## Surgical Pathology of Schistosomiasis

Aminu Z. Mohammed, MBBS, FMCPATH; Steven T. Edino, MBBS, FWACS, FMCS; and Adamu A. Samaila, MBBS, FWACP

Schistosomiasis remains an important health problem in many tropical countries and is being seen with increasing frequency in immigrant populations and tourists in developed countries. The pattern of organ involvement and clinical presentation of schistosomiasis in 80 patients (male: female, 9:1) during a five-year period (2001–2005) was examined from archival histopathology records. The urinary bladder was the most common organ affected [50 (62.5%)]. Gastrointestinal, male and female genital schistosomiasis were detected in 12 (15%), eight (10%) and five (6.1%) cases, respectively. Hematuria was the most common presenting symptom [34 (42.5%)], and bladder cancer was the only malignancy found to be associated with the infection. A high clinical index of suspicion usually allows for a preoperative diagnosis where indicated and avoidance of radical surgery. While research for the development of an effective vaccine continues, a plea is made for the expansion of multinational control programs in sub-Saharan Africa.

**Key words:** schistosomiasis **■** bladder **■** cancer

© 2007. From the Department of Pathology (Mohammed, senior lecturer/consultant pathologist), Department of Surgery (Edino, senior lecturer/consultant surgeon) and Department of Medicine (lecturer 1/consultant physician & gastroenterologist), Bayero University Kano/Aminu Kano Teaching Hospital, Kano, Nigeria. Send correspondence and reprint requests for J Natl Med Assoc. 2007;99:570–574 to: Dr. Aminu Zakari Mohammed, Department of Pathology, Aminu Kano Teaching Hospital, PMB 3452, Kano, Nigeria; phone: 2348034523334; fax: 23464663354; e-mail: aminuzm@yahoo.com

#### INTRODUCTION

caused by parasitic trematode worms of the genus Schistosoma. Of the 10 species that can infect humans, Schistosoma mansoni, haematobium and japonicum cause the vast majority of infections. Schistosomiasis remains the second most important parasitic disease of humans after malaria, with about 600 million people mainly in tropical countries at risk. Of the 200 million people infected worldwide, 120 million are symptomatic, and 20 million have severe disease.

Sub-Saharan Africa bears 85% of the total burden of the disease, while the remainder occurs in South and

Central America, the Caribbean, and the far and Middle East. <sup>1,3,4,5</sup> Travelers to endemic areas (particularly Africa) are at high risk of infection, and with increasing immigration globally, the chances of importing this disease to nonendemic areas are greatly increased. <sup>6-9</sup>

Although mortality related to schistosomiasis has generally been considered to be low,<sup>4</sup> considerable morbidity occurs and life-threatening complications may result with remarkable pathological changes in various organs and tissues depending on the infecting parasite species.<sup>10,11</sup>

Some of the schistosoma-induced lesions could mimic malignant conditions, leading to unnecessary or radical surgery. 12-14 The development of immunodiagnostic assays for serologic diagnosis of schistosomiasis and polymerase chain reaction (PCR) as highly sensitive and specific diagnostic methods have facilitated detection of the disease even though they are mainly utilized in reference laboratories. 15,16 Direct visualization of the parasite ova, however, remains the "gold standard" for diagnosis. 17 While urine, stool, semen and cervical swabs constitute some of the readily available specimens for ova identification, in some cases, ova are not shed even in the presence of active disease. 9,11,18-20 Hence, biopsy of affected tissues or organs provides alternative samples for histologic diagnosis.

Schistosomasis is endemic in the hot, dry northern region of Nigeria, where *S. haematobium* is the predominant parasite species, while *S. mansoni* is less prevalent.<sup>21,22</sup> We therefore analyzed the cases of histologically confirmed schistosomiasis from our surgical pathology records in order to ascertain the pattern of organ involvement and clinical presentation of the disease.

#### MATERIALS AND METHODS

Eighty cases of schistosomiasis diagnosed in the histopathology department of Aminu Kano Teaching Hospital, Kano, Nigeria, between January 2001 and December 2005 constituted the materials for this study. The study was retrospective, and most of the samples were obtained by endoscopic biopsy or during surgical operations.

