Human Fascioliasis: Clinical Features and Diagnostic Difficulties in Egyptian Children

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Summary

Human fascioliasis (HF) has been reported in children worldwide and occasionally from Egypt. In the past 7 years we diagnosed 16 children aged 3.5-11 years (mean age: 6.5 years), 13 of them were boys, as HF. They were referred to Cairo University, Paediatric Hospital (CUPH), with pyrexia of undetermined origin (PUO) and abdominal pain. Diagnosis was based on high peripheral blood eosinophilia (14-82 per cent) in all patients along with *Fasciola hepatica* egg detection on direct stool smear in three or stool concentration in four, antibody detection by indirect haemagglutination test (IHAT) in seven egg-negative patients and ultrasonographic detection of hepatic and/or biliary lesions of HF in two egg-negative patients. Percutaneous liver biopsy confirmed the diagnosis of an eosinophilic abscess (parasitic granuloma) in 12 of 13 patients. Therefore, HF does occur in Egyptian children and its diagnosis needs a high index of suspicion supported by stool microscopy, serology, imaging procedures, and probably liver biopsy.

Introduction

*Fasciola hepatica* is a liver trematode of sheep and other herbivorous mammals. It accidentally infects humans if they ingest fresh vegetables as wild watercress washed in water contaminated by metacercaria. This invading larval stage penetrates the intestines, circulates in the body, and settles by an unexplained hepatotropic mechanism in the liver and biliary radicles, where the hermaphrodite fluke matures and starts oviposition. Two stages of human fascioliasis (HF) have been distinguished: an acute phase which coincides with hepatic invasion by the larva and a chronic phase caused by persistence of the adult fluke in the bile ducts.

Reports of HF are cosmopolitan. They have dramatically increased worldwide in the past few years, and show that HF is becoming an increasingly clinical and epidemiological problem in many provinces in Egypt as well. However, the clinical features and diagnostic criteria of this parasitosis in Egyptian children is not yet sufficiently reported. Herein, we wish to report our experience with HF at the largest paediatric tertiary referral centre in Egypt: Cairo University Paediatric Hospital (CUPH) in a 7-year period (1989-1995).

Patients and Methods

From January 1989 to December 1995, 16 children referred to us at the Hepatology Unit of CUPH with 'obscure liver disease' were suspected of having HF. All had pyrexia of undetermined origin (PUO) for 1 month or more before referral, right upper abdominal pain, tender liver, raised erythrocyte sedimentation rate (ESR), and high peripheral blood eosinophilia.

They were all thoroughly investigated by:

1. interrogation and physical examination;
2. direct stool microscopy for ova and parasites, then concentration over 3 days using the Katz-Kato technique of egg count;
3. complete blood count;
4. ESR;
5. standard biochemical liver function tests (LFT's), including serum bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP), prothrombin time, total serum proteins, and serum albumin;
6. immunodiagnosis of *F. hepatica* antibodies by indirect haemagglutination test (IHAT) using the Diastomiasis Fumouze Kit, Laboratories Fumouze, France;
7. real time abdominal ultrasonographic scanning using a Toshiba 2000 Sonolayer® scanner (3.5 and 5 MHz linear transducers) searching for hepatic and/or biliary fascioliasis as described by Van Beers et al.;
8. abdominal computed tomography (CT) was performed in two patients before referral to us;
9. percutaneous liver biopsy using a disposable modified Menghini suction needle (Surecut®) was performed in 13 patients to settle the diagnosis of this 'obscure liver disease';
10. in patients with ascites, diagnostic tapping was performed.

Results

Over this 7-year period, 16 children aged 3.5-11 years...
(mean age of 6.5 years), were confirmed to have HF, 13 of them were boys. One patient was diagnosed yearly in the first 4 years, then two patients per year for 2 years, and in the last year, eight more were discovered. Five patients were referred from Menofia Governorate, four from Embaba (Giza), three from Cairo, while the rest were from three different provinces in Northern Egypt. All parents admitted ingestion of fresh vegetables washed in potentially contaminated water on several occasions. The presenting symptoms (Table 1) were fever (for 1–20 months) and abdominal pain in all, associated with abdominal distention in five, and a history of jaundice in two. On physical examination, all looked pale and ‘toxic’, but none was icteric. Fourteen had tender hepatomegaly and two had normal-sized, tender liver. The main laboratory investigations are summarized in Table 2.

Fasciola hepatica ova were demonstrated by direct stool microscopy in three patients and by repeat smears in four more, while nine patients had no ova in stools. ESR was significantly raised to >48 mm/h in 12 tested patients and reached a peak of 154. Moderate to severe anaemia with a haemoglobin of 48–96 g/l was present in 12 patients. Peripheral blood eosinophilia of 14–82 per cent with absolute count of $0.58 \times 10^9 - 40.80 \times 10^9/l$ was present in all. One boy with massive ascites had an ascitic fluid eosinophilic count of $0.55 \times 10^9/l$. LFT’s revealed normal serum bilirubin, AST, ALT, and prothrombin time in all, while 12/12 tested had consistently raised AP, and three had serum albumin less than 23 g/l at the time they developed massive transient ascites. IHAT titre of 1:640–1:2,560 was present in all 10 tested patients. Table 3 shows the abdominal ultrasonographic findings in 15 patients. Out of five with hepatobiliary fascioliasis, three were thought to have focal lesions or ‘nodular’ liver; two of them had had an abdominal CT scan before referral to us which showed hypodense, non-enhancing multiple nodules.

