CASE REPORTS

# Gram negative rod meningitis due to *Strongyloides stercoralis*

Nicholas S. Hendren*, Shahzad Chindhy, Kaylee Shepard

*Department of Internal Medicine, The University of Texas Southwestern Medical Center, Dallas, Texas, USA*

**Received:** January 30, 2017 **Accepted:** March 8, 2017 **Online Published:** March 9, 2017
**DOI:** 10.5430/crim.v4n2p28 **URL:** https://doi.org/10.5430/crim.v4n2p28

## ABSTRACT

A 57-year-old male Mexican immigrant living in Dallas presented with altered mental status, progressive confusion, mild headache and fevers. He was diagnosed with embryonal liver sarcoma one year prior to admission and had recently started dexamethasone therapy for metastatic spinal lesions. Blood and cerebrospinal fluid cultures from a lumbar puncture were both positive for *Escherichia coli.* He was diagnosed with spontaneous gram negative rod (GNR) meningitis. Given his travel history, immunosuppression and GNR meningitis, a stool ova and parasite sample was obtained to screen for *Strongyloides stercoralis*. His stool was markedly positive for *Strongyloides stercoralis* larvae and he was further diagnosed with *Strongyloides hyperinfection* syndrome. *Strongyloides* is capable of chronically re-infecting human hosts without an external life cycle via autoinfection. In chronic infections, hyperinfection can be triggered with immunosuppressive medications, especially steroids. Disseminated *Strongyloides* should be considered as the source for unexplained GNR bacteremia or meningitis especially in immunosuppressed patients. Our patient likely had a chronic asymptomatic *Strongyloides* infection acquired in Mexico that became a hyperinfection resulting in GNR meningitis after starting high doses of dexamethasone.

**Key Words:** Strongyloides stercoralis, Gram negative rod meningitis, Strongyloides hyperinfection

## 1. INTRODUCTION

Spontaneous community acquired acute bacterial meningitis due to gram negative rod (GNR) infections is uncommon, occurring approximately in 1%-4% of cases of meningitis.[1] Spontaneous GNR meningitis has been rarely associated with infections of Strongyloides stercoralis as chronic infections can develop into hyperinfection.[2] Strongyloides stercoralis was originally described in 1876 in the stool of French soldiers with severe diarrhea stationed in Vietnam.[3] Strongyloidiasis is a neglected tropical disease that infects an estimated 30-100 million people mainly in developing countries, but remains endemic in rural pockets of the United States.[4,5] Studies in immigrant populations have shown a prevalence of infection up to 38% and living in an endemic area remains strong risk factor for infection.[4,6] We present a case of spontaneous community acquired acute bacterial meningitis due to a GNR infection associated with Strongyloides stercoralis hyperinfection syndrome.

## 2. CASE PRESENTATION

A 57-year-old Hispanic male with a history of embryonal sarcoma of the liver presented with one day of altered mental status. The day prior to admission he had a witnessed mechanical fall without head trauma or a loss of consciousness at a grocery store. He developed progressive confusion, chills, mild headache and fevers in addition to his baseline abdominal pain. A review of systems was otherwise unremarkable. He was diagnosed with stage IV embryonal sarcoma of the liver one year prior to admission. Despite local surgical resection and adjuvant chemotherapy shortly after diagnosis, his cancer progressed with recurrent liver lesions and metastatic spinal disease. His spinal disease required the initiation of palliative radiation and dexamethasone therapy (8 mg three times per day) one month prior to presentation. There were no surgeries or gastrointestinal procedures within one year of presentation. He was an immigrant from Mexico and has lived in Dallas, Texas since immigration in 2008.

*Correspondence: Nicholas S. Hendren, MD; Email: nicholas.hendren@phhs.org; Address: 5323 Harry Hines Blvd., Dallas, TX 75235, USA.

Admission vital signs were unremarkable. On exam he appeared comfortable, but was only oriented to his person. His remaining physical exam was largely unremarkable except for baseline right upper quadrant and back pain. Admission labs were remarkable for a mildly elevated liver enzyme tests attributed to his liver carcinoma, guaic positive stool and a leukocytosis of $27.4 \times 10^9$ per liter without eosinophilia (see Table 1). A review of a complete blood count obtained five days prior to starting steroids and one month prior to admission was notable for an absolute eosinophil count of $2.45 \times 10^9$ per liter. A computed tomography scan of the abdomen demonstrated an interval increase of metastatic disease causing spinal cord stenosis as well as increased size of hepatic lesions consistent with progression of the embryonal carcinoma. Given his altered mental status a lumbar puncture was obtained on admission and revealed glucose < 2 mg/dl, protein of 495 mg/dl, 82,350 nucleated cells per liter and a positive culture for Escherichia coli (see Table 2). Admission blood cultures were positive for *Escherichia coli* on day two of admission. He was treated with intravenous ceftriaxone 2 grams twice daily with a plan for 21 days of intravenous antibiotics.