Information regarding the age, sex, anatomical distribution of lesions, pertinent clinical features and histopathological diagnosis was collated from the surgical pathology register and histology request forms. Analysis was done using SPSS\* version 10.

#### RESULTS

Over the five-year period, 80 cases of schistosomiasis were diagnosed, comprising 72 males (90%) and eight females (10%) with a male:female ratio of 9:1. The age range was 7–80 years, with a mean of 38.1 years. The peak age was between 21–40 years (46.3%) (Figure 1).

The anatomical distribution of schistosoma-induced lesions is shown in Table 1. It reveals the urinary bladder to be the most common organ affected in 50 (62.6%) cases. Coexisting carcinoma of the bladder was found in 15 (30%) of them. Other parts of the urinary tract were involved in five (6.3%) cases. In 12 cases, the gastrointestinal organs were affected, with the vast majority affecting the appendix. The male and female genital organs were affected in eight (10%), and five (6.1%) cases, respectively.

Table 2 summarizes the salient clinical features at presentation, hematuria being the most common symptom.

#### DISCUSSION

The present study provides useful information on the pattern of organ involvement in schistosomiasis. While autopsy studies usually document observations in asymptomatic individuals, this study recognized the clinical presentation in relation to anatomical distribution of lesions. The pathological features of schistosomiasis arise from the host's immune response to eggs deposited in various organs and tissues and the granulomatous inflammatory reaction to soluble egg antigens deposited at these sites.<sup>2,5,11</sup> The mechanism for granuloma formation is through a delayed type hypersensitivity reaction.<sup>23</sup>

S. haematobium primarily affects the genitourinary tract where it leads to hematuria, chronic cystitis, pyelonephritis, obstructive uropathy and increased risk of bladder cancer. 5,9,11,24-28 The ureters, urethra and genital organs of both males and females may also be involved.24 It is therefore not surprising that the bladder recorded the greatest proportion of cases in this study. Bladder affectation was in the form of pathognomonic sandy patches and polyps that clinically presented as painless hematuria. In 30% of cases with bladder lesions, there were associated tumors that were histologically confirmed to be carcinomas, the majority (60%) of which were squamous cell carcinomas. This is in accordance with the firmly established link between this specie with bladder cancer.<sup>27-30</sup> The striking male preponderance may be explained by the greater predisposition of young boys to infection due to frequent contact with water bodies and also the majority of the farmers in the community tend to be males.21

Obstructive uropathy has been recognized to be a common and dangerous sequel of *S. haematobium* infection of the interstitial and juxtavesical portions of the ureter due to the common blood supply with the blad-

Organs	Males	Females	Total (%)
Urinary Tract (n=55)			
Bladder	49	1	50 (62.6)
Ureter	3	_	3 (3.8)
Urethra	1	1	2 (2.5)
Male Genital Organs (n=	8)		
Prostate	4	_	4 (5)
Testis	3	_	3 (3.8)
Epididymis	1	-	1 (1.2)
Female Genital Organs (	n=5)		×
Ovary	· _	2	2 (2.5)
Ovary + fallopian tube	<del>-</del>	1	1 (1.2)
Fallopian tube	_	1	1 (1.2)
Vulva	_	1	1 (1.2)
Gastrointestinal Tract (n=	12)		
Appendix		1	7 (8.8)
Colon	6 2 1	-	2 (2.5)
Rectum		_	1 (1.2)
Liver	2	-	2 (2.5)
Total	72	8	80 (100)

der.<sup>9</sup> Three patients with hydroureter and hydronephrosis presented with this complication, and excision of the site of ureteric stricture demonstrated mural fibrosis with accompanying schistosomal granuloma. The urethra, although rarely involved,<sup>24</sup> was found to be affected in an elderly male with urethral stricture and a female with a small polyp protruding from the urethral orifice.

