

A case of adult hepatic toxocariasis

Jared Hossack*, Paul Ricketts, Helen S Te and John Hart

SUMMARY

Background A 56-year-old female presented to the emergency room with a 2-week history of fevers, chills and right upper quadrant pain. She had no sick contacts, had not traveled recently and denied high-risk sexual behavior. The patient had adopted a stray cat 1 month before presentation.

Investigations Physical examination; laboratory tests (including complete blood count with differential, complete metabolic panel including liver enzymes, and serum *Toxocara* serology); chest and abdominal CT scans; and percutaneous liver biopsy.

Diagnosis Toxocariasis (visceral larva migrans).

Management Supportive care and antihelmintic agents.

KEYWORDS eosinophilic granuloma, granulomatous hepatitis, hepatic toxocariasis, *Toxocara*, visceral larva migrans

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Learning objectives

Upon completion of this activity, participants should be able to:

- 1 Describe the mode of infection with *Toxocara* species.
- 2 Identify the epidemiology of infection with *Toxocara* species.
- 3 Specify useful tools in the diagnosis of toxocariasis.
- 4 Identify the best usual treatment for toxocariasis.

Competing interests

The authors and the journal editor N Wood declared no competing interests. The CME questions author CP Vega declared that he has served as an advisor or consultant to Novartis, Inc.

THE CASE

A 56-year-old African American woman presented to the emergency room with a 2-week history of fever, chills and right upper quadrant abdominal pain. The pain was constant and dull, and it was accompanied by a fever of up to 38.9°C [102°F], chills and drenching night sweats. Furthermore, the patient had unintentionally lost 11 kg [25 lb] in weight in the previous 3 months.

The patient's past medical history was notable for hypertension diagnosed 10 years earlier that had been controlled with amlodipine 10 mg daily and benazepril 20 mg daily for the previous 2 years. She denied high-risk sexual behavior, the use of tobacco, alcohol or illicit drugs, had no sick contacts and had not traveled recently. The patient was a cosmetologist by profession and lived alone with a stray cat that she had adopted 1 month before presentation. She denied having

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Table 1 The patient's notable initial laboratory test results.

Parameter	The patient's values	Normal range
Hemoglobin concentration (g/l)	79	115–155
White blood cell count ($10^9/l$)	23.4	3.5–11.0
Eosinophil fraction	4.6	0.0–0.7
Absolute eosinophil count ($10^9/l$)	10.764	0.027–0.45
Total protein concentration (g/l)	114	60–83
Albumin concentration (g/l)	27	35–50
Alkaline phosphatase concentration (U/l)	167	30–120
Ferritin concentration (pmol/l)	1,348	45–674
Transferrin saturation (%)	8.6	20–50
Erythrocyte sedimentation rate (mm/h)	122	0–20

any visual changes or respiratory symptoms, chest pain, nausea, vomiting, changes in bowel habits, melena or hematochezia.

On physical examination, the patient appeared well and was in no apparent distress. Her sclerae were anicteric, and her heart and lung examination were normal. On abdominal examination, slight tenderness to palpation in the right upper quadrant and hepatomegaly to 3 cm below the costal margin were noted. Rectal examination noted light brown stool that was negative for occult blood. There was no lower extremity edema. Neurologic examination did not reveal focal deficits. There was no cervical, axillary or inguinal lymphadenopathy.

Initial laboratory studies detected that the patient had a low hemoglobin concentration and an elevated white blood count, with a peripheral eosinophilia (Table 1). Her serum electrolyte concentrations were normal. Liver-specific test results were also normal apart from revealing an elevated total protein level, hypoalbuminemia, and an elevated alkaline phosphatase level. The patient's ferritin level was elevated, her transferrin saturation was low and her erythrocyte sedimentation rate prolonged. Serum tests for the presence of viral hepatitis, HIV, syphilis, antinuclear antibodies, and rheumatoid factor were all negative. Both blood and urine cultures were negative. Stool specimens sent for culture and for detection of *Clostridium difficile* and ova and parasites were unremarkable. Serum protein electrophoresis revealed a markedly increased gamma globulin fraction without a clonal spike.