**Table 1.** Admission labs

| Lab | Result | Normal | Lab | Result | Normal |
|---|---|---|---|---|---|
| Sodium | 135 | 135-145 mmol/l | WBC* | 27.4 | 4.22-10.33 × $10^9$/l |
| Potassium | 4.6 | 3.6-5.0 mmol/l | Hemoglobin | 15.1 | 13.2-16.9 g/dl |
| Calcium | 8.8 | 8.4-10.2 mg/dl | Platelets | 213 | 160-383 × $10^9$/l |
| Anion Gap | 16 | 12-16 | Eosinophils | < 0.03 | 0.04-0.62 × $10^9$/l |
| Blood Urea | 24 | 6-23 mg/dl | AST* | 36 | 10-50 units/l |
| Creatinine | 0.54 | 0.67-1.17 mg/dl | ALT* | 74 | 10-50 units/l |
| Albumin | 3.6 | 3.5-5.2g/dl | ALP* | 212 | 20/129 units/l |

*Note.* *ALT: alanine transaminase; ALP: alkaline phosphatase; AST: aspartate aminotransferase; WBC: white blood cell count.

Given his immunosuppression, prior eosinophilia, travel history and GNR meningitis, a stool ova and parasite was obtained to screen for Strongyloides stercoralis. His stool was positive for abundant Strongyloides stercoralis larvae and he was diagnosed with Strongyloides hyperinfection syndrome. He was placed on isolation contact precautions and initiated on a daily oral dose of 200 mcg/kg of ivermectin with initial plans for a two week course pending stool larval clearance and repeat lumbar puncture with parasitic studies. However, given the patient's poor overall prognosis, the patient declined further medical therapy and elected comfort care. He was discharged home with hospice after an abbreviated treatment course of 10 days of ceftriaxone and three days of ivermectin.

## 3. DISCUSSION

Historically screening for Strongyloides has been accomplished with stool samples; however, a single stool screening is inadequate to detect larvae in up to 70% of cases.[3] In chronic asymptomatic infections adult worms may lay as few as 10-15 eggs per day, which makes stool screening difficult.[2] Repeated stool examinations can increase the sensitivity of diagnosis to 50% with three examinations and is further improved to nearly 100% by seven serial examinations.[3] Using a blood agar method with stool to diagnose an active infection improves the sensitivity to 96%, as serpiginous tracks of bacteria grow along the track of mobile larvae.[2,3] Serological tests are available and are sensitive, but not specific for an active infection.[2] For cases of hyperinfection, the stool burden of larvae is usually significantly higher and may result in a higher sensitivity for stool screening than in chronic infection.

**Table 2.** Cerebrospinal fluid studies (CSF) studies

| Lumbar Puncture CSF Studies | | |
|---|---|---|
| **Lab** | **Result** | **Normal** |
| Glucose | < 2 | 40-70 mg/dl |
| Protein | 495 | 15-45 mg/dl |
| RBC | 3,250 | ≤ 0/mcl |
| Nucleated Cells | 82,350 | 0-5/mcl |
| Smear | Many GNRs | Negative |
| Culture | Escherichia coli | Negative |

Strongyloides stercoralis has both free living and parasitic stages.[2] In the parasitic stage adult female worms lay eggs in the intestinal mucosa that hatches into rhabditiform larvae, which are excreted through the stool.[2] Once excreted these free living larvae can progress into free-living adult worms to undergo sexual reproduction or become infectious filariform larvae.[2] Filariform larvae transcutaneously infect a human host and migrate to the small intestine where female larvae begin to lay eggs.[2] Some of the hatched rhabditiform larvae transform into invasive filariform larvae before being excreted and are capable of re-infecting or "auto infecting" the host through the intestine wall or perianal skin.[2] Strongyloides stercoralis therefore can maintain a chronic infection due to its ability to complete an asexual autoinfection that can persist indefinitely as was the case with our patient.[2]

The majority of infected individuals remain asymptomatic.[2] Symptomatic human parasitic infections include acute, chronic, disseminated and hyperinfections.[2] Acute strongyloidiasis can present with local skin irritation at the site of infection. This can be followed by a productive or non-productive cough due to pulmonary irritation from larval migration through the lungs. Manifestations may also include wheezing, chest pain, hemoptysis, palpitations, atrial fibrillation, dyspnea and respiratory alkalosis.[2,3] Gastrointestinal symptoms include diarrhea, constipation, loss of appetite and abdominal pain. Sputum can contain larvae.[2] A chest X-ray can show bilateral or focal pulmonary interstitial infiltrates.[3] Larvae can be isolated from the stool in 3-4 weeks after an initial infection and eosinophilia is seen in a minority of infections.[4] Chronic strongyloides infection is frequently asymptomatic; however, chronic symptoms can include vomiting, diarrhea, weight loss, constipation, anal puritis and larva currens are common.[2] In a non-disseminated infection, the numbers of larvae is increased, but remain confined

to the gastrointestinal and pulmonary tracts.[2] In disseminated infections the larvae migrate through organs other than the gastrointestinal tract and pulmonary system.[2] Extrapulmonary migration appears to routinely occur in chronic infections and does not necessarily imply a more severe infection.[2]

Strongyloides hyperinfection syndrome (SHS) is a rare disorder that results in a high mortality rate documented up to 87%.[3,4] SHS refers to an accelerated autoinfection resulting in a significant increase in the number of larvae with associated signs and symptoms attributable to increased larval migration.[2] Risk factors for developing SHS include autoimmune disorders, hematologic malignancies, solid organ transplants, and human T-lymphotropic virus type 1 infection.[2–4] A review of 133 patients with SHS observed that 83.5% of patients were immunosuppressed with long-term steroids with a median dose of 40 mg daily and average onset of symptoms 42 days after initiating steroids.[4] Our patient was initiated on high dose steroids approximately one month prior to admission and likely prompted SHS in our patient.

