

Case Report: Domestically Acquired Fascioliasis in Northern California

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Abstract. Two cases of domestically acquired fascioliasis are reported. Patient One was a 63-year-old male who developed a febrile illness 2 months after eating watercress in Marin County. Patient Two was a 38-year-old male who had eaten watercress with Patient One, and also developed a febrile illness. Both patients had eosinophilia and liver lesions on imaging. Diagnosis was made by serology and treatment was with triclabendazole.

INTRODUCTION

Fasciola hepatica and *Fasciola gigantica* are tissue-invasive trematodes that infect humans through ingestion of contaminated water or aquatic vegetation such as watercress. Cattle, sheep, and other mammals serve as definitive hosts. Eggs are passed in stool and embryonate in fresh water before releasing miracidia that invade specific aquatic snail species. After further parasite development within the intermediate host snail, *Fasciola* cercariae are released and encyst on aquatic plants.¹ Acute disease is caused by hepatic migration of immature larvae, and is characterized by fever, abdominal pain, hepatomegaly, eosinophilia, and multiple liver lesions on computerized topography (CT) imaging.² Chronic disease occurs as a result of development and persistence of the adult flukes in the biliary tract, and may lead to chronic cholecystitis and cholangitis. Whereas chronic fascioliasis may be confirmed by the presence of eggs in stool, diagnosis of acute fascioliasis requires recognition of clinical and imaging characteristics, and may be confirmed by serologic testing.³

Fascioliasis occurs in the United States in domesticated herbivores,^{4,5} but human disease is uncommonly diagnosed.^{6,7} Most recognized human cases represent imported infection from endemic regions,⁷ and only a handful of domestically acquired *Fasciola* infections have been reported from the continental United States.^{8–10} Two cases of fascioliasis acquired in Northern California are reported here.

CASE REPORTS

Patient One was a healthy 63-year-old male who presented with intermittent fever (103°F), chills, sweats, and headache, along with vague epigastric discomfort and “gurgling” for 20 days in May 2011. Patient One lived in the San Francisco Bay area, and had traveled to France 3 months previously where he ate local vegetables. Two months previously, he picked and ate local watercress in rural Marin County (North of San Francisco). Examination showed minimal epigastric discomfort, and was otherwise unremarkable. Investigation revealed eosinophilia, which peaked at 4,410/ μ L. An abdominal ultrasound showed borderline splenomegaly at 13.6 cm, and a three phase CT showed ill-defined areas of heterogeneous attenuation and enhancement of the liver, along with a borderline enlarged spleen (Figure 1). He was admitted to the hospital for a presumed liver abscess, though malignancy

was also an initial concern. The liver lesions were felt to represent poor targets for biopsy or aspiration, and he was treated with ceftriaxone and metronidazole, with a subsequent change to levofloxacin and metronidazole. Blood cultures were negative, and three stools were negative for ova and parasites. He started nitazoxanide a week later because of concern for fascioliasis. A repeat CT of the liver was unchanged a week later, though his fevers briefly returned. He continued antimicrobial treatment, and finished a 14-day course of nitazoxanide. Eosinophil count gradually declined to 500/ μ L 7 weeks after presentation. Serial *Fasciola* serologies (at presentation, 2 weeks later, and 7 weeks later) at a commercial laboratory by enzyme-linked immunosorbent assay (ELISA) to crude *Fasciola hepatica* extract were all negative with a titer of 1:8, which was below the positive cutoff of 1:32. Multiple stool samples taken in the 2 months after presentation did not show ova or parasites. Serologic testing was negative for *Toxocara*, *Coccidioides*, *Strongyloides*, human immunodeficiency virus (HIV), and other less likely etiologies.

Patient Two was a healthy 38-year-old male who had eaten handpicked watercress with Patient One in March 2011. Ten days after the beginning of Patient One’s illness, Patient Two developed intermittent fever (to 102.5°F) that gradually resolved over 10 days. He was asymptomatic with the exception of occipital neck pain that occurred with fevers, and fatigue that persisted after the fevers resolved. Physical examination was unremarkable. Evaluation revealed eosinophilia, which peaked at 19,176 cells/ μ L 10 days after symptom onset. Other findings included alanine transaminase 131 U/L (9–60 U/L), aspartate transaminase 40 U/L (10–40 U/L), and alkaline phosphatase 115 U/L (40–115 U/L). Initial stool ova and parasite testing showed *Dientamoeba fragilis*, and he was treated with metronidazole. Serologies to *Strongyloides*, *Toxocara*, HIV, and *Coccidioides* were all negative. An abdominal ultrasound showed hepatomegaly with a heterogeneous liver texture.

