Testicular schistosomiasis: a systematic review of the literature

Azadeh Nazemi, MD, Jesse Persily, MD, James S. Wysock, MD
Department of Urology, New York University Grossman School of Medicine, New York, New York, USA

NAZEMI A, PERSILY J, WYSOCK JS. Testicular schistosomiasis: a systematic review of the literature. *Can J Urol* 2022;29(6):11366-11370.

Introduction: *To consolidate reported information on presentation, diagnosis, and treatment modalities in testicular schistosomiasis (TS) to provide a reference tool for this rare disease.*
Materials and methods: *A comprehensive PubMed search was performed using PRISMA guidelines, which yielded 21 articles detailing 22 cases of TS.*
Results: *Testicular schistosomiasis remains a rare disease, presenting at a variety of ages (median age 27). All reports of this condition are associated with exposure to an endemic area. The most common presenting symptoms include nonspecific testicular swelling (54.5%) followed by a testicular mass/nodule (18.4%). Diagnosis relies upon clinical suspicion due to low specificity on laboratory and imaging evaluation, with only 18% of urine evaluations positive for parasitic infection. Final diagnosis was made on biopsy (38.1%), radical orchiectomy (47.6%) or frozen section during partial orchiectomy (14.3%). Treatment included anthelmintic mediation (37%), radical/partial orchiectomy (31%), or some combination of the above.*
Conclusions: *This systematic review of individual patient data reveals that while urine tests and imaging may aid in diagnosis, all patients require definitive histologic diagnosis. It is important to obtain a thorough history to elucidate exposure to endemic areas and inform whether biopsy, and subsequent testicular preservation, may be appropriate.*

Key Words: schistosomiasis, bilharziasis, testicular infections, testicular parasites

Introduction

Schistosomiasis (bilharziasis) is the third most devastating tropical disease in the world, and a major source of morbidity and mortality for developing countries in Africa, South America, the Caribbean, Middle East, and Asia.[1,2] About 240 million people are affected worldwide, with over 700 million people at risk of infection living in endemic areas.[3] Globalization has facilitated cases of schistosomiasis spreading to non-endemic countries.[4] In the United States, it is estimated that over 400,000 individuals are infected, most of whom are immigrants but also includes travelers such as military personnel, expatriates and civilian contractors.[5]

Accepted for publication November 2022

Address correspondence to Dr. James S. Wysock, 222 East 41st St, 12th Floor, New York, NY 10017 USA

Schistosomes are trematode parasites that can infect humans via eggs discarded in standing water, which release parasites that use humans as a definitive host.[6] Once in the human body, they reproduce and eggs are spread throughout via veins and lymphatic vessels. The infectious process that ensues is a result of the intense immune reaction against Schistosoma eggs, with the typical lesion being a granuloma with a spiculated egg in a central position.[6] In this process, there is extensive inflammation, fibrosis, egg deposition and destruction of organ architecture.[6]

The most common species include S. haematobium, which infects the genitourinary tract, and S. mansoni and S. japonicum, which infect the gastrointestinal tract.[1] Schistosomiasis commonly involves the bladder, causing hematuria, while involvement of the testis is very rare.[7] Specifically, worms and ova of S. haematobium infest the urinary bladder (55%), seminal vesicles (54%), vas deferens (39%), to a lesser extent the prostate (20%), and very rarely the testicles.[8-10] Schistosomal infections of the epididymis cause scrotal pain, and infections of the scrotum can cause hydrocele or dermatitis.[11]

Testicular schistosomiasis is attributed to the migration of eggs through venous channels between the internal spermatic and mesenteric veins.[5] The rarity of testicular infection has been attributed to the narrowness of veins of the rete testis, making them out of reach of bilharzia worms.[12] Of the species, only S. mansoni and S. haematobium have been isolated to the testicle.[13]

Thus far, only 22 cases of testicular schistosomiasis have been reported in the literature as individual case reports. There is no current review protocol for this disease. This systematic review aims to consolidate existing data on the presentation and management of testicular schistosomiasis to elucidate trends and to create a reference for clinicians when they encounter this rare disease.

