

## Biliary *Strongyloides stercoralis* With Cholecystitis and Extensive Portal Vein Thrombosis

Laura M. Filkins,<sup>1,2\*</sup> David C. Gaston,<sup>3,4</sup> Blaine Mathison,<sup>2</sup> Timothy Smith,<sup>4</sup> Marc Roger Couturier,<sup>1,2</sup> Ryan D. Murphy,<sup>3</sup> Claire Ciarkowski,<sup>3</sup> Kimberly E. Hanson,<sup>2,4</sup> and Paloma F. Cariello<sup>4</sup>

<sup>1</sup>Department of Pathology, <sup>3</sup>Department of Internal Medicine, and <sup>4</sup>Division of Infectious Diseases, The University of Utah, Salt Lake City, Utah; <sup>2</sup>ARUP Laboratories, Salt Lake City, Utah

We report the rare finding of *Strongyloides stercoralis* rhabditiform larvae in biliary fluid, here associated with cholecystitis and near total portal vein thrombosis. The role of *S. stercoralis* leading to atypical clinical presentations and difficulty diagnosing strongyloidiasis in such patients with appropriate geographic exposure is discussed.

**Keywords.** biliary strongyloidiasis; cholecystitis; *Strongyloides stercoralis* diagnosis.

*Strongyloides stercoralis* is a globally endemic parasitic nematode infecting up to 100 million individuals. Individuals at highest risk are those in high-burden areas, those living in poor sanitary conditions, and those who are immunosuppressed, particularly associated with human T-cell leukemia virus type 1 (HTLV-1) infection and corticosteroid treatment [1].

The complex life cycle of *S. stercoralis* leads to different infection courses ranging from low-burden asymptomatic chronic infection to hyperinfection and dissemination. Host immunosuppression permits hyperinfection and/or dissemination of infectious filariform larvae in nearly any tissue [2]. Isolation of non-infective-stage rhabditiform larvae outside the gastrointestinal (GI) tract is extremely uncommon in immunocompetent hosts. Herein we report the rare finding of *S. stercoralis* rhabditiform larvae in the biliary fluid of an immunocompetent host; this is the first report of associated portal vein thrombus secondary to biliary strongyloidiasis.

## CASE REPORT

The patient is a man in his 50s who immigrated to the United States more than 25 years prior to presentation from Sudan. His medical history is notable only for hypertension. He presented with 4 days of diffuse abdominal pain, nonbilious vomiting, and constipation. He was tachycardic (112 bpm) and hypotensive (77/56 mmHg) on presentation. Admission laboratory analysis revealed leukocytosis (16.2 k/ $\mu$ L; 94% granulocytes, 34% bands, 0.1% eosinophils), thrombocytopenia (75 k/ $\mu$ L), elevated D-dimer (3.9 ug/mL), elevated alkaline phosphatase (408 u/L), hepatitis (AST 181u/L, ALT 281 u/L), hyperbilirubinemia (total bilirubin 5.9 mg/dL), and elevated lipase (1620 u/L). He was admitted with a presumptive diagnosis of cholangitis and pancreatitis, received fluid resuscitation, and was administered piperacillin/tazobactam.

Non-contrast-enhanced abdominal computerized tomography (CT) scan revealed gallbladder distension to 4.5 cm, intrahepatic and extrahepatic biliary ductal dilation, and dilation of the common bile duct (0.9 mm at the ampulla) without visible obstruction. The pancreatic duct was not dilated. Abdominal ultrasound did not identify cholelithiasis. An endoscopic retrograde cholangiopancreatography (ERCP) demonstrated a grossly normal upper GI tract, ampulla, and extrahepatic biliary system. No definitive filling defect was observed. A temporary stent was placed with passage of bile and scant pus.

A contrasted pancreatic dual-phase CT scan was obtained due to persistent hyperbilirubinemia. This study showed near total thrombotic occlusion of the portal venous system, gallbladder distension with circumferential wall thickening, and resolution of biliary ductal dilation following stent placement (Figure 1A). Cholecystitis was diagnosed, and a percutaneous biliary tube was placed.