In the midst of these investigations, Patient One and Patient Two became aware of the other’s illness and fascioliasis was considered a likely diagnosis for both. Patient One had already been treated with nitazoxanide by this time, and commercial laboratory *Fasciola* serologies were pending for Patient One. Blood from both patients was sent to the University of Puerto Rico for *Fasciola hepatica* serology (The Center for Disease Control and Prevention [CDC] preferred the reference laboratory for *Fasciola* testing). While awaiting serology results, Patient Two developed orthostatic-type dizziness with an eventual near syncopal episode. He was not on medications at this time. He later developed urticaria. Serial repeat stool ova and parasite tests from Patient Two

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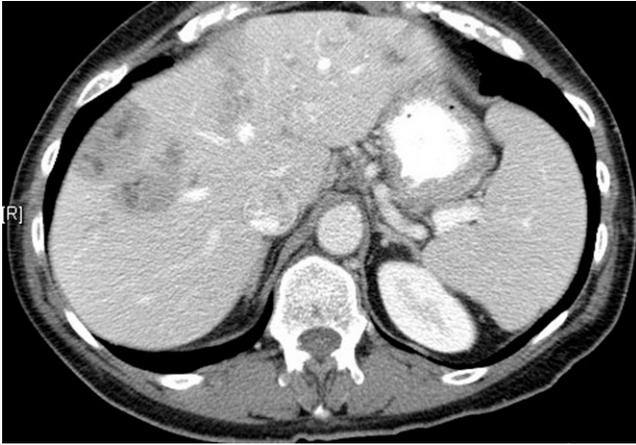


FIGURE 1. Abdominal computerized tomography scan for Patient One, after intravenous contrast, shown in the venous portal phase. A hypodense lesion is seen in the periphery.

showed only recurrence of *D. fragilis* for which he received paromomycin. His eosinophil count fluctuated, but remained as high as 14,579 cells/ μ L 7 weeks after presentation. An abdominal magnetic resonance imaging (MRI) with gadolinium two and one-half months after presentation showed multiple irregular focal lesions with faint enhancement (Figure 2). These lesions were located centrally and peripherally, and were most prominent around the portal veins. With the rise in eosinophilia and urticaria suggesting an ongoing or worsening process, and the initial negative *Fasciola* serologies for Patient One, Patient Two received a short course of albendazole while awaiting the reference laboratory *Fasciola* serology (to cover less likely possibilities such as pre-neurologic *Baylisascaris procyonis* infection or seronegative toxocariasis).

Fascioliasis diagnosis was confirmed when both patients tested positive for *F. hepatica* excretion-secretion antigen by ELISA.¹¹ Repeat testing with new samples was again positive. After Institutional Review Board approval and informed consent, both patients received 10 mg/kg of triclabendazole under the Food and Drug Administration (FDA) Investigational New Drug (IND) program. Each patient submitted several additional stools in the week after treatment, but all were

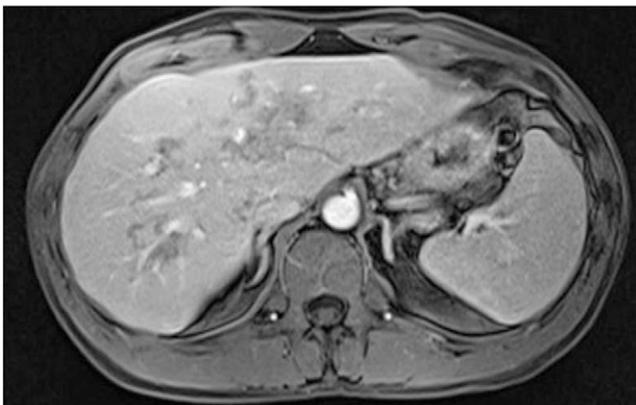


FIGURE 2. T1 weighted image of abdominal magnetic resonance imaging (MRI) with gadolinium for Patient Two. Multiple peripheral and central lesions are seen.

negative for ova and parasites. Patient Two's eosinophil count declined after treatment, but did not return to normal. Repeat stool testing 1 month after treatment did not show *D. fragilis* or *Fasciola* eggs. A repeat abdominal MRI four and one-half months after treatment showed marked improvement and near resolution of enhancing hepatic lesions, with persistent mild prominence of portal venous structures. Because of the persistent low level eosinophilia, Patient Two received a repeat dose of triclabendazole. His eosinophil count subsequently normalized, and repeat MRI 5 months later showed stable hepatomegaly and no liver lesions.

Both Patient One and Patient Two remain in good health. A limited public health investigation did not reveal additional cases.

DISCUSSION

Fascioliasis is a global disease¹² with an estimated prevalence of 2.6 million¹³ infected and 91 million at risk,¹ though these may be underestimates.¹⁴ Prevalence varies significantly within larger geographic regions^{2,15} with focal areas of increased prevalence.¹⁶ The worldwide burden of disease has been calculated at 35,000 disability adjusted life years,¹³ though this may also be a significant underestimate.³ The global expansion of fascioliasis has resulted in disease in diverse ecosystems, with a range of definitive herbivore hosts and intermediate lymnaeid snail hosts.¹⁴

In the United States, veterinary disease is prevalent in multiple areas,^{4,5} and may be expanding.¹⁷ *Fasciola hepatica* has long been present in cattle in California,¹⁸ and in some areas 90% of adult cattle are infected.¹⁷ This does not necessarily imply significant human population risk, as human fascioliasis prevalence does not always correlate with increased regional veterinary prevalence.^{14,15} Nevertheless, the persistence of this zoonotic cycle in herbivores provides a reservoir that may lead to current or future human cases of fascioliasis. Future changes in snail, cattle, or sheep populations, human population center expansion, climate change,¹⁹ and the reemerging practice of food foraging⁶ have the potential to increase human exposure to the agents of fascioliasis.

