Rev. Inst. Med. trop. São Paulo
38 (1): 69-73, janeiro/fevereiro, 1996.

HEPATIC FASCIOLIASIS: CASE REPORT AND REVIEW

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SUMMARY

A well documented case of hepatic fascioliasis (HF), successfully treated with triclabendazole, is reported. Predominant clinical manifestations were fever, marked eosinophilia and abdominal pain. Triclabendazole was given as two single oral doses of 10 mg/kg each. Neither side effects nor clinical or parasitological relapses were seen after three months of follow up

Based on this experience and few other similar reports in the literature, triclabendazole might be a valid therapeutical alternative in the treatment of human fascioliasis.

KEYWORDS: *Fasciola hepatica*; Hepatic fascioliasis; Eosinophilia; Triclabendazole.

INTRODUCTION

Fascioliasis is a zoonotic disease caused by the liver trematode *Fasciola hepatica*, [25] that affects herbivorous animals, specially sheep, goats and cattle, which may accidentally affect humans as well [6, 26].

In Venezuela, the human infection has rarely been recognized. Indeed, only five additional cases of human fascioliasis have been reported [27, 35] since the original case by RISQUEZ, in 1910 [10, 11].

The purpose of this communication is to report a new case of indigenous hepatic fascioliasis in Venezuela and discuss its clinical, laboratory, and radiological findings. The occurrence in this patient of fever and hypereosinophilia, along with other characteristic clinical manifestations, indicate that the infection was in an invasive phase (migratory stage). Excellent therapeutic response was seen with triclabendazole (Fasinex®), a fasciolicide of veterinary use, which has recently been suggested as a therapeutic alternative in those patients that fail to respond to the administration of other human fasciolicides.

CASE REPORT

E. G., a 60-year-old Venezuelan woman, from the rural Andean Region but currently living in Caracas, was admitted to the University Hospital of Caracas complaining of intermittent right upper quadrant pain radiating to the back, chills, mild fever, myalgias, asthenia and 8 Kg weight loss during the previous two months. On interrogation, she mentioned the frequent ingestion of wild raw watercress *(Rorippa nasturtium aquaticum)*.

Physical examination revealed a firm and tender liver, about 4 cm below the right rib margin.

Relevant laboratory results included: 35,800/mm^3 white blood cells (WBC) with 77% eosinophils; alkaline phosphatase 338U (NV=31-115U), SGOT 90U (NV=10-40U), SGPT 77U (NV=10-40U). Multiple parasitological stool samples were negative during this period.

An abdominal ultrasound exploration disclosed an enlarged liver with three irregular anechogenic parenchymal images, two in the right lobe and one between

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both lobes, approximately 23 and 22 mm in diameter, respectively, and irregular echogenic rings. An abdominal CT scan disclosed multiple hypodense images in both lobes. Both image diagnostic studies were initially reported as suggestive of metastatic liver disease.

On laparoscopy, multiple white, irregular nodular lesions, approximately 5 to 10 mm in diameter, were observed on the hepatic surface. Histopathology revealed eosinophilic infiltrates in the portal spaces, as well as portal, septal and parenchymal fibrosis.

The original symptoms progressively subsided spontaneously. On a follow up performed four months later, the patient remained asymptomatic. WBC were 10,000/mm^3 with 19% eosinophils. Both a new stool sample and a duodenoscopic bile aspiration revealed *Fasciola hepatica* eggs. An endoscopic retrograde cholangiography disclosed multiple linear filling defects in the biliary ducts (Figure 1). She was given two single 630 mg (10 mg/kg) oral doses of triclabendazole, postprandially, with a 48-hour interval. No toxic side effects were observed. All previously abnormal laboratory findings became normal. A new endoscopic retrograde cholangiography showed remarkable improvement (Figure 2). Both CT scan and ultrasound explorations, performed two months after therapy, became normal.

No *Fasciola hepatica* eggs were observed in four stool sample and one duodenoscopic bile aspiration carried out 3 months after treatment.

DISCUSSION

Fasciola hepatica, the first described digenetic trematode, [25, 33] is a lance-shaped parasite (2-4 cm long by 1-2 cm wide) that inhabits the gallbladder and biliary ducts of herbivorous animals, specially cattle, sheep and goats. Large operculated eggs are passed in the stools of infected animals and hatch into ciliated miracidia in the water. The miracidium must find an intermediate host, a fresh-water snail (*Lymnaea* spp.) where multiplication ordinarily takes place over a period of 20 days. Various authors [7, 32] have documented *Lymnaea* (galba) *cubensis* as an intermediate host in Venezuela. Cercariae emerge from the snail and encyst on aquatic vegetation, specially the wild watercress