A CT scan of the patient's chest and abdomen detected calcifications within the lungs and

hila and diffuse patchy infiltrates in the liver (Figure 1). To evaluate the liver findings further, a core liver biopsy was taken. Histologic analysis of the biopsy sample revealed the presence of eosinophilic granulomatous lesions with central necrosis (Figure 2). This finding was highly suggestive of visceral larva migrans (VLM), and a diagnosis of toxocariasis was confirmed by the detection of elevated levels of *Toxocara* in the serum (1.3 OD units; normal range 0.0–0.5 OD units) using an enzyme-linked immunosorbent assay (ELISA) that detects antibodies against a second-stage larval excretory-secretory antigen. As the patient had debilitating symptoms, she was treated with albendazole 400 mg twice daily for 5 days. Despite treatment, the patient continued to have fevers, so she was then given mebendazole 200 mg twice daily for 5 days. After 1 month the patient's symptoms had resolved; laboratory studies revealed reduced eosinophilia (18%; absolute count 1,810 per mm^3) and lower alkaline phosphatase levels (122 U/l).

DISCUSSION OF DIAGNOSIS

Toxocara canis and *Toxocara cati* are ascarid nematodes that use dogs and cats, respectively, as their definitive host. They are common parasites that have a worldwide distribution. In North America, the prevalence of *Toxocara* infection is approximately 20% for adult dogs,¹ 80% for puppies¹ and 28–42% for cats.²

Definitive and paratenic hosts, which include humans, become infected when they ingest embryonated ova present in contaminated soil or uncooked meat. Definitive hosts can also become infected by transplacental or transmammary

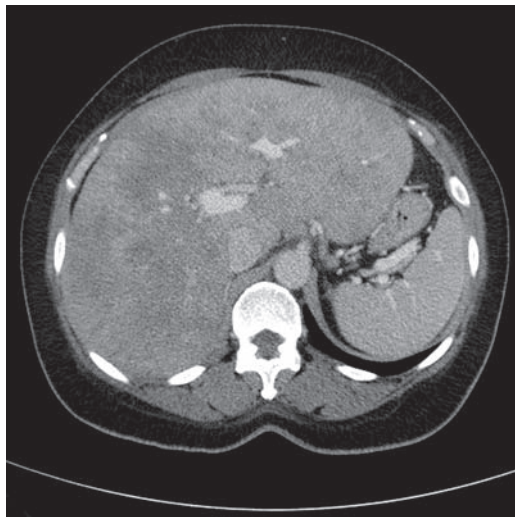


Figure 1 An abdominal CT scan of the case patient showing diffuse, heterogeneous low-density infiltrative liver lesions.

transmission of embryonated ova. The embryonated ova hatch and release larvae that penetrate the wall of the small intestine. The larvae are then able to enter the bloodstream and migrate to many different organs throughout the body. In humans, these second-stage larvae are unable to fully mature and reproduce. In the definitive host, however, the juvenile larvae develop into adult worms and live in the lumen of the small intestine. In these definitive hosts reproduction occurs and unfertilized ova are excreted with the fecal mass. Embryonation occurs in the soil 1–2 weeks after deposition.³

Toxocariasis is the clinical term for the parasitic infection of a human host by either *T. canis* or, less commonly, *T. cati*. As *Toxocara* ova are excreted in dog or cat feces, outdoor parks and playgrounds with sandboxes in urban or suburban settings and areas of poor sanitation are locations likely to harbor infectious ova.³ For this reason, toxocariasis is most commonly seen in young children aged 1–5, especially those who have pica and/or geophagia.⁴ Several cases of food-borne adult toxocariasis have been reported in regions where the consumption of raw liver is customary.⁵ As cases of larva migrans syndromes are not required to be reported to public health departments, the exact incidence of toxocariasis is unknown in the US. However, approximately 3,000–4,000 serum specimens from patients with presumptive diagnoses of toxocariasis are sent for serodiagnostic testing and confirmation of infection each year.⁶

The two main syndromes of toxocariasis—VLM and ocular larva migrans—are defined by the major organs that are affected by the migrating juvenile larvae. In 1952, Beaver and colleagues were the first to describe VLM in a series of children who presented with fever, hepatomegaly, pulmonary infiltration, hypergammaglobulinemia and peripheral eosinophilia.⁷ In patients with VLM, the liver is the visceral organ most commonly affected.⁴ When larvae gain access to the portal venous circulation (after migrating through the bowel wall and into blood vessels), they move through the liver and leave a trail of tissue disorganization, in the form of necrosis, interstitial edema, eosinophilic infiltrates and hemorrhage, resulting in granulomatous inflammation.⁸ This inflammation can lead to the development of granulomatous hepatitis.⁹