The problem of male genital schistosomiasis, though previously neglected, has being receiving renewed interest because of its association with hemospermia, particularly in travelers to endemic areas from nonendemic areas. 18,31,32 The prostate and seminal vesicles have been shown by postmortem studies to be as frequently involved by egg-induced lesions as the urinary bladder. 10,33 The four cases of prostatic involvement in this study were incidental findings in men who had prostatectomy for benign nodular hyperplasia. An earlier study from our center has previously documented the paucity of prostatic involvement by the disease.34 Although schistosomiasis is rarely associated with male infertility,35 testicular or epididymal lesions can occur, where they may simulate malignancy<sup>14</sup> or infarction,<sup>36</sup> or cause acute scrotal pain.<sup>37</sup> Diagnosis, therefore, requires a high index of suspicion, as in our cases, where incision biopsy aided in confirmation of diagnosis, allowing for a conservative approach in management and avoidance of unnecessary radical surgery.

Female genital schistosomiasis (FGS) has been regarded as a common complication of *S. haematobium* infection, occurring in 50–80% of parasitized females.<sup>38</sup> Its significance in *S. mansoni* infection is not precisely known but is also considered not to be uncommon.<sup>38</sup> Only five of our patients demonstrated lesions in fe-

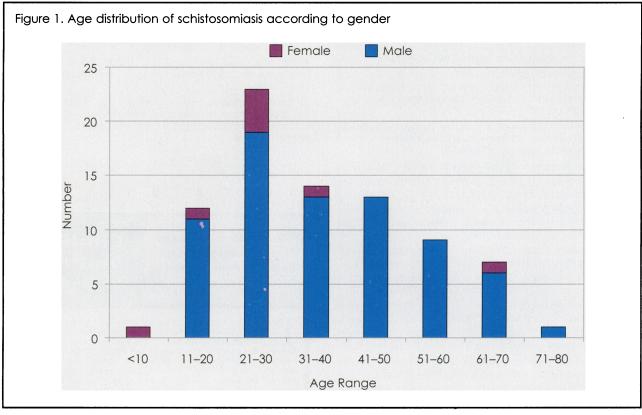
male genital organs, the ovary being most commonly involved. Considerable research on FGS has focused on its effect on fertility and pregnancy,<sup>39-42</sup> but renewed interest now lies in its role in facilitating transmission of sexually transmitted infections, including human immunodeficiency virus (HIV) and human papilloma virus (HPV).<sup>32,43,44</sup> This is of immense concern in sub-Saharan Africa considering the high rates of HIV and HPV-associated cervical cancer even though a clear link with cervical cancer and HIV is yet to be established.<sup>17,38</sup>

The appendix was the organ mainly affected in the gastrointestinal tract. In four of the cases, there was significant deposition of ova, granulomatous reaction, congestion and edema to suggest that schistosomiasis was the primary event that led to appendicitis. In the remainder, acute inflammation was associated with scant ova and granulomas. In the colon and rectum, polyps or inflammatory masses are frequent manifestations, and S. mansoni is the most common parasite associated.<sup>2,5,10</sup> Some investigators have proposed a link between colorectal cancer and schistosomiasis, 13,45 but none of our cases had coexistent bowel cancer. Recognition of pertinent clinical information again prompted incision biopsy and permitted a suitable surgical approach for one of the patients who presented with intestinal obstruction, while the others were treated conservatively.

Hepatic disease, which was observed in two teenagers, was characterized by remarkable regression of the liver and spleen, which were significantly enlarged at presentation following administration of praziquantel and correction of anemia.

Our findings call for enhanced strategies to control the infection. In order to decrease morbidity associated

Anatomical Sites	Main Clinical Presentation	Number
Urinary bladder	Bladder mass	16
	Hematuria	34
Ureter	Hydronephrosis	3
Urethra	Urethral stricture	1
	Polyp	. 1
Prostate	Benign nodular hyperplasia	4
Testis	Scrotal mass	2
	Acute scrotal pain	1
Epididymis	Chronic epididymo-orchitis	1
Ovary	Ovarian cyst	2
Tube/fallopian tube	Tubo-ovarian mass	1
Fallopian tube	Ruptured ectopic gestation	1
Vulva	Polyp	1
Appendix	Acute appendicitis	7
Colon	Intestinal obstruction	1
	Abdominal mass	1
Rectum	Bleeding per rectum	1
Liver	Hepatosplenomegaly	2
Total		80



with schistosomiasis, the best approach to control may well be prevention. Even though the urinary and genital organs are most frequently affected, ecological changes in the future may conceivably alter the distribution of parasite species which may have public health implications.<sup>2,22,27</sup> For an effective control program to achieve any success, modification of snail habitats and employment of molluscicides should complement current strategies utilizing large-scale, population-based chemotherapy even as ongoing research in development of an effective vaccine continues to show promise. 5,46,47 Despite significant advances in chemotherapy of schistosomiasis over the last two decades, the emergence of resistance to praziquantel poses new challenges to the control of this infection. 48-50 The expansion of the multinational control program in Africa funded by the Bill and Melinda Gates Foundation provides new hope for millions of affected individuals in sub-Saharan Africa.