Materials and methods

This review was performed using the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA-IPD) guidelines. All reported cases of testicular schistosomiasis were identified using PubMed. Search terms included: "testicular schistosomiasis" (MeSH Terms), OR "testicle schistosomiasis" OR "testicular bilharzia," OR "testicle bilharzia." The initial search yielded 95 distinct results. Of these, 49 were not related to testicular schistosomiasis, two were non-English with no full-text translation available and 20 were not accessible through the extensive academic library network used for this review, and were thus excluded. An additional three were excluded because they lacked quantitative data on individual patients. The remaining 21 articles yielded the 22 cases included in this review, Figure 1. Patient demographics, presenting symptoms, associated work up, and treatment modalities were recorded. Relevant individual patient data were extracted from the included 21 articles. Data was consolidated and subsequently summarized with descriptive statistics. Statistical analyses were performed using SPSS 21 software (IBM Corp., Armonk, NY, USA).

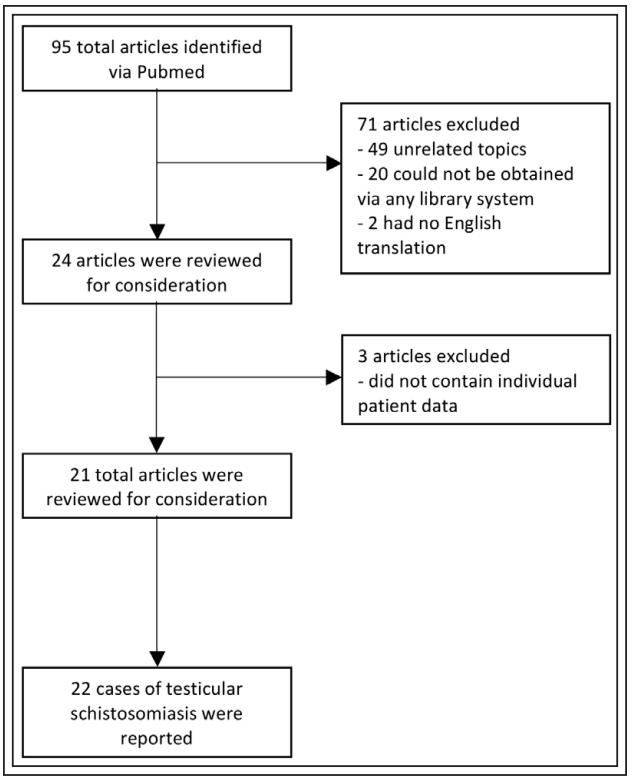

Figure 1. PRISMA flow diagram summarizing the steps involved in the systematic review of testicular schistosomiasis. From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and MetaAnalyses: The PRISMA Statement. PLoS Med 2009;6:e1000097. doi:10.1371/journal.pmed1000097.

Results

The median age at presentation was 27 (IQR 14.5-37.5). The most common ethnicities included Egyptian (22.7%), Nigerian (27.3%), Brazilian (22.7%), other African country (13.6%), Puerto Rican (9.1%) and Caucasian (4.5%), Figure 2.

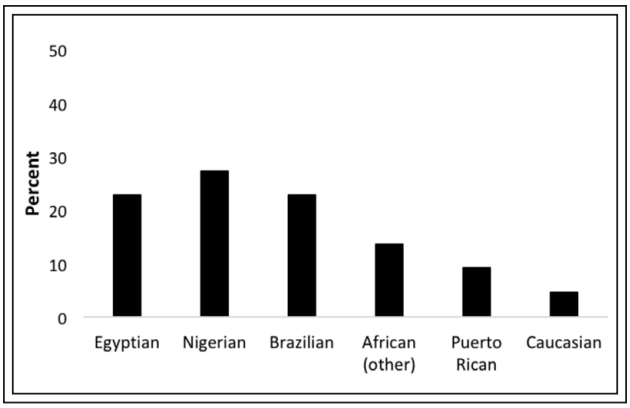

Figure 2. Demographic breakdown of reported cases.

Presenting symptoms included painless unilateral testicular swelling, testicular nodule/mass, infertility, hematuria, incidental diagnoses during work up for difficulty voiding, and incident diagnosis during workup for congenital bilateral absence of vas deferens, Table 1. Two cases presented with associated hydroceles (9.1%). Patients presenting with infertility had semen analyses showing oligospermia and azoospermia.

