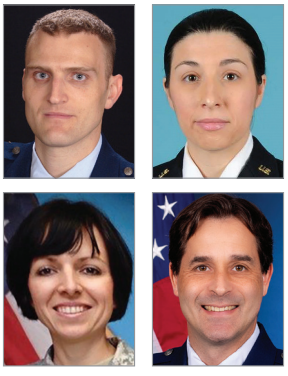
Neuroschistosomiasis

Complete neurologic recovery after acute cauda equina syndrome

By Paul M. Elsbernd, MD; Kathryn J. Lago, DO; Tatjana P. Calvano, DO; and John H. Sladky, MD



Case Report

Clinical Presentation

Mr. M, age 30, presented to a US hospital with severe headaches and abdominal pain with no clearly identifiable cause. He was discharged with a diagnosis of suspected kidney stones. He returned twice more to the same emergency room with similar symptoms and was discharged home after both visits. After 10 days of progressive symptoms, he developed paresthesias, saddle anesthesia, and urinary/fecal retention. He returned to the same hospital and was subsequently transferred emergently to a hospital with neurologic specialty capability.

History and Physical Examination

Mr. M, from the central African country Chad, had been in the US for the prior 6 months and had no known medical history. He denied any tobacco, alcohol, or recreational drug use. He reported having lived in the capital city of Chad for his entire life and denied drinking, swimming or bathing in untreated freshwater, or any other unusual exposures. He denied any medical family history. On arrival after his emergent transfer, his neurologic examination revealed near-complete sensory loss of the right lower extremity, perianal area, and genitalia with a spinal cord sensory level at L1/T12. Neurologic examination also demonstrated hyporeflexia of the right lower extremity and loss of the cremasteric reflex bilaterally with reduced rectal tone.

Diagnostic Studies

The findings of Mr. M's initial laboratory evaluation were notable for mild eosinophilia (absolute eosinophil count [AEC] 550) and elevated C-reactive protein (CRP) of 0.90 (reference value=0-0.49). Before catheterization, urinalysis was notable for mild hematuria (10 red blood cells (RBCs) / high-power field (HPF); reference value=0.3 RBCs/HPF). Whole spine MRI showed central spinal cord enhancement from T1 through the conus medullaris with mild cord expansion and profound anterior cord enhancement from T8 through T11 with nerve root enhancement in the cauda equina (Figures 1 and 2).

A lumbar puncture was subsequently performed and cerebrospinal fluid (CSF) analysis findings were notable for elevated protein (130 mg/dL) and increased nucleated cells (65/mcL in tube 2 and 70/mcL in tube 4) with pathology review demonstrating mature-appearing lymphocytes and increased eosinophils. Importantly, the CSF RBC count was normal, cytology revealed no malignant cells, and a comprehensive infectious evaluation was negative. All relevant lab results and reference values are presented in the Table.

Based on the peripheral and CSF eosinophilia and Mr. M's country of origin, both general serum schistosomiasis IgG and species-specific antibody tests were ordered. Urine was tested for ova and parasites on multiple occasions and findings were negative.

Diagnosis and Treatment

Mr. M was admitted to the hospital, and on the third day of his stay, while awaiting further testing, methylprednisolone 1 g/day was started empirically and continued for 5 days with no improvement in neurologic symptoms. Although a parasitic infection was on the differential diagnosis, antiparasitic treatment was not initiated because of Mr. M's denial of swimming or wading in any freshwater at any time in his life, his lifelong residence in an urban setting, and the appropriately broad differential diagnosis for transverse myelitis in the setting of mild eosinophilia. Consultations with experts in parasitic infections of the central nervous system (CNS) also expressed concern for potential adverse effects of praziquantel in the setting of alternate CNS parasitic infections (eg, angiostrongyliasis), which contributed to the decision not to give empiric antiparasitic treatment. Mr. M was discharged from the hospital after 7 days.

