

Human infection by *Fasciola hepatica* in Venezuela: report of a geriatric case.

Renzo Nino Incani¹, Juan Manuel Vieira², Mercedes Pacheco¹, Sandra Planchart¹, Manuel Amarista³ and Janis Lazdins⁴.

¹Departamentos de Parasitología y ²Medicina Interna, Facultad de Ciencias de la Salud, Universidad de Carabobo, Valencia. ³Instituto de Altos Estudios en Salud Pública “Dr. Arnoldo Gabaldón”, Ministerio de Salud y Desarrollo Social, Maracay, Venezuela.

⁴World Health Organization, Geneva, Switzerland.

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Abstract. A new case of human infection due to *Fasciola hepatica* is reported in the Venezuelan parasitological literature. The patient is an 81-year-old female asymptomatic, with an eosinophilia of 21% and eritrosedimentation rate of 26 mm/h and was found during a routine check up. These values were normal at the time of treatment (4 months later), as were several tests of hepatic function, blood chemistry and peripheral blood haematological values. The number of eggs of the parasite were between 90 and 130/g of faeces. The patient was successfully treated with the human formulation of triclabendazole at 2 single doses of 10mg/kg, each separated by 24h. The same laboratory tests mentioned above did not show modifications, except for a slight increase in the eosinophil counts at 2 and 11 days and erythrocytation rate at 11 days post-treatment. Coproparasitological observations carried out at 12, 18, 60 and 120 days post-treatment were negative. No clinical symptoms were registered up to 2 months after treatment. The patient most probably acquired the infection at home through the ingestion of commercially available lettuce from an endemic area of bovine fascioliasis, very distant from home, and between 4 and 7 months previous to treatment. We stress the need to investigate *F. hepatica* infections which have been neglected, probably because of limited knowledge by health workers, lack of specific symptoms and absence of more sensitive diagnostic procedures.

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Palabras clave: *Fasciola hepatica*, fascioliasis, eosinophilia, triclabendazole, Venezuela.

Resumen. Se reporta para la literatura parasitológica venezolana, un nuevo caso de infección humana por *Fasciola hepatica*. Se trata de una paciente de 81 años, asintomática, quien presentó durante exámenes de rutina, una eosinofilia de 21% y una eritrosedimentación de 26 mm/h. Estos valores fueron normales para el momento del tratamiento (4 meses después), así como también lo eran varias pruebas de funcionamiento hepático, química sanguínea y valores hematológicos. El número de huevos del parásito fue de 90 a 130/g de heces. La paciente fue exitosamente tratada con la formulación humana de triclabendazol en 2 dosis simples de 10 mg/kg cada una separadas por 24h, resultando negativas las evaluaciones coproparasitológicas realizadas a los 12, 18, 60 y 120 días post-tratamiento. Los mismos tests de laboratorio arriba mencionados no mostraron modificaciones excepto por un incremento leve en el conteo de eosinófilos en los días 2 y 11, así como un incremento en los valores de eritrosedimentación al día 11 post-tratamiento. Así mismo, no se registraron síntomas durante 2 meses de seguimiento post-tratamiento. La paciente probablemente adquirió la infección en su hogar, a través de la ingestión de lechuga adquirida en el comercio local, originalmente proveniente de un área endémica de *F. hepatica* bovina distante de su hogar, entre 4 y 7 meses previos a su tratamiento médico. Enfatizamos la necesidad de investigar esta parasitosis, la cual ha sido subvalorada como infección humana en Venezuela, probablemente debido al limitado conocimiento que de ella tiene el personal de salud, su sintomatología poco específica y la ausencia en el país de procedimientos diagnósticos más sensibles.