Diagnostic work up included obtaining serum tumor markers, urine/stool studies for ova and parasites, and imaging, though not all cases underwent complete work up prior to surgical intervention. Tumor markers were obtained in four cases where a nodule was felt on physical exam and five cases of generalized testicular swelling, with all cases having normal tumor marker levels. Of all cases that submitted a urine or stool sample for analysis, only 18% (two cases) were positive for ova and parasites. In all three cases where MRI was performed, the presenting symptom was a testicular nodule. When presenting symptom was generalized testicular swelling, ultrasound was performed in five cases (62.5%) and for cases presenting with a discrete nodule, ultrasound was obtained in three cases (37.5%).

TABLE 1. **Presenting symptoms of patients with testicular schistosomiasis varied**

Presenting symptoms	**% (n)**
Testicular swelling	54.5 (12)
Nodule/mass	18.4 (4)
Infertility	13.6 (3)
Incidental finding	9 (2)
Hematuria	4.5 (1)

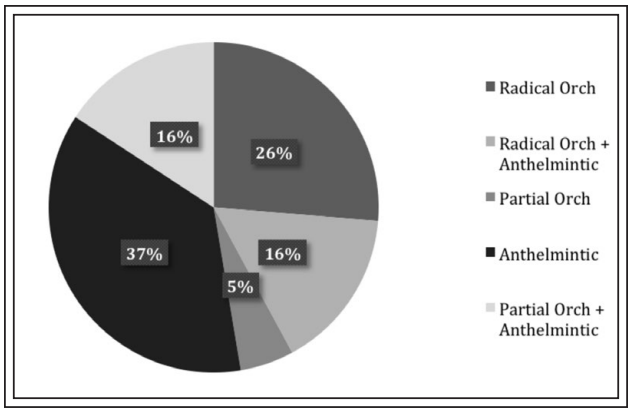

Figure 3. All cases were treated with radical orchiectomy, partial orchiectomy, an anthelmintic drug, or some combination of the aforementioned.

All cases of schistosomiasis were diagnosed on histology. Histologic sample was obtained by biopsy in 38.1% of cases. The remaining cases were diagnosed on pathology during treatment with radical orchiectomy (47.6%) or frozen section during partial orchiectomy (14.3%). Treatment modality is shown in Figure 3.

One case did not report treatment. All reported cases experienced resolution of disease. Additionally, two cases were noted to have concurrent hydroceles, with hydrocelectomy performed during treatment. Figure 4 demonstrates a diagnostic and therapeutic algorithm for testicular schistosomiasis based on these findings.

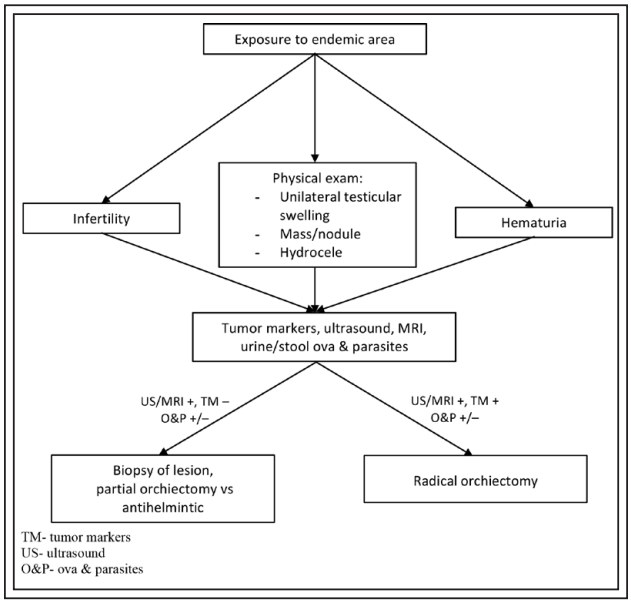

Figure 4. Diagnostic and therapeutic algorithm for patients suspected of having testicular schistosomiasis.

Discussion

Schistosomiasis is a parasitic infection that rarely infects the testis. Given its rarity, there is no large study on this disease with current literature comprising solely of case reports or small case series. This systematic review using PRISMA criteria quantitatively consolidates data on existing cases of testicular schistosomiasis to elucidate patterns in presentation, work up and treatment to serve as a reference for clinicians in this diagnostically challenging disease.

The highest incidence of cases is in sub-Saharan Africa in Nigeria, consistent with the findings of this study.[14] Risk factors for disease include poor sanitation, lack of safe water, malnutrition and overcrowding.[14] All cases in this report were either from an endemic area or had a history of recent travel to an endemic area.

