Diagnosis and management of urogenital schistosomiasis in a young adult; a case report

G. De Win, T. Van den Broeck, B. Van Cleynenbreugel, F. Claus, E. Lerut

Schistosomiasis is rarely diagnosed in Western European countries. However, due to the popularity of exotic vacations, more and more western patients can get infected by schistosomiasis. Awareness of this disease is important, as an infection can lead to non-transitional cell bladder carcinoma in the long run (squamous cell carcinoma; SCC)
In this article, we present a rare case of urogenital schistosomiasis in a 27-year old Belgian male. Extensive patient history together with eosinophil count and bladder biopsy, is the key to making the diagnosis. Medical treatment with praziquantel is often sufficient.
(Belg J Med Oncol 2012;6:97-101)

Introduction

In most African countries, bladder cancer is the most frequent malignancy with a mean age of 46 years (as opposed to 72.9 years in patients with transitional cell carcinoma (TCC) of the bladder in the United States). Most of these tumours are squamous cell carcinomas (SCC), arising on a background of Schistosoma haematobia infection.[1-4] Roughly 200 million people in 74 countries suffer from schistosomiasis, of whom 100 million people are affected by bilharziasis of the urogenital tract, caused by S. haematobium.[1] A very rare disease in Europe, it is endemic and a common health problem in Malawi and other African countries.[1,2] Due to increasing migration and tourism, European urologists are currently more frequently confronted with infected people travelling from these endemic zones. Therefore, awareness of the disease and thorough patient history are of vital importance.

Patient History

A 25-year old Belgian male consulted the outpatient clinic with complaints of dysuria, bilateral testicular pain and urgency. Ultrasound examination showed acute prostatitis and epydimitis while urine cultures were negative. He was treated with quinolones for six weeks but his symptoms did not completely disappear, resulting in the diagnosis of Chronic Pelvic Pain syndrome. At the age of 27, he presented with persisting urethralgia, frequency, microhaematuria, leukocyturia and slightly elevated PSA of 1.54 ng/mL. Because of his severe symptoms in combination with persisting microhaematuria, a thorough anamnesis with special attention to his travel history was performed, revealing that he went on a diving-trip in Lake Malawi in Malawi two years before. A few weeks after his return in Belgium his complaints had started.

In Malawi, Schistosomiasis haematobium is

Authors: G. De Win MD, T. Van den Broeck, B. Van Cleynenbreugel MD, Department of Urology, University Hospitals KULEUVEN, Leuven, Belgium; F. Claus MD PhD, Department of Radiology, Uro-radiology, University Hospitals KULEUVEN, Leuven, Belgium; ms. E. Lerut MD PhD, Department of Histology and Pathology, University Hospitals KULEUVEN, Leuven, Belgium.
Please send all correspondence to: G. De Win MD, Department of Urology, UZA, University Hospital Antwerp, Wilrijkstraat 10, B-2650 Edegem, Tel +32 3 821 30 00, email:gunterdewin@me.com
Conflict of interest: the authors have nothing to disclose and indicate no conflicts of interest.
Key words: Schistosoma haematobium, squamous cell carcinoma, Chronic Pelvic Pain syndrome, Bladder cancer.

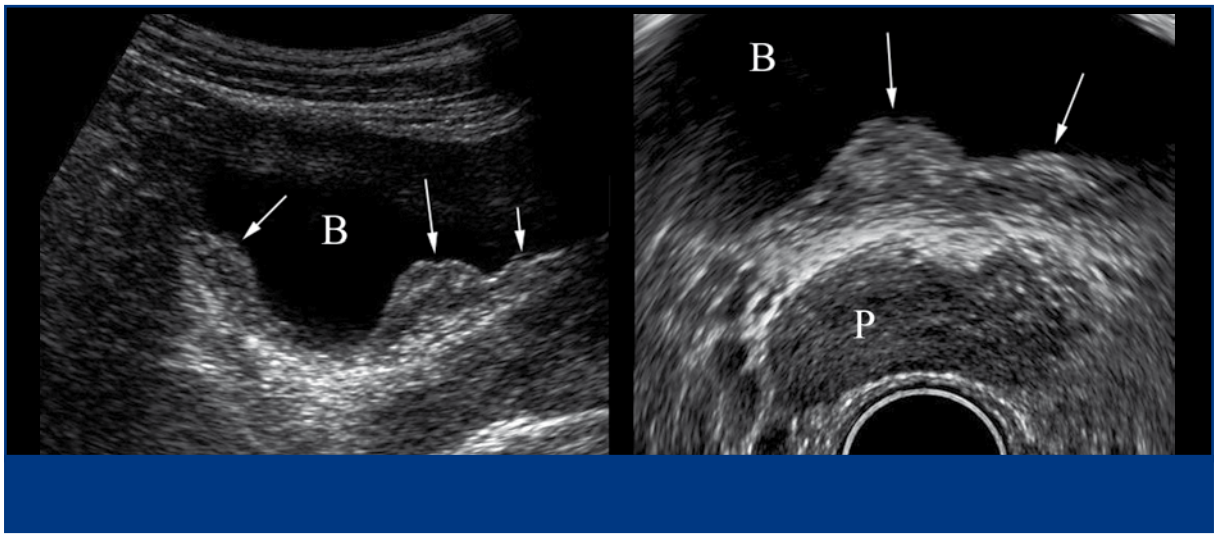

Figure 1. Transabdominal (left panel) and transrectal (right panel) sonography of the bladder (B) and the base of the prostate (P), showing a pathological nodular thickening (white arrows) of the posterior bladder wall. These iso-echoic nodular laesions showed vascularisation on Doppler imaging (not shown on this figure).

highly endemic.[2] Therefore, his travel history, together with his symptoms, were very suspicious for schistosomiasis. Bloodanalysis showed eosinophilia, but urine egg count and serology were negative. Cystoscopy showed atypical granulomata in the trigone, sparing the ureteral orifices. Transrectal ultrasound was repeated and showed thickening and hyperechogenicity of the irregular bladder wall, coexisting with a submucosal mass protruding into the lumen at the bladder base (*Figure 1*). A transurethral endoscopy with biopsies of the laesions - with the impression of egg-excretion- was performed. Postoperatively, one dose of praziquantel 3g (40mg/kg) was administered orally. The next day, the patient left the hospital pain-free.