To date, three instances of fascioliasis acquired in the continental United States have been reported in the medical literature. Norton and Monroe⁸ described a 50-year-old female with a 9-year history of recurrent abdominal pain with a *F. hepatica* fluke identified at cholecystectomy in 1960. The patient and three neighbors developed fever, abdominal pain, and eosinophilia after eating watercress in 1951 in Calistoga, California (East of Marin County and North of San Francisco). Hauser and Bynum¹⁰ described a 42-year-old woman with a long history of "chronic active hepatitis," and inflammatory bowel disease over almost 20 years. Subsequent evaluation showed findings consistent with sclerosing cholangitis and a liver cyst with parasitic contents. *Fasciola hepatica* serology was positive. Finally, dual reports describe a 51-year-old male in Florida with fascioliasis acquired from eating watercress in Florida.^{9,20} In addition to the above, over 20 cases were described in various locations in Hawaii in the 1950s.²¹

Aside from the domestically acquired cases mentioned, a limited number of cases have been diagnosed and reported in immigrants.^{7,22} It is perhaps surprising that fascioliasis in the United States is rarely diagnosed in the United States despite immigrant populations from endemic regions, and a domestic

reservoir of disease. However, the paucity of diagnosed disease does not necessarily mean that fascioliasis is rare in a region or country. A recent cross-sectional serologic study in Haiti highlighted that fascioliasis subpopulation seroprevalence may be higher than would be expected from reported cases.²³ Similarly, unsuspected seroprevalence has also been found in Mexico City schoolchildren, where 1.51% (and 2.48% from other Mexican states) were seropositive to *F. hepatica*.²⁴ These studies raise the question of whether similar unsuspected infected populations exist in the United States, both among immigrants and within domestic endemic areas. Further study is required to clarify the true prevalence of imported and domestic human fascioliasis in the United States, and to characterize the burden of undiagnosed disease.

These cases further highlight difficulties in diagnosis of acute fascioliasis. Diagnosis first requires recognition of potential cases. Familiarity of clinicians and radiologists with the epidemiology, clinical presentation, and the typical imaging findings such as hypodense subcapsular lesions²⁵ on computed tomography scans would aid disease diagnosis. Serology is a cornerstone of acute fascioliasis diagnosis. Serology testing at a commercial laboratory, which uses a delipidized crude extract of adult *F. hepatica* worms, was consistently below the positive cutoff for Patient One. Patient Two's commercial laboratory did not offer *Fasciola* serology testing. Multiple barriers were encountered in getting both patients' blood drawn and sent off to the reference laboratory. Commercial laboratories for both patients were alerted to the concern for fascioliasis when stools were sent for analysis, though communication with the actual laboratory technicians was difficult. Ongoing advances in serologic, antigen-based, and molecular diagnosis³ will be most useful in hyperendemic regions, but would hopefully filter back to aid diagnosis in domestic locales.

Triclabendazole is a recommended treatment of fascioliasis,²⁶ though it is an investigational drug in the United States. Nitazoxanide, which is available in the United States, has shown some efficacy in chronic infection.²⁷ Patient One improved clinically and had reduction in eosinophil counts with nitazoxanide. Nitazoxanide was not used for Patient Two, because it was anticipated he would receive triclabendazole as soon as the diagnosis was confirmed. The other question that arose was how to adjudicate successful treatment. Patient Two experienced marked improvement in eosinophilia after receiving triclabendazole, but still had residual eosinophilia 5 months later. Eosinophilia resolves within 60 days in patients treated for acute²⁵ and chronic fascioliasis,²⁸ though in other parasite-endemic settings persistent eosinophilia is common 3 months after treatment.²⁹ Patient Two also had recent *D. fragilis*, which is associated with low level eosinophilia,³⁰ though eosinophilia persisted after eradication of this coinfection. Patient Two's eosinophil count normalized eventually after a second treatment with triclabendazole suggesting a response to the second dose.

The diagnosis of fascioliasis was based on clinical scenario, epidemiology with shared watercress ingestion, characteristic imaging findings, and serologic testing. Although identification of eggs in stool would have further confirmed the etiology, both patients were identified in the acute stage where eggs are not yet present. We did rely on off-site commercial laboratories for stool ova analysis. Other potential etiologies for their clinical syndromes were evaluated. *Toxocara* serol-

ogies were negative for both patients. *Baylisascaris procyonis* is endemic in California, though both patients lacked definitive brain or eye involvement typical of diagnosed cases.³¹ Other migrating parasites were considered much less likely or were excluded by serologic testing. Although we cannot identify the species, infection was likely *F. hepatica*, largely because it is more prevalent than *F. gigantica*.

CONCLUSION

Fascioliasis may be acquired and cause disease in Northern California. Further study is needed to determine if the disease is rare or simply underdiagnosed. Patients with eosinophilia and unexplained liver processes should be assessed for fascioliasis.

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