#### **REFERENCES**

- 1. Neafie RC, Marty AM. Unusual infections in humans. *Clin Microbiol Rev.* 1993;6:34-56.
- 2. Wu GY, Halim MH. Schistosomiasis: progress and problems. World J Gastroenterol. 2000;6:12-19.
- 3. Chitsulo L, Engels D, Montresor A, et al. The global status of schistosomiasis and its control. *Acta Trop.* 2000;77:41-51.
- 4. Pincock S. Schistosomiasis initiative extended to five more countries. BMJ. 2003;327:1307.
- 5. Ross AGP, Bartley PB, Sleigh AC, et al. Schistosomiasis. N Engl J Med. 2002;346(16):1212–1220.
- 6. Grobusch MP, Muhlberger N, Jelinek T, et al. Imported Schistosomiasis in Europe: Sentinel Surveillance data from Trop Net Europ. J Travel Med.

2003;10:164-169.

- 7. Patz J, Graczyk T, Geller N, et al. Effects of environmental change on emerging parasitic diseases. *Int J Parasitol.* 2000;30:1395-1405
- 8. Corachan M. Schistosomiasis and international travel. Clin Infect Dis. 2002;35:446-450.
- 9. Neal PM. Schistosomiasis—an unusual cause of ureteral obstruction. A case history and perspective. Clin Med Res. 2004;2(4):216-227.
- 10. Edington GM, Von Lichtenberg F, Nwabuebo I, et al. Pathological effects of Schistosomiasis in Ibadan, Western state of Nigeria. 1. Incidence and intensity of infection, distribution and severity of lesions. Am J Trop Med Hya. 1970;19:982-995.
- 11. Edington GM, Gilles HM. Schistosomiasis. In: Edington GM, Gilles HM, eds. Pathology in the tropics, 2nd ed. London: Arnold. 1976:145-180.
- 12. Poon RT, Chu KW. Inflammatory cecal masses in patients presenting with appendicitis. World J Surg. 1999;23:713-716.
- 13. Mandong BM, Madaki AJK. Missed diagnosis of schistosomiasis leading to unnecessary surgical procedures in Jos University Teaching Hospital. *Trop* Doct. 2005;35:96-97.
- 14. Githae GM. Testicular schistosomiasis simulating a malignant tumour or tuberculosis. S Afr Med J. 1992;81:338.
- 15. Koneman EW, Allen SD, Janda WM, et al. Parasitology: Blood and tissue parasites. In Color Atlas and Text book of Diagnostic Microbiology 5th ed. Philadelphia, PA: Lippincott, Williams & Wilkins: 1997:1111-1119.
- 16. Rabello A, Pontes LA, Dias-Neto E. Recent advances in the diagnosis of schistosoma infection: the detection of parasite DNA. *Mem Inst Oswaldo Cruz*. 2002;97:171-172.
- 17. Kameh D, Smith A, Brock MS, et al. Female genital schistosomiasis: case report and review of the literature. South Med J. 2004;97(5):525-527.
- 18. Durand F, Brion JP, Terrier N, et al. Funiculitis due to Schistosoma haematobium: uncommon diagnosis using parasitologic analysis of semen. Am J Trop Med Hyg. 2004;70:(1):46-47.
- 19. Poggensee G, Kiwelu I, Saria M, et al. Schistosomiasis of the lower reproductive tract without egg excretion in urine. Am J Trop Med Hyg. 1998;59:782-783.
- 20. Helling-Giese G, Sjaastad A, Poggensee G, et al. Female genital schistosomiasis (FGS): relationship between gynaecological and histopatho-

logical findings. Acta Trop. 1996;62:257-267.