Commercial lab initial results (returned 4 days postdis- *Schistosoma* antibody titer (0.36 optical density [OD],

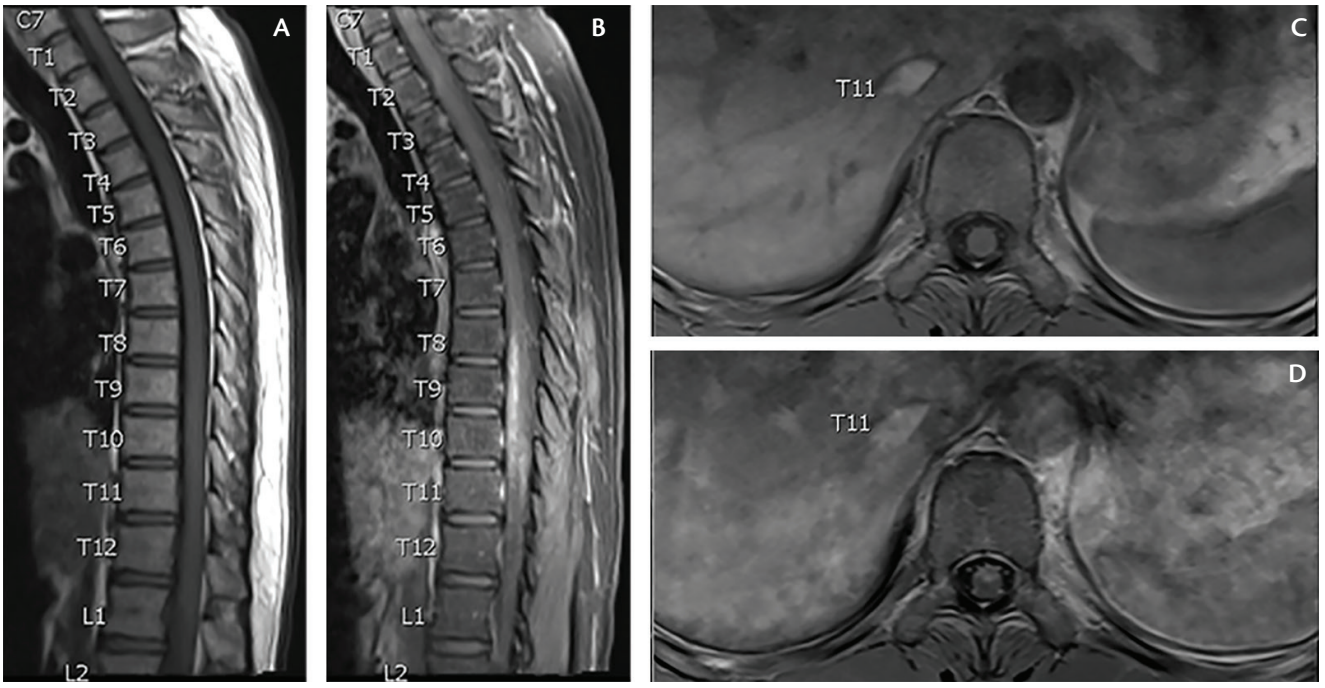


Figure 1. Sagittal T1 pre- (A) and postcontrast (B) MRI of the thoracic and lumbar spine showing anterior cord enhancement from T8 through T11 and axial T1 pre- (C) and postcontrast (D) MRI showing enhancement of the conus medullaris and nerve roots from T2 through L1.