Clinically, testicular schistosomiasis may present as infertility, hydrocele, testicular enlargement, or as a testicular mass.[15] While hematuria may be present, there may be no urinary bladder symptoms or history of hematuria due to a subclinical infection.[11] Thus, it is important to consider schistosomiasis as a differential diagnosis in patients residing in or with exposure to an endemic area regardless of bladder symptoms.[14]

Identifying presence of ova in a urine sample confirms the diagnosis, however accuracy of this varies depending on the phase of the disease.[16] This review confirmed the low sensitivity of laboratory diagnosis, with only 18% of patients demonstrating evidence of ova in urine or stool evaluation.

Confirming diagnosis with imaging also presents challenges. Echographically, schistosomiasis lesions typically present as a well delineated hypoechoic nodule with adjacent hyperechogenicity.[5,15,17] However, hyperechogenicity is the most common radiographic pattern for testicular cancer, making it difficult to distinguish between benign and malignant lesions, thus preventing exclusion of testicular neoplasm and subsequent orchiectomy. Scrotal imaging with MRI may offer improved evaluation of intratesticular abnormalities than ultrasonography.[5] In this review, MRI was performed in two cases that presented with a discrete nodule. These studies reported either a solid, hypervascularized nodule with ectasia of the veins of pampiniform plexus, or mass with low signal intensity on T2 indicating a fibrous component ultimately insufficient to rule out testicular neoplasm.[5,18] A prior report suggests MRI may be sensitive by showing irregular tunica, however it still cannot definitively rule out a neoplasm.[11]

Due to low sensitivity in urine/stool studies and nonspecific findings on imaging, in many cases tissue evaluation is indicated.[5,16,19] For many patients, benign cases are treated by radical orchiectomy when frozen biopsy is inconclusive.[20] This review identified that thirteen (59%) cases were identified after undergoing orchiectomy and eight cases (36.4%) diagnosed on testicular biopsy. Only one of these (12.5%) went on to receive partial orchiectomy and the remainder were treated with anthelmintic agents. With appropriate index of suspicion, biopsy facilitates accurate diagnosis and avoids unnecessary orchiectomy. Treatment with anthelmintic agents included oxamniquine or praziquantel and success rates of 100%.[21]

In general, parasitic infections of the testicles are relatively rare. Filariasis is the only other commonly reported infection and is caused by Wuchereria bancrofti or Brugia malayi. Similar to schistosomiasis, it has a geographic predilection and is most common in sub-Saharan Africa, Southeast Asia, India and the Pacific Islands.[22] Infection spreads to the testicles through lymphatic channels to cause inflammation of the tunica vaginalis or impaired lymphatic drainage through the spermatic cord. Hydroceles account for 90% of genital presentations, with other clinical manifestations include an acute inflammatory disease like epididymo-orchitis, lymph varix, testicular nodule, or elephantiasis of the genitalia.[22,23] Diagnosis is difficult and is usually based on clinical presentation prompting Giemsa-stained blood smears, IgG testing, or testicular biopsy, as ultrasound imaging is non-specific.[23] Diethylcarbamazine is the standard treatment.[22]

Despite the rarity of parasitic testicular infections, specifically schistosomiasis, recent cases have been noted in non-endemic areas thus necessitating improvement in understanding the presenting characteristics and diagnostic evaluation of this disease. Limitations of this study include the relatively small number of cases due to the rarity of the disease. Thus, findings here should continue to be updated and reassessed with increased reporting of cases. To the best of our knowledge, however, this study provides the broadest review assessing presentation, workup and treatment of testicular schistosomiasis to date.

Conclusions

Testicular schistosomiasis is a rare disease that was previously only found in endemic areas. Due to increased tourism and travel in the current era, more cases have presented in non-endemic areas showing that this disease has potential for wider spread. With low specificity on laboratory and imaging evaluation, diagnosis relies upon clinical suspicion, showing the

importance of remaining mindful and up to date on this less common, often forgotten disease. With a thorough history and appropriate index of suspicion, a properly directed diagnostic approach with more conservative treatment may be undertaken, resulting in less morbidity. In the appropriate scenario, patients would truly benefit from a physician with broad clinical suspicion who remains aware of all possible differential diagnoses and utilizes the proposed diagnostic and therapeutic algorithm presented herein during work up and management. □