The clinical signs and symptoms seen in patients with toxocariasis are a direct consequence of the damage caused by migrating larvae and the host's subsequent inflammatory response. The tissues most sensitive to invasion include the liver, lungs, eyes and central nervous system (CNS). Inflammation manifests as eosinophilic granulomas. Common signs and symptoms of toxocariasis include fever, abdominal pain, hepatomegaly, splenomegaly, and lower respiratory findings, such as cough, dyspnea or bronchospasm.^{3,10} Less common manifestations, such as myocarditis, nephritis, and CNS involvement leading to seizure, neuropsychiatric symptoms and encephalopathy, have been described. In addition, more subtle clinical syndromes including asthma, functional bowel disorders, prurigo and urticaria have been linked to chronic exposure to migrating larvae.³

Laboratory evaluation of patients with toxocariasis almost always reveals leukocytosis with notable eosinophilia (eosinophil fraction 1.7–8.5).¹⁰ Other tests can often reveal hypergammaglobulinemia and elevated anti-A or anti-B isohemagglutinin titers.⁴ Granulomas or abscesses can appear on abdominal CT scans as ill-defined nodules that are similar in appearance to other inflammatory lesions.¹¹

As hepatic toxocariasis has a nonspecific appearance on a CT scan, it can be mistaken for another diagnosis. The differential diagnosis for multiple low-density liver nodules also includes microabscesses, other granulomatous diseases (i.e. sarcoidosis), hepatocellular carcinoma or liver metastases. When these findings

are accompanied by peripheral eosinophilia, hepatic toxocariasis must be considered and further serologic or pathologic testing should be pursued.¹² Two other helminthiases can result in similar CT findings—human fascioliasis and capillariasis. Capillariasis, which is caused by an infection with *Capillaria hepatica*, is most often a disease of young children, and hepatic biopsy samples reveal the presence of *C. hepatica* eggs. Fascioliasis, which is caused by an infection with *Fascioliasis hepatica* or *Fascioliasis gigantica*, is typically associated with ingestion of freshwater plants, such as watercress.¹³

A finding of eosinophilic granulomas on tissue biopsy is strongly suggestive of VLM, and a causative organism should be sought.⁸ However, samples containing intact *Toxocara* larvae are rarely found and are not required for a diagnosis to be made. An ELISA that detects antibodies against a second-stage larval excretory-secretory antigen is one of the best indirect methods for diagnosis (sensitivity 78–91%, specificity 86–93%).¹⁴ Immunologic tests, however, do show some degree of cross-reactivity to both *T. canis* and *T. cati*.^{4,15} Stool examination for ova and parasites is generally not helpful because the infective juvenile larvae do not multiply in paratenic hosts. Thus, a clinical history with laboratory findings of eosinophilia, hypergammaglobulinemia and positive serologies along with eosinophilic granulomas detected histologically from tissue biopsy samples confirm the diagnosis of toxocariasis.

Cases of toxocariasis are typically asymptomatic or mild; however, severe cases and, rarely, fatalities have been reported.^{16,17} In the case discussed here, a female adult presented with fever, chills and right upper quadrant pain. Given the patient's subsequent laboratory and histopathologic findings—in addition to the fact that she had recently adopted a stray cat, did not have risk factors for fascioliasis and did not have *Capillaria* eggs in her liver biopsy sample—she was diagnosed as having toxocariasis and the causative agent was determined to be *T. cati*.

TREATMENT AND MANAGEMENT

Most cases of toxocariasis are benign and self-limited, and medical treatment of even prolonged mild cases is unnecessary.¹⁰ More severe cases of toxocariasis require treatment with albendazole (400 mg twice a day for 5 days). Sturchler showed that albendazole was superior to the older antihelmintic drug, thiabendazole, with