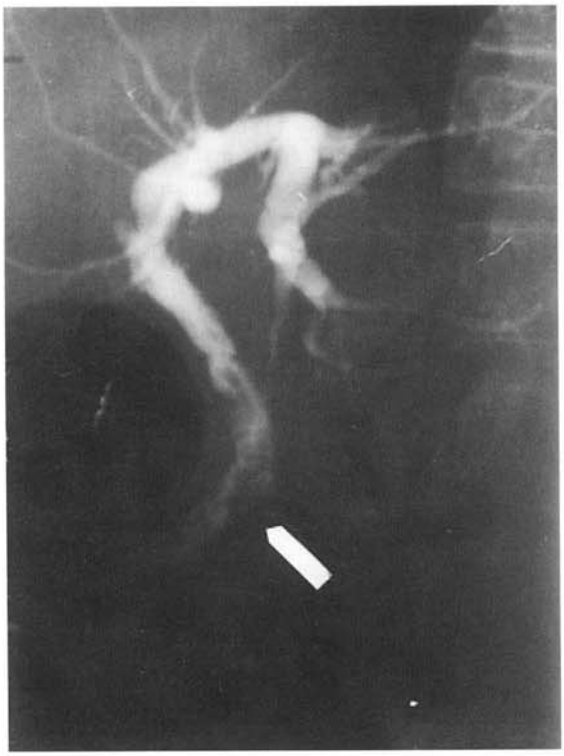

Fig. 1 - Endoscopic retrograde cholangiography before treatment with the common bile duct markedly irregular and multiple radiolucent defects.

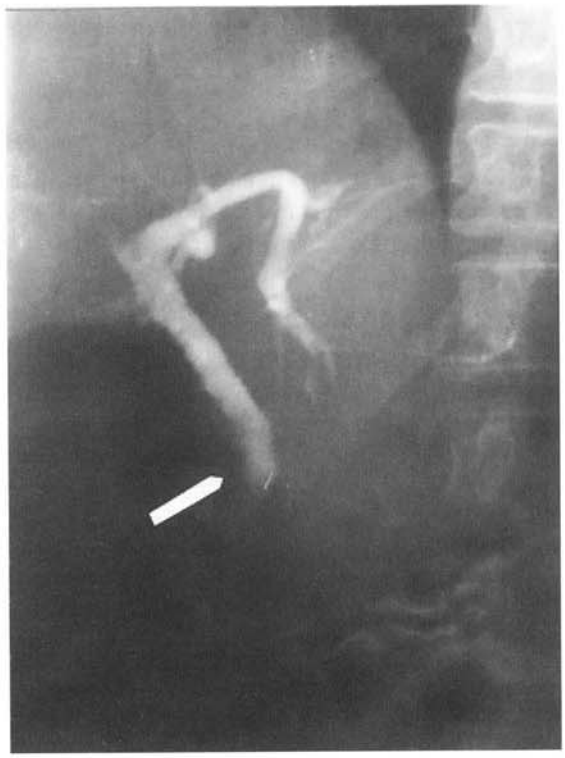

Fig. 2 - Endoscopic retrograde cholangiography after treatment with remarkable improvement.

(Rorippa nasturtium aquaticum), [5, 9, 16, 26, 27] producing multiple metacercariae, which are infectious to the definitive host [8, 26]. Humans may occasionally become accidental hosts by ingesting these vegetables.

Metacercariae excyst in the host's duodenum, perforate peritoneum and Glisson's capsule, reaching the biliary ducts through the liver parenchyma [8, 26]. In this stage, patients exhibit varied clinical symptoms, including: fever, jaundice, abdominal pain, myalgias, and asthenia. Hepatomegaly, leukocytosis and high eosinophilia are common [2, 15, 16, 26, 29]. Such clinical picture may mimic many other hepatobiliary diseases [24, 28, 31] and, since the infection is at an early migratory stage, stool samples are negative for eggs. In the current case, all these symptoms and signs were present, except for the jaundice.

Marked eosinophilia, such as that observed in the initial phase of fascioliasis, [2, 9, 16, 22, 26, 29] often represents an important reason for consultations in tropical areas. Since most of those patients, such as occurred in this case, will eventually have common parasitic diseases, [16, 29, 33] among them intestinal or tissue invading helminths, it appears reasonable to routinely perform simple diagnostic parasitologic techniques before asking for more complicated or expensive explorations.

Once the parasite reaches the biliary ducts, the early clinical symptoms and the eosinophilia tend to abate [8] and eggs begin to appear in the stools, as in the present case.

Image diagnostic findings in this case are coincident with those described in previous reports [17, 23, 28]. The multiple hepatic peripheral hypoechogenic images on ultrasonography and the hypodense hepatic images on abdominal CT scans, are very similar to those seen in metastatic liver disease [6, 22, 23].