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INTRODUCTION

Fasciola hepatica is a hepatic trematode parasite of herbivores with a world-wide distribution (1, 2). Human infections are less common although epidemics have been described in several countries (3). There are indications that human infection is underestimated, perhaps because of neglect or lack of available sensitive diagnostic procedures. For example, human infection in Bolivian highlands

have been found to reach up to 70% prevalence in certain localities (reviewed by 1, 4), supporting the contention that the reported cases are far below the real figures. Indeed, estimates of the number of people infected world-wide vary from 2,4 million (5) to 17 million (6). In Venezuela, the number of reported cases are very few. The first case was reported in 1910 (7) and the same author (8) refers to 9 additional but non-published cases between 1911 and 1921 (also reviewed by 9). Since then

there has been a major dearth of publications, barely interrupted by 3 cases reported individually in 1975 (10), 1996 (11) and the most recent in 1999 (12). This contrasts with the high rate of bovine infection found in certain regions (13, 14). In this paper we report a new case of human fascioliasis and discuss its epidemiology, clinical aspects and successful chemotherapy with triclabendazole.

MATERIAL AND METHODS

Patient

The patient was an 81-year-old female German-born Venezuelan, a retired nurse with 50 years residence in Valencia, Venezuela. She presented values of 21% eosinophilia and erythrocyte sedimentation rate (ESR) of 26 mm/h during a routine check up. On interrogation, the patient only complained of mild hypertension, scoliosis and a 50-year old history of constipation. She had referred hepatitis in the 1950s, but no hepatic or biliary involvement since then. Physical examination did not show any relevant finding.

Laboratory

Faecal examination. Three stool samples pre-treatment were obtained during a period of 3 months, starting 2 months after the reported eosinophilia. Samples were processed using the following methods: direct with isotonic saline and iodine, Kato-Katz, Baermann and Faust. A 2% (w/v) KOH digestion of 5 g of faeces at 37°C for 24 h was also carried out, after sieving and 3 spontaneous sedimentations in water. One mL samples were screened in 7x5cm-gridded slides after methylene blue counterstaining of faecal debris, and observed at total magnification of 40x. Kato-Katz and KOH digestion were also carried out at 12, 18, 60 and 180 days after treatment.

Haematology and blood chemistry. Blood haemogram, ESR, SGOT, SGPT, acid and alkaline phosphatases, pancreatic amylase, total, direct and indirect bilirubin, serum proteins, total cholesterol, cholesterol HDL, LDL, and VLDL, triglycerides, urea, creatinine and glycaemia, were performed pre- and at 2 and 11 days post-treatment.

Abdominal CT scan. An helicoidal CT scan with contrast was performed pre-treatment to search for hepatic lesions or evidence of the presence of *F. hepatica* adult worms (15).

Drug treatment. Triclabendazole human formulation (Egaten®, Novartis) was used at 10 mg/kg single oral dose after breakfast for 2 days as recommended by the manufacturer.

Clinical follow up. Clinical interrogation for side-effects of the drug and evolution of infection was pursued daily for 15 days and then weekly for 2 months.

RESULTS

Side-effects post-treatment

Interrogation and clinical examination of the patient did not show any evidence of symptoms up to 2 months after the administration of triclabendazole.

Coproscopy

Faecal examination pre-treatment revealed the presence of large, oval, operculated eggs with unembryonated granular content, measuring $129.1 \pm 7.5 \mu\text{m}$ length ($107.5\text{-}140 \mu\text{m}$), $68.5 \pm 2.7 \mu\text{m}$ width ($65\text{-}75 \mu\text{m}$) ($n=30$), compatible with the diagnosis of *F. hepatica* eggs (16) as the only parasite present, with a parasitic load of 90, 118 and 130 eggs/g measured by the Kato-Katz method (3 stool samples in 3 months, 6 slides per sample) and 87/g by KOH digestion of faeces of the first sample. No *F. hepatica* eggs were found by the Kato-Katz or in 5 g KOH digests of faeces

carried out at 12, 18, 60 and 180 days post-treatment, after which time we considered that the patient was cured parasitologically.