Presenting symptoms of SHS commonly include fever, respiratory symptoms, gastrointestinal symptoms, septic shock and the need for mechanical ventilation.[4] Occult blood secondary to esophagitis, gastritis, duodenitis and colitis is not uncommon.[2] Larva currens along the lower trunk, thighs and buttocks are common and associated with intense pruritis.[2] Larvae have been found in essentially every organ in cases of hyperinfection including the spinal fluid, epidural, subdural and subarachnoid spaces.[2] Gram negative rod infections often complicate SHS likely due to bacterial gut translocation due to filarial worm invasion through the intestine wall.[2,3] In a review of 133 patients with SHS, bacterial infections were observed in 51 patients with 34 cases of bacteremia, 23 cases of pneumonia and 14 cases of meningitis.[4] Causative organisms of infections have been previously reported as *Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae, Pseudomonas, Enterococcus faecalis* and *Streptococcus bovis*.[2–4]

Treatment with albendazole, thiabendazole or ivermectin is effective for chronic infections; however, a single dose of enteral ivermectin taken twice two weeks apart appears to be the most effective.[4,7] Treatment of hyperinfection should continue until clinical symptoms abate and until fecal larval cultures are negative, which typically takes at least two weeks.[2] The preferred agent for extended treatment is ivermectin due to better efficacy and fewer side effects.[2,4,7] If possible, immunosuppression should be discontinued or tapered. Given the on-going need for steroids and relative safety of ivermectin we elected to continue daily treatment until the patient elected comfort care.

In sum, our patient presented with SHS which is a rare cause of GNR meningitis and bacteremia. Given his prior residence in Mexico, previous eosinophilia and immunosuppression a stool ova a parasite test was obtained and markedly positive. Eosinophilia is not always present during Strongyloides infections with or without complications and steroids may mask eosinophilia in SHS.[2] Unrecognized Strongyloides stercoralis infections with associated bacteremia have a high mortality and screening for Strongyloides stercoralis infections should be considered for high risk patients prior to starting long-term steroids. The case serves as a reminder that clinicians should have a high level of suspicion for Strongyloides stercoralis in patients with unexplained GNR infections, immunosuppression and a history of travel to endemic areas of transmission.

## ACKNOWLEDGEMENTS

We would like to thank our colleagues at the University of Texas Southwestern for their insight and expertise as well as the staff, staff support and our patient for providing us with the support and permission to author this paper.

## CONFLICTS OF INTEREST DISCLOSURE

The authors have no competing interests to declare.

## REFERENCES

[1] Bouadma L, Schortgen F, Thomas R, et al. Adults with spontaneous aerobic Gram-negative bacillary meningitis admitted to the intensive care unit. Clin Microbiol Infect. 2006; 12(3): 287-90. PMid:16451418 https://doi.org/10.1111/j.1469-0691.2005.01346.x

[2] Keiser PB, Nutman TB. Strongyloides stercoralis in the Immunocompromised Population. Clin Microbiol Rev. 2004; 17(1): 208-17. https://doi.org/10.1128/CMR.17.1.208-217.2004

[3] Siddiqui AA, Berk SL. Diagnosis of Strongyloides stercoralis infection. Clin Infect Dis. 2001; 33(7): 1040-7. PMid:11528578 https://doi.org/10.1086/322707

[4] Geri G, Rabbat A, Mayaux J, et al. Strongyloides stercoralis hyperinfection syndrome: a case series and a review of the literature. Infection. 2015; 43(6): 691-8. PMid:26008854 https://doi.org/10.1007/s15010-015-0799-1

[5] Schar F, Trostdorf U, Giardinaet F, et al. Strongyloides stercoralis: Global Distribution and Risk Factors. PLoS Negl Trop Dis. 2013; 7(7): e2288. PMid:23875033 https://doi.org/10.1371/journal.pntd.0002288

[6] Nuesch R, Zimmerli L, Stockliet R, et al. Imported strongyloidosis: a longitudinal analysis of 31 cases. J Travel Med. 2005; 12(2): 80-4. PMid:15996452 https://doi.org/10.2310/7060.2005.12204

[7] Suputtamongkol Y, Premasathian N, Bhumimuang K, et al. Efficacy and safety of single and double doses of ivermectin versus 7-day high dose albendazole for chronic strongyloidiasis. PLoS Negl Trop Dis. 2011; 5(5): e1044. PMid:21572981 https://doi.org/10.1371/journal.pntd.0001044