A thorough evaluation did not reveal an etiology for the portal vein thrombus other than cholecystitis. The patient was anticoagulated, and antibiotics were transitioned to ciprofloxacin and metronidazole. Blood cultures remained negative. Biliary fluid culture grew *Enterobacter gergoviae* and *Enterobacter cloacae* susceptible to all administered antibiotics, as well as *Candida glabrata*.

Incidentally, bacterial growth morphology consistent with tracks made by mobile parasites was noted on blood agar plates incubating biliary fluid from the percutaneous drain (Figure 1B). Ova and parasite (O&P) examination of the biliary fluid was performed, which revealed *S. stercoralis* rhabditiform larvae (Figure 1C). Serology for *Strongyloides*, HIV-1, HIV-2, and HTLV-1 was negative. The patient had no known corticosteroid use or history of immunosuppression. Ivermectin 15 mg

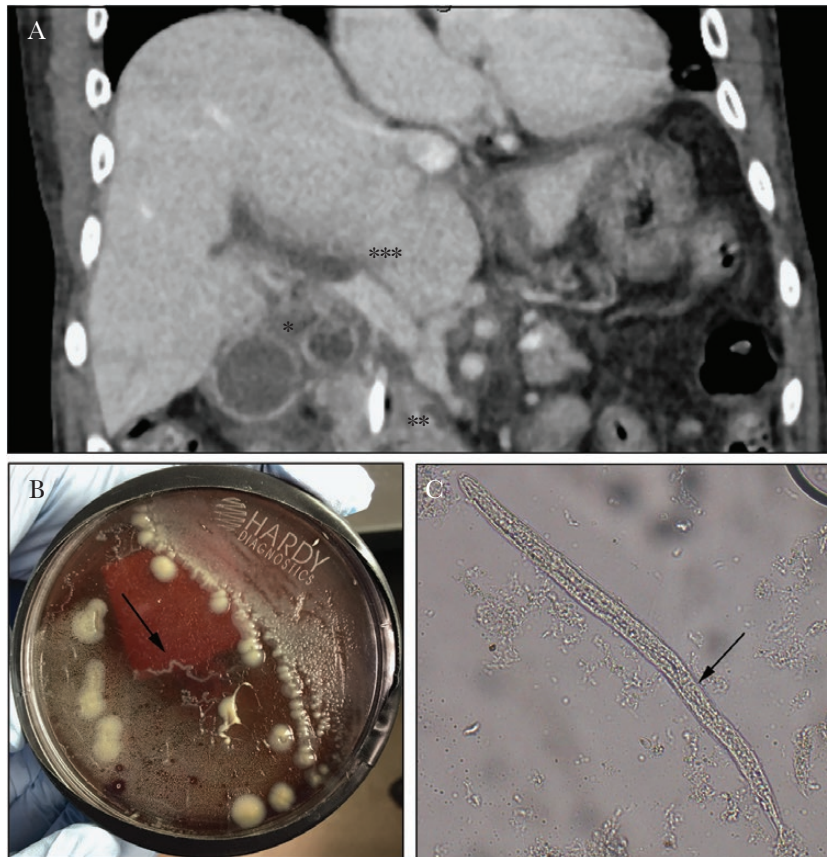
Received 15 June 2017; editorial decision 28 September 2017; accepted 4 October 2017.

Correspondence: L. M. Filkins, PhD, ARUP Laboratories, Department 115, 500 Chipeta Way, Salt Lake City, UT 84108 (laura.filkins@aruplab.com).

\*Equal contribution

### Open Forum Infectious Diseases®

© The Author 2017. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (<http://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact [journals.permissions@oup.com](mailto:journals.permissions@oup.com). DOI: 10.1093/ofid/ofx217



**Figure 1.** (A) Coronal view of contrasted pancreatic-phase computed tomography scan. The image exhibits gallbladder dilation with circumferential wall thickening consistent with cholecystitis (right and left of \*), presence of biliary stent with decompression of biliary system (\*\*), and thrombotic occlusion of the portal vein (\*\*\*, contrast media abuts radiolucent thrombus). (B) Culture of the gallbladder fluid on Columbia agar + 5% sheep's blood showing *Strongyloides stercoralis* trails of bacterial growth indicated by the arrow. (C) Wet mount examination of rhabditiform larva in gallbladder fluid + 10% formalin. Larva size ~200 µm; genital primordium is indicated by the arrow (400× magnification).

daily was administered for 2 days without complication. He was discharged with appropriate follow-up.