Haematology and blood chemistry

At the time of drug administration (4 months after the detection of eosinophilia), the total and differential white blood cell counts and ESR were normal, as also were the levels of SGOT, SGPT, acid and alkaline phosphatases, pancreatic amylase, total, direct and indirect bilirubin, serum proteins, total cholesterol, cholesterol HDL, LDL, and VLDL, triglycerides, urea, creatinine and glycaemia. Evaluations of the same tests at 2 and 11 days post-treatment showed that the only abnormalities were a modest eosinophilia at day 2 (8%, 493/ μ L) and day 11 (7%, 478/ μ L) and an ESR of 30mm/h at day 11.

Abdominal CT scan

A CT scan carried out pre-treatment did not show any evidence of hepatic lesions or adult *Fasciola* worms in the bile ducts.

Epidemiology

The patient has always been a city dweller and the relevant data for *F. hepatica* transmission was an increased intake of lettuce (about 200 g/day) during a 3-month period previous to the detection of eosinophilia, to alleviate her chronic constipation. The patient's main source of lettuce was a local branch of a known national chain of supermarkets, that obtains lettuce from farms in regions of the Andes (Mérida and Trujillo states) where *F. hepatica* infection in bovines is prevalent (12, 14). An additional minor and irregular source of lettuce was from farms in Colonia Tovar (in the high lands of Aragua state), where no records of bovine *F. hepatica* infection has been found. The patient has not been a water cress eater, a traditional major vehicle of infection.

DISCUSSION

In this paper we report a new case of human fascioliasis for the Venezuelan literature, with the peculiarity that the infection has probably been acquired not directly by living in an endemic area, but receiving the infection through a vegetable (lettuce) that was obtained in a city market, but was cultivated and transported from endemic areas far away from the city. This potentiates the probability of dispersion of the infection, since vegetables obtained from *F. hepatica* endemic areas are sold nationwide. Scorza et al. (12) commented on this problem, since they observed wild water cress been harvested on the shores of creeks in an endemic area of the Andes, by workers from a nationwide supermarket chain. It is possible that we may have a widespread underestimated infection, which is not been diagnosed because of lack of knowledge on the parasite by health workers and/or non-specific symptoms. The acute period of the infection, which occurs basically during the invasion of the metacercaria through the intestinal wall, peritoneum and liver parenchyma, is classically characterised by fever, abdominal pain, gastrointestinal disturbances, urticaria and eosinophilia (reviewed by 1). The latter also may be found in latent and chronic-obstructive phases, but tends to disappear after the invasive phase. Eosinophilia and increased ESR, were the only signs observed in our patient and were detected at the end of a 3-month period, during which there was probable contact with the parasite through the reported high intake of lettuce. Since the eosinophilia was no longer detected in 2 opportunities around the time of treatment, i.e. 4 months after the detection of this sign, we could conclude that the time of infection may have occurred between 4 and 7 months be-

fore treatment. Thus, the patient was treated during the latent phase.

Despite the absence of symptoms, this aged patient was treated because of the risk of developing biliary fibrotic disease if the disease had been left to develop to a chronic stage, and because triclabendazole has been shown to produce high cure rates with low side effects (1, 16, 17). The manufacturers do not mention any report on the use of the drug in aged patients. This drug has been in use for the treatment of fascioliasis of livestock for around 20 years and is at present the best drug of choice for treatment for human fascioliasis. Unfortunately, the drug has been certified for human use only in Egypt, but has been listed by the World Health Organization as one of the essential drugs (18). Endemic countries should be encouraged to press for approval, since former less efficient drugs (eg Bithionol, Emetine) are difficult to obtain. Our results indicate that triclabendazole is an effective therapeutic option, without side-effects for the treatment of aged patients infected with *F. hepatica*, with an apparent moderate parasitic load, and with a relative short time of evolution. To our knowledge, this is the first successful treatment reported of a geriatric case of fascioliasis with this drug.

Research on this neglected disease should be encouraged in Venezuela in view of the possibility of widespread infection with no necessary contact with an endemic zone. Patients with eosinophilia of unknown origin, symptoms of cholelithiasis, cholecystitis and cholangitis should be placed in a protocol for *F. hepatica* detection. Since it is difficult to detect eggs in the faeces of some patients (19), efforts should be directed to antibody detection methods or detection of antigens in the faeces.

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