In our patient, diagnosis was made by demonstration of characteristic eggs in the stools and bile, as well as by the occurrence of multiple filling detects in the biliary ducts on cholangiography, corresponding to adult parasites. Endoscopic retrograde cholangiography has been mentioned as useful in the literature [5, 30].

Although specific serology and cutaneous reactions were not carried out in this case, they might be useful when an early diagnosis in required, since *Fasciola hepatica* eggs are seen in the stools only when the parasites have reached their sexual maturity, around twelve weeks after the moment of infection [26, 30].

The enzyme-linked immunosorbent assay (ELISA) is a widely used diagnostic serological method in fascioliasis [6, 26]. Although ELISA is considered highly sensitive (100%) and specific (97.8%) in detecting antibodies against excretion-secretion antigens of the adult stages of *Fasciola hepatica*, [26, 29] some studies have reported cross-reactivity with *Schistosoma* spp [18, 26, 29]. The levels of antibodies to excretion-secretion antigens of *Fasciola hepatica* may remain high for many years in actively infected individuals [26]. In contrast, ELISA titles steadily decrease after a successful antiparasitic treatment [12, 26]. A new DOT-enzyme-linked immunosorbent assay (DOT-ELISA) has recently been used for seroepidemiological studies [29]. In individual patients, specific serum antibodies to *Fasciola* may also be detected by counterimmunoelectrophoresis [1, 29]. The complement fixing reaction is also useful, even though it may show cross-reactivity with hydatidosis and trichinellosis [1]. Finally, a specific rapid-reading intradermal test has also been used [1].

The treatment of fascioliasis has been complex in terms of drugs efficacy and toxicity [21, 26]. Traditional therapy included the parenteral administration of highly toxic drugs such as the dehydroemetine or chloroquine [4, 26, 34]. Despite initial encouraging reports, praziquantel has not proved an effective drug for acute or chronic fascioliasis [13, 15, 19, 26, 33, 34]. Bithionol, at the dose of 1g three times a day for 15 days, has been recommended as the drug of choice for treating fascioliasis since 1982 [2, 15, 26, 30, 33]. Some reports show 100% effectiveness for the compound [2]. Side effects are minimal and mainly restricted to the gastrointestinal tract [2, 26, 33]. Therapeutic response to triclabendazole (Fasinex ® Ciba-Geigy, Basle, Switzerland) for veterinary use [19, 21, 22, 34] was very effective.

Triclabendazole [6-chlorine-5 (2-2 diclofenoxi) 2-methil tiobenzimidazol] is chemically related to the antihelminthic benzimidazole -2 carbamate, which is active against *Fasciola* and other closely related trematodes [14, 34]. Triclabendazole is fasciolicide not only against the adult worms present in biliary ducts, but also against the immature larval stages of *Fasciola* migrating through the hepatic parenchyma [4, 34]. The exact mechanism of action of triclabendazole is not thoroughly understood [3, 34]. This drug can induce im-

mobilization and death of *Fasciola* within 24 hours, with corresponding changes in the inactive parasite's tegumentary membrane, strongly inhibiting the release of proteolytic enzymes of mature and immature worms, a process which appears critical to the survival of the parasite [3, 14].

In domestic animals, doses of 5 mg/kg of weight nearly kill all adult *Fasciola* and about 85% of the immature stages. A dose of 10-12 mg/kg is nearly 100% effective against these immature parasites [4, 34]. Therapeutic doses of triclabendazole do not produce teratogenic, mutagenic or embryotoxic effects in rats, sheep and bovines [14, 34]. Ninety five per cent of the orally administered drug is eliminated by the stools, 2% through the urine and less than 1% by the milk [14].

Good clinical and laboratory tolerance of a cumulative total dose of 38 mg/kg has been demonstrated [21, 34]. Similarly to albendazole, postprandial administration significantly increase the absorption of the drug [20, 21].

Triclabendazole (Fasinex ®) seems a good alternative in the treatment of both acute and chronic human fascioliasis [19, 21, 22, 34].

This case and few other reports in literature indicate that triclabendazole represents an attractive therapeutic option in the treatment of human fascioliasis.

RESUMO

Fasciolíase hepática. Relato de um caso e revisão da literatura

Os autores relatam um caso bem documentado de fasciolíase hepática (FH) tratado com êxito com triclabendazole.

As manifestações clínicas predominantes foram febre, eosinofilia marcante e dor abdominal. Triclabendazole foi dado em duas doses únicas orais de 10 mg/kg cada. Não houve efeitos colaterais, nem recaídas clínicas ou parasitológicas até três meses após tratamento.

Baseados nesta experiência e em outros poucos dados revistos na literatura, triclabendazole poderia ser uma alternativa terapêutica válida no tratamento da fasciolíase humana.

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Recebido para publicação em 23/03/1995.
Aceito para publicação em 05/02/1996.