- 21. Pugh RNH, Bell DR, Gilles HM. Malumfashi Endemic Diseases project XV. The potential medical importance of Bilharzia in northern Nigeria: a suggested rapid, cheap and effective solution for control of Schistosoma haematobium infection. Ann Trop Med Parasitol. 1980;74:597-613.
- 22. Bitterton C, Ndifon GT, Bassey SE, et al. Schistosomiasis in Kano state, Nigeria (1). Human infections near dam sites and the distribution and habita preferences of potential snail intermediate hosts. *Ann Trop Med Parasitol.* 1988;82:561-570.
- 23. Samuelson J, Von Lichtenberg F. Infectious Diseases In: Cotran RS, Kumar V, Robbins SL (eds). Robbins Pathologic Basis of Disease, 5th ed. Philadelphia, PA: WB Saunders Co.; 1994:305-377.
- 24. Ghoneim MA. Bilharziasis of the genitourinary tract. Br J Urol. 2002;89:22-30.
- 25. El-Nahas AR, Shoma AM, El-Baz M. Bilharzial Pyelitis: a rare cause of secondary ureteropelvic junction obstruction. *J Urol.* 2003;170:1946-1947.
- 26. Christie JD, Crouse D, Smith JH, et al. Patterns of Schistosoma haematobium egg distribution in the human lower urinary tract. Il Obstructive Uropathy. Am J Trop Med Hyg. 1986;35:752-758.
- 27. Abdel-wahab MF, Strickland GT, El-Sahly GT, et al. Schistosomasis in an Egyptian village in the Nile Delta. Am J Trop Med Hyg. 1980;29:866-874.
- 28. Mostafa MH, Sheweita SA, O'Connor PJ. Relationship between Schistosomiasis and bladder cancer. *Clin Microbiol Rev.* 1999;12:97-1111.
- 29. Vizcaino AP, Parkin DM, Baffetta P, et al. Bladder cancer: epidemiology and risk factors in Zimbabwe. Cancer Causes Control. 1994;5:517-522.
- 30. Attah EDB, Nkposong EA. Schistosomiasis and cancer of bladder. A critical appraisal of causal relationship. *Trop Geogr Med.* 1976;28:268-275.
- 31. Feldmeier H, Leutscher P, Poggensee G, et al. Male genital schistosomiasis and haemospermia. *Trop Med Int Health*. 1999;4:791-793.
- 32. Richens J. Genital manifestations of tropical diseases. Sex Transm Infect. 2004;80:12-17.
- 33. Patil PS, Elem B. Schistosomiasis of the prostate and seminal vesicles: observations in Zambia. *J Trop Med Hyg.* 1988;91:245-248.
- 34. Mohammed AZ, Alhassan SU, Edino ST, et al. Histopathologic review of prostatic diseases in Kano, Nigeria. Nig Postgrad Med J. 2003;10:1-5.
- 35. Girgis SM, Wassef NF. Bilharziasis and azoospermia. Arch Androl. 1980;5:369-372.
- 36. Steinberger RM, Lindsay KG, Alassandri R, et al. Infarction of testicle and Schistosoma mansoni. *Urology*. 1975;5:567-569.
- 37. Yakubu AA, Mohammed AZ, Sheshe A, et al. Testicular schistosomiasis an unusual cause of acute scrotal pain. *Afr J Urol.* 2005;11:258-260.
- 38. Feldmeier H, Daccal RC, Martins MJ, et al. Genital manifestations of schistosoma mansoni in women: important but neglected. *Mem Inst* Oswaldo Cruz Rio de Janeiro. 1998;93:127-133.
- 39. Kjetland E, Poggensee G, Helling-Giese G, et al. Female genital Schistosomiasis due to schistosoma haematobium. Clinical and parasitological findings in women in rural Malawi: Acta Trop. 1996;62:239-255.
- 40. Leutscher P, Raharisolo C, Pecarrere JL, et al. Schistosoma haematobium induced lesions in the female genital tract in a village in Madagascar. Acta Trop. 1997;66:27-34.
- 41. Richter J, Poggensee G, Kjetland E, et al. Reversibility of lower reproductive tract abnormalities in women with schistosoma haematobium infection after treatment with praziquantel- an interim report. Acta Trop. 1996;62:289-301.
- 42. Mohammed AZ, Uzoho CC, Galadanci HS, et al. Ruptured tubal gestation: an unusual presentation of Schistosoma haematobium infection of the fallopian tube. Trop Doct. 2004;34:48-49.
- 43. Feldmeier H, Krantz I, Poggensee G. Female genital schistosomiasis: a neglected risk factor for the transmission of HIV?. Trans R Soc Trop Med Hyg. 1995;89:237.
- 44. Poggensee G, Feldmeier H. Female genital schistosomiasis: facts and hypotheses. *Acta Trop.* 2001;79:193-210.
- 45. Ojo OS, Odesanmi WO, Akinola OO. The surgical pathology of colorectal carcinoma in Nigerians. *Trop Gastroenterol.* 1992;13:64-69.
- 46. Hagan P, Doenhoff MJ, Wilson RA, et al. Schistosomasis vaccines: a response to a devil's advocate's view. *Parasitol Today*. 2000;16:322-323.
- 47. Capron A, Capron M, Riveau G. Vaccine development against Schisto-