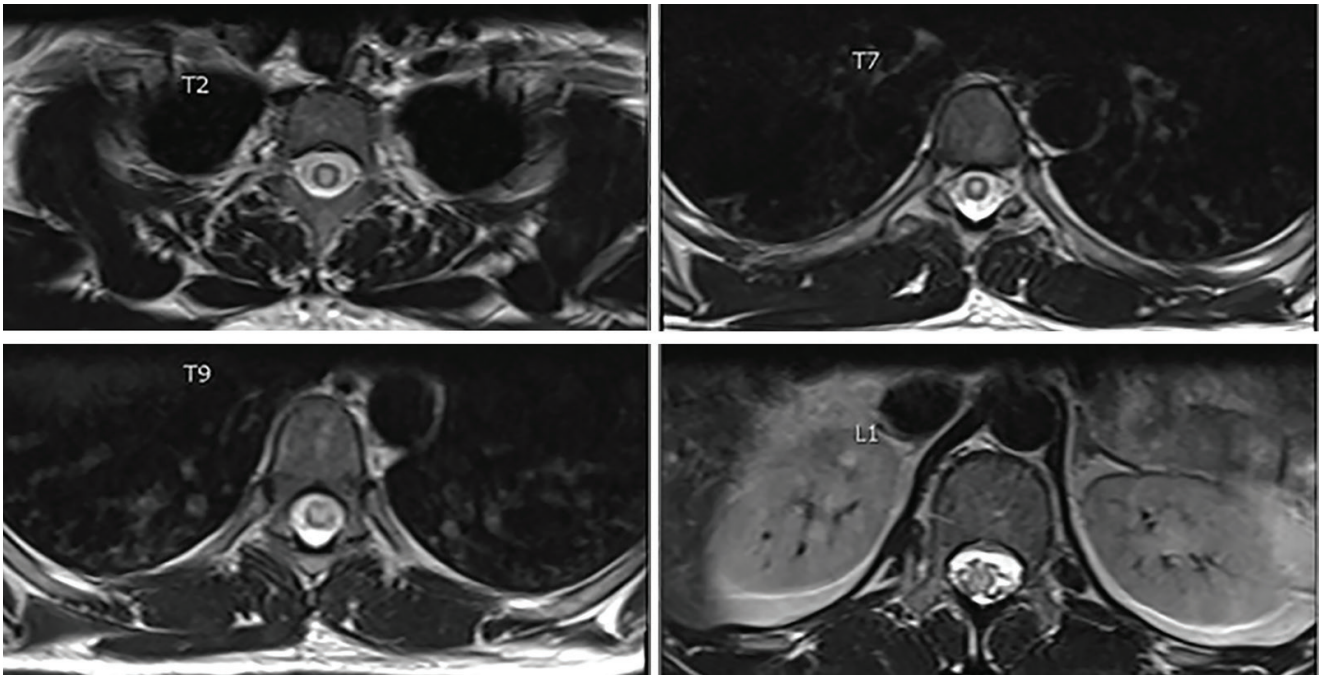


Figure 2. Axial T2 postcontrast MRI showing central cord hyperintensity and enhancement of T2 through L1.

TABLE. MR. M'S LABORATORY TEST FINDINGS

Laboratory Test	Results	Reference Value
Serum		
Complete blood count (CBC)	6.79>14.9 45.7<328 8.2% eosinophils (AEC=550)	<6.0% eosinophils
Erythrocyte sedimentation rate (ESR)	20	≤20
C-reactive protein (CRP)	0.90	≤0.49
Antibody (Ab) panels (antinuclear Ab, aquaporin 4, paraneoplastic Abs)	Negative	Negative
Viral and borrelial panel (HIV/EBV/RPR/ FTA/ Lyme/Coxiella)	Negative	Negative
Hepatitis panel (acute and chronic)	Negative	Negative
Quantiferon gold	Negative	Negative
Coccidioides	Negative	Negative
Schistosomal FMI	0.36 optical density (OD)	0-0.19 OD
Schistosomal FAST-ELISA	100, positive for *S. mansoni*	Negative (<10)
Schistosomal immunoblot	Positive for *S. mansoni*	Negative
Cerebrospinal fluid (CSF)		
Protein	130mg/dL	15-40mg/dL
Glucose	52mg/dL	40-70mg/dL
Red blood cells (RBCs)	1/mcL	0-8/mcL
Nucleated cells	70/mcL	0-8/mcL
Cytology	Eosinophilia	No eosinophils
Gram stain and culture	Many white blood cells (WBCs) no organisms	No growth
Meningitis encephalitis panel (PCR)	Negative	Negative
West Nile virus IgG/IgM	Negative	Negative
HTLV 1/2 IgG	Negative	Negative
Urinalysis		
RBC Count	10 RBC/HPF	0-3 RBC/HPF
Ova & parasites	None	None

Abbreviations. AEC, absolute eosinophil count; EBV, Epstein-Barr virus; HPF, high-power field; FAST ELISA, Falcon assay screening test enzyme-linked immunoassay; FMI, fluorescent microscopy immunoassay FTA, fluorescent treponemal antibody; HTLV, human T-cell lymphocyte virus; PCR, polymerase chain reaction; RPR, rapid plasma reagin

reference value=0-0.19 OD), making a diagnosis of neuroschistosomiasis more likely. Mr. M was readmitted and treated with a 5-day course of praziquantel 50 mg/kg/day in 3 divided doses, 7 days of intravenous (IV) methylprednisolone 15 mg/kg, and then a 4-week prednisone taper for presumptive neuroschistosomiasis.

