidney function tests, abdominal ultrasonographic (US) examination, and routine stool examination to exclude parasitic infection.

Further investigations were conducted for cases following the clinical picture, and results of the routine investigations include:

1. Indirect hemagglutination assay (IHA) using Distomatose Fumouze (Laboratoires Fumouze Diagnostic, Levallois Perret, France). A titer of 1/320 or more was considered to be positive according to the manufacturer's instructions.
2. Abdominal CT scan.
3. Endoscopic retrograde cholangiopancreatography (ERCP).

All patients were given two doses of triclabendazole at a dose of 10 mg/kg body weight/day. Patients were clinically followed up with for at least 3 months. Stool analysis, abdominal US and/or CT, and serology were used according to each case's needs.

This study was approved by our Institutional Review Board and ethical committee.

RESULTS

Twenty-three patients (14 males; mean age: 21.2 ± 10.6 years) were diagnosed to have hepatic fascioliasis among inpatients of the Assiut University Hospitals. All patients presented with clinical symptoms, except for two who had HFLs on routine abdominal US. The main complaint was pyrexia of unknown origin (PUO) for more than 1 month ($N = 10$), followed by distended abdomen ($N = 4$), epigastric pain ($N = 4$), and jaundice ($N = 3$). Nineteen patients came from rural areas and had farm animals at their residences (data shown in Table 1).

Routine stool analysis revealed operculated eggs of genus *Fasciola* in two cases (Figure 1A and B), while the remaining cases were negative when tested for any intestinal parasites. Routine complete blood count showed absolute eosinophilia ranging between 30% and 70% in all patients. Such high eosinophilia was a milestone to suspect parasitic infection. A routine liver function test detected elevated transaminases in all cases and elevated total bilirubin in 15 cases.

Abdominal US examination revealed just ascites in 7 cases, HFLs in 10 cases (3 of which also had ascites), dilated common bile duct (CBD) in 3 cases, and gall bladder stones in 2 cases.

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TABLE 1
Clinical and demographic data of patients recruited in this study showing the main complaint and percentage of eosinophilia

	Sex	Age	Residency	City/Governorate	Farm animals	Main complaint	Absolute eosinophilia (%)
1	Female	5	Rural	Manfalut/Assiut	Yes	Distended abdomen	70
2	Male	4	Rural	Manfalut/Assiut	Yes	Distended abdomen	55
3	Male	10	Rural	Manfalut/Assiut	Yes	Prolonged fever	45
4	Male	6	Rural	Dayr Mawas/Minya	Yes	Prolonged fever	70
5	Female	11	Rural	Mallawi/Minya	Yes	Distended abdomen	30
6	Male	12	Rural	Dayrout/Assiut	Yes	Prolonged fever	70
7	Male	14	Rural	Manfalut/Assiut	Yes	Jaundice	50
8	Male	16	Rural	Mallawi/Minya	Yes	Jaundice	55
9	Male	19	Urban	Sohag/Sohag	No	No symptoms	40
10	Female	19	Urban	Assiut/Assiut	No	Epigastric pain	40
11	Male	20	Rural	Dayrout/Assiut	Yes	Epigastric pain	50
12	Male	22	Rural	Edfu/Aswan	Yes	No symptoms	70
13	Female	22	Rural	Dayr Mawas/Minya	Yes	Prolonged fever	70
14	Female	23	Rural	Esna/Qena	Yes	Prolonged fever	30
15	Male	24	Rural	Dayrout/Assiut	Yes	Prolonged fever	50
16	Male	27	Rural	Edfu/Aswan	Yes	Jaundice	60
17	Female	29	Rural	Manfalut/Assiut	Yes	Prolonged fever	55
18	Male	30	Rural	Manfalut/Assiut	Yes	Epigastric pain	30
19	Male	31	Rural	Mallawi/Minya	Yes	Distended abdomen	45
20	Male	33	Rural	Manfalut/Assiut	Yes	Epigastric pain	30
21	Female	34	Rural	Dayr Mawas/Minya	Yes	Prolonged fever	70
22	Female	39	Urban	Assiut/Assiut	No	Prolonged fever	55
23	Female	39	Urban	Assiut/Assiut	No	Prolonged fever	35

All cases with HFL underwent an abdominal CT scan and in three cases liver biopsy was taken from the lesion. CT revealed multiple hypodense HFL suggestive of liver abscess (Figure 2A). Histopathological examination of biopsy tissue revealed necrotic tissue in one case and eosinophilic liver abscess in two cases. ERCP was performed in three cases with dilated CBD, and necrotic remains of worms were extracted (data shown in Table 2).

All patients received two doses of triclabendazole at a dose of 10 mg/kg body weight/day. Those who had HFL with ascites were given a low dose of cortisone (15 mg/day) for 2 weeks. Follow-up at 1-month interval was conducted using clinical examination, abdominal US, abdominal CT (for those who had HFL), and serology using IHA to measure antibodies titer. All patients showed signs of disease regression with no ova detectable in stool analysis and healing of HFL as shown in CT (Figure 2B). However, two patients maintained the same antibody titer 3 months after treatment.

It is noteworthy that one female patient developed severe hypotension and cyanosis 1 hour post-CT-guided liver biopsy, a picture similar to anaphylactic shock, and she was admitted

to the intensive care unit until she regained normal blood pressure and blood oxygen tension.