## DISCUSSION

This is the first report describing cholecystitis and portal vein thrombosis associated with biliary strongyloidiasis as the suspected underlying etiology. The biliary system is not known to be involved in the *S. stercoralis* parasitic life cycle, and detection of *S. stercoralis* larvae in biliary fluid is infrequently reported. A review of published cases revealed 3 prior reports of *S. stercoralis* rhabditiform larvae in biliary fluid [3–5]. Although larval presence outside of skin, lungs, or intestines defines dissemination, we do not propose that this patient had disseminated disease. True disseminated infection occurs when filariform larvae penetrate tissue and reside in organs atypical of their normal life cycle. In the current case, only rhabditiform larvae (which are unable to penetrate tissue) were observed in the biliary fluid, indicative of larval migration from the intestines to connected organs. In contrast, in disseminated disease, rhabditiform larvae may only be present within extra-intestinal organs due to the continued parasitic life cycle and are expected in the

copresence of filariform larvae. Further, dissemination typically occurs in patients with a suppressed immune response [6]. This patient had no evidence of immunosuppression but presented with *S. stercoralis* extra-intestinal disease, representing a diagnostic middle ground between disseminated strongyloidiasis and classic infection. The presence of biliary strongyloidiasis in this immunocompetent host highlights the importance of considering *S. stercoralis* infection when evaluating patients with hepatobiliary disease and geographic exposure to *S. stercoralis*.

The precise role of *S. stercoralis* alone or in combination with *Enterobacter* spp. leading to cholecystitis is difficult to determine. Likely explanations include *S. stercoralis* causing cholecystitis, *S. stercoralis* passively depositing *Enterobacter* spp. and leading to cholecystitis, or the pathogens cooperatively precipitating cholecystitis [2]. Alternatively, the cholecystitis may be due to *Enterobacter* spp. alone with incidental presence of rhabditiform larvae and *Candida glabrata*. We propose that entry of *S. stercoralis* rhabditiform larvae into the patient's gallbladder precipitated cholecystitis with inflammation, leading to portal vein thrombosis and other associated findings. Parasite burden in the duodenum has been reported to produce inflammation

of the ampulla, papillitis, and subsequent biliary dilation with cholangitis, cholecystitis, and/or pancreatitis [3, 5, 7]. This mechanism did not underlie the presentation of this patient as duodenal inflammation and papillitis were not apparent on ERCP. Rather, we hypothesize that reflux of duodenal contents through a dysfunctional sphincter of Oddi introduced rhabditiiform larvae from the duodenum [8]. Interestingly, this patient received 1 month of tramadol prior to presentation due to an unrelated injury. Tramadol has been reported to cause sphincter of Oddi relaxation and could have contributed to sphincter dysfunction [9]. Alternatively, introduction from duodenal contents could occur upon ERCP and biliary stent placement, in which case larval presence would not underlie cholecystitis. The prevalence of low-level migration of *S. stercoralis* rhabditiiform larvae causing colonization of the biliary system has not been documented but should not be ruled out as another possible explanation. This patient also presented with idiopathic dilation of his common bile duct, similar to prior reports [4, 10, 11]. Accordingly, involvement of the hepatobiliary system with biliary dilation, cholangitis, cholecystitis, and/or pancreatitis may be an underappreciated component of *S. stercoralis* pathogenesis.

Diagnosis of strongyloidiasis can be challenging despite the high global burden of *S. stercoralis* infections. Clinical manifestations vary extensively, and risk of exposure may precede presentation by many years. Eosinophilia (>400 eosinophils/ $\mu$ L) occurs in less than 50% of chronic strongyloidiasis cases for some populations [12]. As seen in the current patient, lack of eosinophilia does not rule out infection. Stool analysis (microscopic O&P examination or agar culture) is the primary method of diagnosis for active infection, but larvae are often shed transiently and in low numbers, requiring up to 7 consecutive stool analyses [13]. Stool O&P examination was not clinically necessary for diagnosis of strongyloidiasis in this patient and therefore not performed. Serology for *S. stercoralis* may aid in the diagnosis of chronic strongyloidiasis. However, the clinical sensitivity of serological methods for *S. stercoralis* range from 70% to 95%, and agreement between commercial tests can be as low as 65% [14, 15]. Serologic testing for *S. stercoralis* IgG was negative in this patient. The serologic test used for this patient's serum (SciMedx enzyme-linked immunosorbent assay) has a reported clinical sensitivity of 85.5% [15]. False negatives are most common in patients with severe immune suppression or acute infection, and in patients without hyperinfection or disseminated infection; the latter is consistent with this case. Despite negative serology, a definitive diagnosis

of strongyloidiasis was made via identification of live larvae in bile fluid.