References

1. Abdel-Naser MB, Wollina U, Lohan M, Zouboulis CC, Altenburg A. Schistosomiasis (Bilharziasis) ova: An incidental finding in testicular tissue of an obstructive azoospermic man. *Andrologia* 2018;50(10):8-10.
2. Adisa J, Egbujo EM, Yahaya BA, Echejoh G. Primary infertility associated with schitosoma mansoni: A case report from the Jos Plateau, north central Nigeria. *Afr Health Sci* 2012;12(4):563-565.
3. Schistosomiasis (Bilharzia). World Health Organizationhttps://www.who.int/news-room/fact-sheets/detail/schistosomiasis (accessed 11/30/2022).
4. Periyasamy P, Subramaniam SR, Rajalingham S. An increasingly notorious mimicker of testicular tumours; crossing borders. *BMJ Case Rep* 2011:9-11.
5. Hassan A, El-Mogy S, Zalata K, Mostafa T. Testicular schistosomiasis: a case study. *Fertil Steril* 2011;95(6):2124.e1-e4.
6. Alves LS, Estanislau C, Barreto L, Batista F, Toppa N. Concomitant testicular infection by Zika virus and Schistosoma mansoni in a Brazilian young boy. *Rev Assoc Med Bras* 2017;63(6):500-503.
7. Elem B, Patil PS, Lambert TK. Giant fibrous pseudomotor of the testicular tunics in association with schistosoma haematobium infection. *J Urol* 1989;141(2):376-377.
8. Abdel-Naser MB, Altenburg A, Zouboulis CC, Wollina U. Schistosomiasis (bilharziasis) and male infertility. *Andrologia* 2019;51(1):1-6.
9. Elbadawi A, Davis R, Cockett A. Schistosomiasis presenting with testicular enlargement in elderly male. *Urology* 1978;XIL(1):11-14.
10. Athanazio D, Athanazio P. Asymetric testicular schistosomal infection. *Brazilian J Infect Dis* 2008;12(6):461.
11. Rambau PF, Chandika A, Chalya PL, Jackson K. Scrotal swelling and testicular atrophy due to schistosomiasis in a 9-year-old boy: a case Rreport. *Case Rep Infect Dis* 2011;2011:1-3.
12. Girgis SM, Wassef NF. Bilharziasis and azoospermia. *Arch Androl* 1980;5(4):369-372.
13. Ekenze SO, Modekwe VO, Nzegwu MA, Ekpemo SC, Ezomike UO. Testicular schistosomiasis mimicking malignancy in a child: a case report. *J Trop Pediatr* 2015;61(4):304-309.
14. Oguntunde OA, Ikhisemojie S, Sonusi SE, Oyebode A, Abdulkareem FB, Banjo AA. Testicular schistosomiasis mimicking hydrocele in a child: a case report. *Pan Afr Med J* 2020;35:1-5.
15. Lopes R, Lopes R, Leite K, Prando D. Testicular schistosomiasis simulating malignancy. *Lancet Infect Dis* 2003;3:556.
16. Wedel PG, Jess P. Testicular schistosomiasis simulating malignancy case report. *Scand J Urol Nephrol* 1991;25(3):237-238.
17. Soans B, Abel C. Ultrasound appearance of schistosomiasis of the testis. *Australas Radiol* 1999;43(3):385-387.
18. Ferreira TN, Higa HCM, Rondina RG et al. Testicular schistosomiasis as differential diagnosis for testicular nodules: A case report. *Rev Soc Bras Med Trop* 2015;48(4):501-503.
19. Joshi RAMA. Total granulomatous infarction of testis due to Schistosoma haematobium. *J Clin Path* 1967;20:273-275.
20. Neto NM, Grando JPS, Moreira HA. Testicular schistosomiasis mimicking tumour. *Int Braz J Urol* 2004;30(6):502-503.
21. Dauda MM, Rafindadi AH. Testicular schistosomiasis simulating malignancy. *Trop Doct* 2006;36(3):182-183.
22. Ho CCK, Ideris N. Testicular mass: do not forget filariasis. *Infection* 2013;41(4):893-896.
23. Marcos LA, Shapley NP, Eberhard M et al. Case report: testicular swelling due to lymphatic filariasis after brief travel to Haiti. *Am J Trop Med Hyg* 2014;91(1):89-91.