DISCUSSION

Cases of human fascioliasis are increasing worldwide, making it an emerging threat to humans. *Fasciola* has previously existed in Egypt, and human cases are increasing with endemic areas in the Nile Delta.^{1,5} The overall prevalence is unknown as only limited-size data samples are available. Soliman⁵ assumes that the prevalence of *Fasciola* is approximately 3% among humans. This presumption is based on a survey of 3,000 children in an endemic village in the Nile Delta where 3% were found to be infected. Such data are opposed by the fact that overall rates of *Fasciola* infection in animals slaughtered in slaughterhouses in Egypt were 2.02% for sheep and goats, 3.54% for cattle, and 1.58% for buffaloes, as stated by the same author. Moreover, a recent study in the Minia district, Upper Egypt, showed that *Fasciola* species eggs were not detected in both immunocompromised and immune-competent children in that study.¹¹

FIGURE 1. *Fasciola* eggs seen in two cases under $\times 40$ objective lens. Size variation makes it hard to diagnose the exact species especially in areas where both *Fasciola gigantica* and *F. hepatica* coexist (A and B).

FIGURE 2. (A) Abdominal computed tomography (CT) image of a 29-year-old female, shows multiple heterogeneous hepatic focal lesions “arrows,” and mild ascites (before treatment). A picture suggestive of hepatic abscess. (B) Abdominal CT scan of the same patient after 3 months from receiving treatment.

This outcome is consistent with our findings. Although we report an increasing number of cases admitted to Assiut University Hospitals (23 cases in 21 months: 11 cases in 2012 and 12 cases in 2013) while we used to see one or two isolated cases per year. The number of cases is still low per the total population of Upper Egypt, where Assiut University is located. Although Soliman⁵ cite higher rates of fascioliasis in animals by the Ministry of Agriculture, we tend not to accept those numbers that depend on veterinary convoys for which only sick animals are presented. In Assiut, a study of slaughterhouses all over the governorate state that the infection rates were 1.2% for sheep, 0.5% for goats, 5.3% for cattle, and 3.5% for buffaloes.¹² In a more recent study in 2008, a limited sample number of slaughtered goats in Assiut revealed infection rate of 3.5% for fascioliasis.¹³

The infection rate was higher among males than females, adults than children, and those who came from rural areas and had farm animals than those from urban areas with no farm animals. The higher prevalence in adults can be explained through the pattern of age distribution among nonendemic areas.¹⁴ Higher infection rates among males may be explained by lifestyle factors as men are usually responsible for feeding animals and working in the fields in rural areas in Upper Egypt. The presence of *Fasciola* as an endemic parasite in the Nile Delta may be due to the fact that the lymnaeid snail lives in slow or shallow water habitats, which are more common in the Nile Delta than in Upper Egypt. The infection rate of fascioliasis ranged from 5.2% to 19% in an endemic area in the Nile Delta, such infection rate was comparable to *Schistosoma mansoni*.^{15,16} This result supports the theory of snail habitat compatibility in the Nile Delta, where rice fields

and slow canals are common. In addition, the low infection rate of *S. mansoni* in Upper Egypt supports the comparably low fascioliasis infection rate finding.^{17,18} As infection is due to ingestion of metacercariae contaminating water or vegetables, the recent increase of the number of cases in Upper Egypt may be due to political instabilities that have occurred since January 2011, which may have affected the snail control programs of the Ministry of Health. The increase could also be due to the use of partially processed sewage water, intended to grow trees used for wood and not meant to plant vegetables for irrigation.

Although finding an egg in stool analysis is the main diagnostic test for fascioliasis,⁴ eggs were detected in only two cases in this study. This outcome may be due to the fact that diagnosis occurred in the hepatic phase, where an immature worm feeds on liver tissue with no egg production as all cases had eosinophilia and HFL, which are observed in early infection.⁶ It also can be an indicator that *Fasciola* is not yet an endemic disease for humans in Upper Egypt as the immune systems react strongly to the parasites giving rise to severe symptoms. While in endemic areas, immune system tends to be exposed to parasite antigens through whole life leading to moderate immune reaction. This phenomenon was seen in U.S. soldiers who were in filariasis endemic areas, they tend to show lymphadenitis and microfilariae were detected in rare cases.¹⁹ HFL, found in 10 cases, was detected in both abdominal US and abdominal CT and had a picture suggestive of liver abscess. This outcome is consistent with the previous studies finding that during the early infection phase, immature worms dig through liver parenchyma forming minute cavities, which mainly come from tissue necrosis, unlike a pyogenic abscess where a single large cavity is observed.^{9,20} Histopathology of biopsies revealed necrosis with eosinophilic infiltrations. Thus, imaging could be quite useful for screening and suspecting cases in nonendemic regions.

Indirect hemagglutination test (IHA) was very helpful in diagnosing cases, and it can be used for follow-up to detect the falling titer of antibodies after treatment. Human fascioliasis should not be ignored, unless IHA or more specific enzyme-linked immunosorbent assay of *Fasciola hepatica* cysteine proteinase antigen 2 (ELISA Fas2) is performed.

In conclusion, human fascioliasis should be suspected in patients who exhibit fever, eosinophilia, and hepatic infiltrates.

TABLE 2

Imaging findings using abdominal ultrasonographic (US) examination and or abdominal computed tomography (CT) scan

Imaging findings (US and/or CT)	Frequency (%)
Normal	1 (4.3)
HFLs	7 (30.4)
Dilated CBD	3 (13)
Ascites	7 (30.4)
GB stones	3 (13)
HFL with ascites	7 (30.4)

CBD = common bile duct; HFL = hepatic focal lesion; GB = gallbladder.

Physicians also need to become familiar with this presentation, especially, in areas where *Fasciola* is common. The rising number of cases in Upper Egypt should be alarming and call for more work on studying the snail infection rate and snail control programs to avoid an epidemic of fascioliasis or appearance of new endemic foci in this locality.

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