Follow-Up

At his initial 1-week follow-up visit, Mr. M's sensory symptoms and gait were improving, but he was still unable to obtain an erection or urinate independently, requiring intermittent catheterization. The prednisone taper was continued, and subsequent species-specific serum antibody immunoblotting from the Centers for Disease Control (CDC) confirmed the presence of IgG for *Schistosoma mansoni*. Findings of an enzyme-linked immunoassay (ELISA) for *Schistosoma* ELISA were also positive (100, reference value<10). At his 1-month follow-up, Mr. M was able to urinate, defecate, and obtain an erection independently. His reflexes and gait had normalized, and his sensory symptoms had nearly resolved with minimal residual numbness of the right plantar foot. Serial repeat serum testing showed sustained resolution of peripheral eosinophilia.

Discussion

Epidemiology

Neuroschistosomiasis is an underrecognized complication of the second most common parasitic infection in the world. It affects between 1% and 4% of the estimated 200 to 300 million people with systemic schistosomal infections.[1] *Schistosoma mansoni* is 1 of 5 major schistosomal species and is found throughout Africa within the freshwater of the great lakes, rivers, and smaller bodies of water. Worldwide, 90% of cases of neuroschistosomiasis are found in sub-Saharan Africa,[2] although the ever-increasing frequency of global travel has resulted in an increasing number of cases of neuroschistosomiasis outside of endemic areas.[3-6] Although neuroschistosomiasis is thought to be rare, there is well-documented morbidity. Approximately 1% to 4% of spinal cord lesions in sub-Saharan Africa are thought to be caused by schistosomal infections,[2,6,7] and seizure occurrence in endemic areas is 8 times higher than in nonendemic areas.

CLINICAL GEMS

Schistosomiasis is the second most common parasitic infection worldwide after malaria and can be asymptomatic for weeks to years; symptoms can occur at any time

Pathophysiology

Schistosoma infection is acquired when a person comes into contact with infected fresh water and the parasite penetrates the skin. Freshwater snails serve as the intermediate host for the parasite and release thousands of infective schistosomal larvae into freshwater. Larvae, termed cercaria, penetrate human skin with proteolytic enzymes and mechanical activity and invade the lymphatic system. The organisms enter the systemic circulatory system and migrate to the lungs where they mature. Mature *Schistosoma* then reenter the bloodstream via the hepatic portal system.[1,8] In spinal infections, the adult *Schistosoma* lay eggs in the hepatic portal system that travel through the valveless paravertebral veins of Batson (Batson's plexus) to reach the lower spinal cord. More rarely, adult worms migrate to the CNS.[3] Eggs can then spread throughout the CNS via normal CSF circulation.

Clinical Presentation

Neuroschistosomiasis can involve the brain, spinal cord, or both. Sites of involvement vary significantly among species. Cerebral involvement is more common with *Schistosoma japonicum*, and spinal complications are more common with *Schistosoma mansoni* and *Schistosoma haematobium*. Cerebral schistosomiasis can cause seizures, diffuse encephalopathy, cerebral vasculitis and stroke-like symptoms, or a cerebellar syndrome.[9] Rarely, granulomatous inflammation can cause obstructive hydrocephalus.[6,7] Spinal schistosomiasis typically presents as acute myelopathy with transverse myelitis or as cauda equina syndrome with symptoms of flaccid paraparesis, urinary retention, and variable paresthesias. Often, back or flank pain precedes neurologic symptoms.[2]

Diagnosis

Lack of timely recognition and treatment of neuroschistosomiasis is an increasingly recognized cause of neurologic morbidity and mortality in the developing world.[8]

Diagnosis of neuroschistosomiasis requires clinical signs of CNS involvement (eg, altered mental status, seizures, or myeloradiculopathy), typical imaging findings (eg, obstructive hydrocephalus, transverse myelitis, or vasculitis), demonstration of schistosomal infection, and exclusion of other causes.