somiasis from concepts to clinical trials. Br Med Bull. 2002;62:139-148.

- 48. Guisse F, Polman K, Stelma FF, et al. Therapeutic evaluation of two different dose regimens of praziquantel in a recent schistosoma mansoni focus in Northern Senegal. Am J Trop Med Hyg. 1997;56:511-514.
- 49. Picquet M, Vercruysse J, Shaw DJ, et al. Efficacy of praziquantel against Schistosoma mansoni in Northern Senegal. *Trans R Soc Trop Med Hyg.* 1998:92:90-93.
- 50. Brindley PJ, Sher A. Anti-schistosomal drugs: observations on the mechanism of resistance to Hycanthone, and on the involvement of host antibodies in the mode of action of praziquantel. Mem Inst Oswaldo Cruz. 1987:82:157-161. ■

### CAREER OPPORTUNITIES

#### The University of Texas Health Science Center at San Antonio School of Medicine

# CHAIR Department of Medicine

The School of Medicine at the University of Texas Health Science Center at San Antonio (UTHSC-SA) seeks an accomplished, dynamic academic leader as candidate for the position of Chair, Department of Medicine. Reporting to the Dean of the School of Medicine and Vice President for Medical Affairs, Dr. William Henrich, the Chair will be responsible for continuing to build and maintain world-class programs in basic and translational research, as well as for all clinical services of the department and maintaining fully accredited, high quality residency and fellowship programs.

The School of Medicine was chartered in 1959, and in 1972 UTHSC-SA became a unit of the UT System. The University is one of six health science centers within the UT System and now includes five professional schools and an Area Health Education Center in South Texas as an extension of the School of Medicine. The Health Science Center is designated as a Hispanic-Serving Institution.

Candidates must be a professor of medicine at an LCME accredited medical school and be board certified. The ideal candidate will have national recognition in the field of Medicine as a clinician, research scientist, educator, and/or physician leader. The candidate should have ten years of practice experience, five years of experience in operational and financial management, and leadership in a hospital, academic health center, or group practice environment. The ability to foster a culture of collaboration, innovation, accountability, and business literacy across the divisions and across the Health Center is important.

Nominations, expressions of interest and questions should be directed, via email, to the chair of the search committee, Dr. Robert Schenken, M.D., via the University's executive search consultants:

Marvene Eastham/Ryan Hubbs • Witt/Kieffer 10375 Richmond Avenue, Ste 1625 • Houston, TX 77042 713/266.6779 P • 713/266.8133 F • UT\_Chair@wittkieffer.com

Equal Employment Opportunity/Affirmative Action Employer. All faculty appointments are designated as security sensitive positions.

WANTED: Chief Residents or PGY-4's in general surgery interested in traveling to Nigeria during the last two weeks of July 2007 to assist with surgery. Interested parties must use their vacation time. Travel expenses will be covered from home of record. Passport, visa and inoculations are required. Interested persons should contact Eddie L. Hoover, MD, (716) 862-3291 or eddie.hoover@med.va.gov