## CONCLUSIONS

This is the first case report of portal vein thrombosis associated with strongyloidiasis and the fourth case documenting *S. stercoralis* rhabditiiform larvae in biliary fluid. Involvement of the hepatobiliary system may be an underappreciated component of the *S. stercoralis* life cycle. This case further highlights the clinical and laboratory challenges of diagnosing *S. stercoralis* infections and the importance of considering strongyloidiasis in patients with suspected geographic exposure.

## Acknowledgements

The authors appreciate the contributions of Jackie Bohn in clinical care, Richard Leake, MD, for radiographic review of CT images, and Sanefumi Tsuha, MD, for translation of articles in Japanese.

**Potential conflicts of interest.** All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

## References

1. Puthiyakunnon S, Boddu S, Li Y, et al. Strongyloidiasis—an insight into its global prevalence and management. *PLoS Negl Trop Dis* **2014**; 8:e3018.
2. Keiser PB, Nutman TB. *Strongyloides stercoralis* in the immunocompromised population. *Clin Microbiol Rev* **2004**; 17:208–17.
3. Hata H, USA F, Okamoto Y, Okubo H. A case of cholecystitis in which rhabditiiform larvae of *Strongyloides stercoralis* were detected by duodenal intubation. *J Kansai Med Univ* **1983**; 35:264–72.
4. Ishida H, Inoue T, Nishioka Y, et al. A case of biliary strongyloidiasis. *J Jpn Soc Clin Surg* **1991**; 52:2151–5.
5. Delarocque Astagneau E, Hadengue Antoine, Degott C, et al. Biliary obstruction resulting from *Strongyloides stercoralis* infection. Report of a case. *Gut* **1994**; 35:705–6.
6. Buonfrate D, Requena-Mendez A, Angheben A, et al. Severe strongyloidiasis: a systematic review of case reports. *BMC Infect Dis* **2013**; 13:78.
7. Ikeuchi N, Itoi T, Tonozuka R, et al. *Strongyloides stercoralis* infection causing obstructive jaundice and refractory pancreatitis: a lesson learned from a case study. *Intern Med* **2016**; 55:2081–6.
8. Berkmen YM, Rabinowitz J. Gastrointestinal manifestations of the strongyloidiasis. *Am J Roentgenol Radium Ther Nucl Med* **1972**; 115:306–11.
9. Wu SD, Zhang ZH, Jin JZ, et al. Effects of narcotic analgesic drugs on human Oddi's sphincter motility. *World J Gastroenterol* **2004**; 10:2901–4.
10. Dearden JC, Ayaru L, Wong V, van Someren N. The double duct sign. *Lancet* **2004**; 364:302.
11. Pijls NH, Yap SH, Rosenbusch G, Prenen H. Pancreatic mass due to *Strongyloides stercoralis* infection: an unusual manifestation. *Pancreas* **1986**; 1:90–3.
12. Biggs BA, Caruana S, Mhrshahi S, et al. Management of chronic strongyloidiasis in immigrants and refugees: is serologic testing useful? *Am J Trop Med Hyg* **2009**; 80:788–91.
13. Nielsen PB, Mojon M. Improved diagnosis of strongyloides stercoralis by seven consecutive stool specimens. *Zentralbl Bakteriol Mikrobiol Hyg A* **1987**; 263:616–8.
14. Bisoffi Z, Buonfrate D, Sequi M, et al. Diagnostic accuracy of five serologic tests for *Strongyloides stercoralis* infection. *PLoS Negl Trop Dis* **2014**; 8:e2640.
15. Anderson NW, Klein DM, Dornink SM, et al. Comparison of three immunoassays for detection of antibodies to *Strongyloides stercoralis*. *Clin Vaccine Immunol* **2014**; 21:732–6.