CLINICAL GEMS

Eosinophilia of cerebrospinal fluid (CSF) strongly suggests a parasitic/helminthic infection of the central nervous system (CNS)

Making the diagnosis can be difficult because diagnostic modalities are limited. The standard for testing remains direct visualization of *Schistosoma* eggs from stool or urine samples. However, visual diagnosis is challenging, and diagnostic yield is dependent on the timing of an individual's presentation, timing of sample collection, and the experience of the microbiology lab. *Schistosoma* eggs do not appear in the urine until at least 2 months after the initial infection, and eggs are shed at different times in the stool or urine depending on the species.[10] For *Schistosoma mansoni*, a Kato-Katz thick stool smear is 85% sensitive and 100% specific.[10] Our hospital, however, did not have this testing modality available because the prevalence of schistosomiasis is very low in the US.

CLINICAL GEMS

Diagnostic testing for schistosomiasis is challenging in the developed world because visualization of eggs or organisms in the urine or stool remains the standard but has a poor diagnostic yield

Serologic tests for schistosomiasis include the Falcon assay screening test (FAST) ELISA, fluorescent microscopy immunoassay (FMI), and immunoblot (IB) testing. The FAST ELISA and FMI both use microsomal fractions of adult *Schistosoma mansoni* as an antigen and are therefore highly specific and sensitive for *Schistosoma mansoni* but are less sensitive for other *Schistosoma spp*.[11,12] The IB uses species-specific adult worm microsomes and is used mainly when there is a concern for *Schistosoma haematobium* or *Schistosoma japonicum*.[12] The FMI is commercially available and used initially for this case with an elevated but indeterminate result. Because a high clinical suspicion for *Schistosoma* infection remained, samples were sent to the CDC for further confirmatory testing. The CDC performed the FAST ELISA test and IB, both of which were positive for *Schistosoma mansoni* only. To definitively make a diagnosis of CNS schistosomiasis, a brain or spinal cord biopsy is required and hematoxylin and eosin staining will show a *Schistosoma* granuloma with ova and a refractile shell surrounded by fibroblasts, eosinophils, and macrophages.[13] We did not pursue surgical confirmation because of Mr. M's rapid improvement with praziquantel and the high morbidity associated with the procedure.

Treatment

Although established treatment regimens exist for more common manifestations of systemic schistosomal infection (eg, swimmer's itch and Katayama fever), there are no consensus guidelines or randomized controlled trials for the treatment of neuroschistosomiasis. Regimens have been established based on anecdotal evidence and expert opinion that combine antiparasitics, corticosteroids, and surgery with minimally metabolized seizure medications

when needed.[1,7,8] Praziquantel is the antiparasitic of choice for schistosomiasis because of a reported cure rate of 70% to 90% for parasitic infections.[7] Dosing regimens vary from 40 to 60 mg/kg/day given in divided doses and treatment duration varies widely from 1 to 14 days. After review of several case reports published in the literature,[6,14-17] few of which listed the dose and duration of therapy used, we chose a moderately aggressive regimen of 5 days of praziquantel at 50 mg/kg based on a case with good neurologic recovery.[6] This case highlights the importance of publishing the duration and dose of praziquantel used as well as clinical outcome achieved, because there is a paucity of information in the published literature.

CLINICAL GEMS

Early recognition and treatment of neuroschistosomiasis are critical for good neurologic outcomes, but empiric treatment can possibly worsen other parasitic central nervous system (CNS) infections

In addition to praziquantel, steroids are typically administered. The role of steroids in CNS schistosomiasis is multifactorial. In animal models, steroids have been shown to decrease the size of granulomas. Steroids also decrease the inflammatory reaction that results from the death of the adult worms and can worsen neurologic symptoms.[14] Steroid dosing and duration varies widely. For our case, we chose 7 days of IV methylprednisolone 15 mg/kg followed by a 4-week prednisone taper, again based on reported regimens outlined in other case reports. Surgery is typically reserved for people with neuroschistosomiasis who have severe neurologic symptoms and evidence of CSF flow obstruction.[1]

Summary

Neuroschistosomiasis is a rare but serious cause of treatable neurologic disability. Although typically it is seen only in endemic areas, more cases are being reported in the developed world, presumably due to increased global travel and emigration from endemic areas. Among the most important features of this case was the remarkable functional recovery by the patient with minimal-to-no residual disability. This is rarely reported in the scant available literature, with only 2 known cases of similar recovery,[3,4] and most cases resulting in at least some degree of permanent paraparesis and bowel or bladder dysfunction. Although neuroschistosomiasis is exceedingly rare in the US (and outside endemic areas in general), *Schistosoma* infection should always be considered in patients with the proper exposure history and associated neurologic symptoms. Prompt recognition and initiation of appropriate treatment are critical to improving clinical outcomes and minimizing permanent neurologic sequelae. ■