![Figure 1](https://example.com/fig1.jpg)

**Fig. 1.** High power view showing eosinophilic abscess with large number of eosinophils and foreign body giant cell (x400). Reduced by 50% in preparation.
interpreted as metastatic lymphoma. Consequently, one of these two patients was biopsied under CT guidance, while the other underwent an exploratory laparotomy. Neither procedure would arrive at the correct diagnosis, and revision of the biopsies by our pathologist confirmed the diagnosis of HF.

Hepatic histopathology was compatible with eosinophilic abscess (or parasitic granuloma) in 12 of 13 patients (Table 4), with areas of coagulative necrosis in seven and Charcot-Leyden eosinophilic birefringent crystals in 6 (Figs 1 to 4). One biopsy showed no abnormalities probably because it was taken 4 months after therapy with triclabendazole. Trials of therapy for our patients are being evaluated and will be published as a separate report.

Discussion

HF is becoming a public health problem in many developing countries, including Egypt. It might be also a problem in residents of developed countries who travel to endemic regions. The highest prevalence of HF reported to date is in North Western Bolivia in Latin America. HF was thought to be uncommon in Egyptian children because only a few reports, each including a few children, have been published. Most of them came from Alexandria province. Our report indicates that HF might be uncommon in Egyptian children referred to tertiary care centers with various clinical presentations, but probably being underdiagnosed due to lack of awareness of the problem. Our patients who came from Cairo, as well as different provinces in Northern Egypt, experienced delay in diagnosis for 1–20 months; two of them were thought to have abdominal malignancies. A high index of suspicion in children with PUO and right upper abdominal pain associated with high ESR and eosinophilia is needed to diagnose HF. Dizia et al. coined the term ‘the febrile eosinophilic syndrome’ as a clinical indicator of HF; this syndrome consists of fever, high eosinophilic count and abdominal pain. Eosinophilia is common in all tissue parasitosis, and in endemic areas it should raise the suspicion of HF. Eosinophilic counts were strikingly high in all our patients.

Direct stool microscopy for Fasciola hepatica ova is not always diagnostic of HF, particularly in the early larval stage; in the chronic biliary stage, eggs may be detected in stools. Duodenal and biliary aspirates are far more sensitive in diagnosis, but were not attempted in our children because of technical difficulties. Serology helps in diagnosis of egg-negative cases and is the mainstay in field survey. Various serologic tests have been standardized in diagnosis of HF including the one we used (IHAT), counter-immuno-electrophoresis (CIE), enzyme-linked immunoassay (ELISA), Falcon assay screening test-enzyme-linked immunosorbent assay (FAST-ELISA) and enzyme-linked immuno-electrotransfer blot (EITB). Seven of our 16 patients passed eggs in stools, while all 10 tested for IHAT were positive; two of those IHAT positive had negative stool findings.

LFT’s showed normal serum bilirubin, AST, ALT, and prothrombin time in all tested patients, while AP was
always elevated. This is in accord with most previous reports. However, Wessely et al. reported modest elevations of aminotransferase in HF.

Abdominal ultrasonography (Figs 5 and 6) was the basis of diagnosis of two egg-negative patients, and assisted in diagnosis of seven egg-positive and five IHAT-positive. Results of non-invasive imaging help in the diagnosis of both acute hepatic invasion and chronic biliary stage of HF. Han et al. described three characteristic ultrasonographic features of the acute hepatic phase:

1. cluster of micro-abscesses arranged in tract-like fashion (burrow tract);
2. subcapsular location of the hepatic lesions;
3. very slow evolution of the lesions on follow up.

They also described the characteristics of the chronic phase as multiple, conglomerated filling defects in the common bile ducts. However, the very early larval stages with no or tiny parasitic granulomas cannot be diagnosed by ultrasonography and serology is more sensitive in these early stages. CT scan has become a useful technique in the diagnostic work-up of HF. It shows nodular and/or tortuous lesions of diminished attenuation. Nodular lesions are non-specific and cannot be distinguished from necrotic neoplasms or usual abscesses, whereas tortuous lesions should raise

FIG. 5. Ultrasonographic scan of a case of HF showing hypoechoic lesion in the liver (right) and dilated common bile duct (left) (hepatobiliary fascioliasis).

FIG. 6. Ultrasonographic scan of another case of HF showing thickened wall of gall bladder with echogenic masses (worm) inside (biliary fascioliasis).
the diagnostic considerations of HF.\textsuperscript{25,26} A careful consideration of HF in our two patients with nodular CT lesions could obviate the need for CT-guided biopsy and laparotomy.

Eosinophilic abscess on hepatic histopathological examination is almost always pathognomonic of HF.\textsuperscript{23} However, this investigation should not be routine in patients suspected of having HF as less invasive investigations might be more diagnostic. The vague presentations and the late referral of our patients prompted us to perform percutaneous liver biopsy which showed eosinophilic abscess in 12 of 13 patients. It is well known that HF does not result in extensive hepatic fibrosis or cirrhosis unless the worm causes severe biliary obstruction with obstructed jaundice; it rarely causes ascites.\textsuperscript{3,27} None of our patients had hepatic fibrosis or cirrhosis, while three developed massive transient ascites with ascitic fluid eosinophilia in one and spontaneous bacterial peritonitis (SBP) in another. Three patients developed minimal transient ascites detected only by ultrasonography. Apart from SBP, we can attribute this ascites to the undernutrition and hypoproteinemia and/or to larval invasion, not to hepatocellular failure.

In conclusion, HF does occur in Egyptian children in various parts of the country. Its diagnosis is not always easy and needs a high index of suspicion particularly in children presenting with the 'febrile eosinophilic syndrome'. Surveys are needed to estimate the actual prevalence of this parasitosis.

References