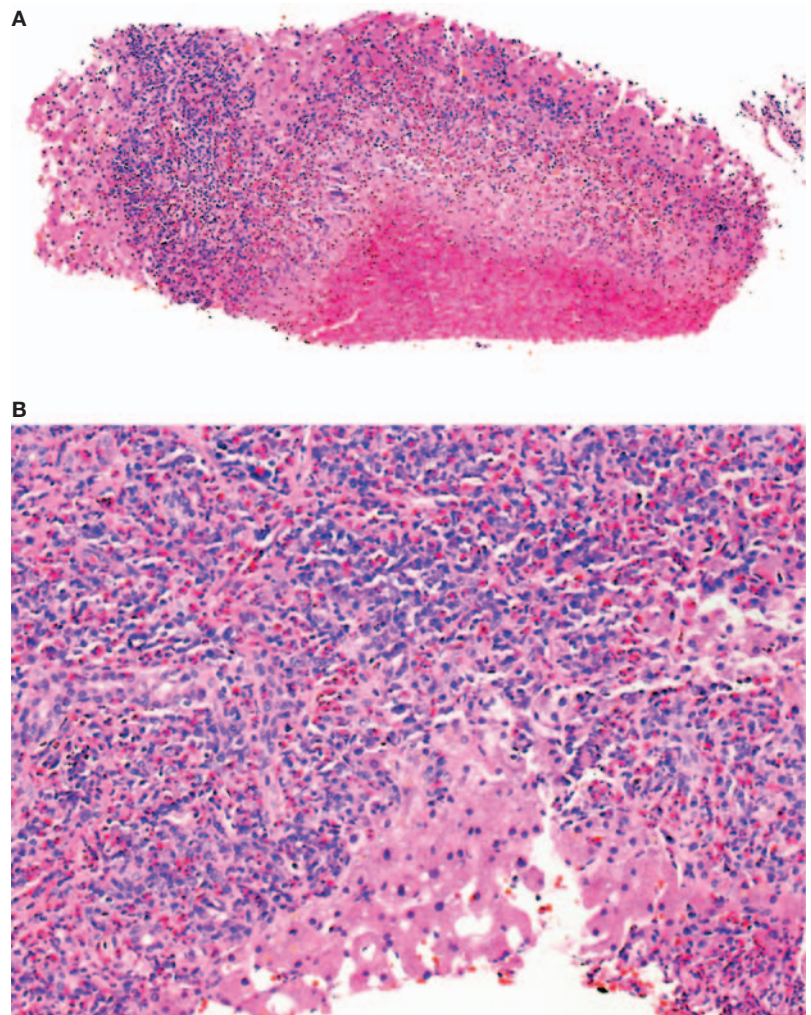


Figure 2 Histology of the case patient's liver biopsy sample. (A) A low-powered view displaying geographic hepatocyte necrosis surrounded by a granulomatous inflammatory reaction rich in eosinophils (hematoxylin and eosin staining, magnification $\times 10$). (B) A high-powered view showing diffuse eosinophilic infiltrates (hematoxylin and eosin staining, magnification $\times 100$). The histopathologic detection of eosinophilic granulomatous hepatitis was a key finding and, in our opinion, is almost pathognomonic of toxocariasis in patients with typical risk factors.

regard to improvement in clinical symptoms and reduction of eosinophilia.¹⁸ Mebendazole (100–200 mg twice daily for 5 days) can also be used, but it is considered second-line therapy because it is relatively poorly absorbed outside the gastrointestinal tract. Corticosteroids have been reported to improve symptoms related to the intense allergic response to infection, but these reports are anecdotal.³ The case patient had severe and debilitating symptoms that improved after she was given two courses of antihelmintic agents without the use of corticosteroids.

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Competing interests

The authors declared no competing interests.

Strategies for the prevention of toxocariasis focus most importantly on personal hygiene, appropriate preventative pet-health maintenance and limiting indiscriminate fecal deposition in public areas, in particular play areas used by children. The routine treatment of dogs and cats with ivermectin or other deworming agents is effective in limiting the spread of ova. Placing vinyl covers over sandboxes at night or removing sandboxes entirely from public parks could also help to reduce human exposure to infection.

CONCLUSIONS

Although VLM caused by toxocariasis is classically described as a benign disease of young children, it can also present as a debilitating febrile illness in adults. The case patient was an adult who presented with clinical features typical of toxocariasis and had confirmatory laboratory and histopathologic findings. Toxocariasis should be considered in the differential diagnosis of both children and adults who present with hepatomegaly with infiltrative liver lesions, particularly in the presence of other signs of parasitic infections, such as fever and eosinophilia.

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