1. Vale TC, de Sousa-Pereira SR, Ribas JG, Lambertucci JR. Neuroschistosomiasis mansoni: literature review and guidelines. *Neurologist*. 2012;18(6):333-342.
2. Clerinx J, Van Gompel A. Schistosomiasis in travellers and migrants. *Travel Med Infect Dis*. 2011;9(1):6-24.
3. Kim AH, Maher CO, Smith ER. Lumbar intramedullary spinal schistosomiasis presenting as progressive paraparesis: case report. *Neurosurgery*. 2006;58(5):E996.
4. Szekeres C, Galletout P, Jaureguiberry S, et al. Neurological presentation of schistosomiasis. *Lancet*. 2013;381(9879):1788.
5. Clerinx J, van Gompel A, Lynen L, Ceulemans B. Early neuroschistosomiasis complicating Katayama syndrome. *Emerg Infect Dis*. 2006;12(9):1465-1466.
6. Joshi TN, Yamazaki MK, Zhao H, Becker D. Spinal schistosomiasis: differential diagnosis for acute paraparesis in a US resident. *J Spinal Cord Med*. 2010; 33(3):256-260.
7. Carod-Artal FJ. Neurological complications of Schistosoma infection. Trans R Soc Trop Med Hyg. 2008;102(2):107-116.
8. Ross AG, McManus DP, Farrar J, Hunstman RJ, Gray DJ, Li YS. Neuroschistosomiasis. *J Neurol*. 2012; 259(1):22-32.
9. Chen MG. Progress in the assessment of morbidity due to Schistosoma haematobium infections: a review of the recent literature. *Trop. Dis. Bull*. 1989;48:2643-2648.
10. Gray DJ, McManus DP, Li Y, Williams GM, Bergquist R, Ross AG. Schistosomiasis eliminations: lessons from the past guide the future. *Lancet Infect Dis*. 2010;10(10):733-736.
11. Weerakoon KG, Gobert GN, Cai P, McManus DP. Advances in the diagnosis of human schistosomiasis. *Clin Microbiol Rev*. 2015;28(4):939-967.
12. Tsang VC, Wilkins PP. Immunodiagnosis of schistosomiasis. Immunologic Invest. 1997;26(1-2):175-188.
13. Berkowitz AL, Raibagkar P, Pritt BS, Maateen FJ. Neurologic manifestations of the neglected tropical diseases. *J Neurol Sci*. 2015;349(1-2):20-32.
14. Suchet I, Klein C, Horwitz T, Lalla S, Doodha M. Spinal cord schistosomiasis: a case report and review of the literature. *Paraplegia*. 1987;25(6):491-496.
15. Lighter J, Kim M, Krasinski K. Intramedullary schistosomiasis presenting in an adolescent with prolonged intermittent back pain. *Pediatr Neurol*. 2008;39(1):44-47.
16. Ueki K, Parisi JE, Onofri BM. Schistosoma mansoni infection involving the spinal cord: case report. *J Neurosurg*. 1995;82(6):1065-1067.
17. Olson S, Rossato R, Guazzo E. Spinal schistosomiasis. *J Clin Neurol*. 2002:9(3):317-320.

Paul M. Elsbernd, MD
Neurology Resident
Department of Neurology
Brooke Army Medical Center
Fort Sam Houston, TX

Kathryn J. Lago, DO
Infectious Disease Fellow
Department of Infectious Diseases
Brooke Army Medical Center
Fort Sam Houston, TX

Tatjana P. Calvano, DO
Associate Program Director
Internal Medicine Residency
Infectious Disease Physician
Brooke Army Medical Center
Fort Sam Houston, TX

John H. Sladky, MD
Associate Professor Neurology
Uniformed Services University of the Health Sciences
Director of Neurological Research
711HPW/USAFSAM/FES/59MDW
Lackland Air Force Base, TX

Disclosures
PME, KJL, TPC, and JHS report no disclosures