Histopathological examination of the bladder biopsies confirmed the presence of granulomatous laesions with active form of schistosomiasis (*Figure 2*) and excluded (squamous) bladder carcinoma. Two months later, the patient's symptoms were completely resolved and cystoscopy was negative. Eosinophil count was again within normal range. One month later, a second dose of praziquantel was administered. Yearly follow-up with cystoscopy and cytology (risk of bladder SCC), medical imaging of the higher urinary tract (risk of obstruction) and eosinophil count were planned.[4-7,12]

Discussion and conclusions

Urogenital schistosomiasis is caused by the digenetic trematodes S. haematobium and is frequently the result of unprotected contact (eg. bathing, swimming, fishing,…) with contaminated fresh water in endemic areas.[1,2,4] Indeed, S. haematobium eggs are excreted in the water, hatch and release miracidia that penetrate their intermediate host, the aquatic bulinid snails. They excrete cercaria, which penetrate (non-injured) human skin during contact with contaminated water. Mature worms mate and migrate to the pelvic venous plexuses to begin oviposition, after which the eggs migrate into the surrounding organs causing micro-mucosal perforation. Non-excreted eggs remain in the submucosa of the pelvic organs, encapsulated in fibrous granulomas.

The ulcerative stage of the infection frequently presents with urethralgia, frequency, suprapubic pain and haematuria but the presentation may differ greatly depending on the stage of the disease, severity of the infection and localisation of the eggs of the parasite. It may cause local complications, such as upper urinary tract obstruction with consequent hydronephrosis and kidney damage, nephrotic syndrome and ectopic localisations due to aberrant worm migration.[1,4,9,10]

Moreover, the association between schistosomiasis and the late (10-20 years post-infection) develop-

ment of non-transitional cell bladder carcinomas (SCC) is well known. Bladder SCC was the most common malignant disease in Egypt until a reduction of schistosomasis in Egypt resulted in an important shift in the epidemiology of bladder cancer in Egypt, which is nowadays characterised by a lower incidence, a higher age at diagnosis, a lower male predominance and lower proportion of SC histology, but with increased incidence of transitional cell carcinoma. This shows the remarkable cause-effect relation between the eradication of schistosomiasis and the subsequent radical decline in SCC of the bladder.[13] Over 90% of bilharzial SCC patients present with T3 and T4 tumours, due to the overlap of symptoms of bilharzial cystitis with early malignant disease. In regions where Schistosomiasis is rare, it is is even more likely to miss these early stages if one is not aware of this disease. Morphologically, SCCs are nodular, ulcerative, or infiltrative. Papillary laesions are rare. Lymph node invasion is rare (19%), even though the tumours are mostly diagnosed at advanced stages. Distant metastases are much lower in incidence than those reported for the transitional cell carcinoma. Management of SCC of the urinary bladder should be the same as that of advanced muscle-invasive TCC.[5-7] Radical cystectomy remains the main treatment giving a 5-year survival rate of 50%.

The importance of a thorough anamnesis and travel history can therefore not be stressed enough. In the early phase of the disease, ultrasound may not show the typical laesions as seen in our case but when the classic therapy for prostatitis fails, schistosomiasis still has to be incorporated in the differential diagnosis if there is an anamnesis for travelling in endemic areas.

Diagnosis is based on the detection of S. haematobium eggs in the urine, which should be collected on several consecutive days between 11.00 and 14.00, because of the peak output of the eggs at this time. Urinanalysis looking for microhaematuria and proteinuria and urine cytology in the screening for malignancy should be performed as well. When the egg count is positive, the viability of the eggs can be checked through the egg hatch procedure and diagnosis is confirmed for which medical treatment should be started.[1] However, the sensitivity of urine filtration for parasitologic diagnosis is known to be lower in individuals with minimal infections. Such

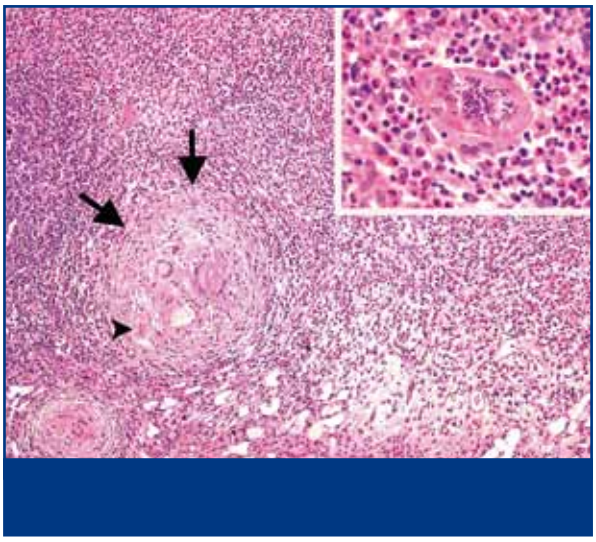

Figure 2. Transurethral biopsy of the bladder showed an extensive granulomatous inflammation (arrow) with an abundant accompanying eosinophillic inflammatory infiltrate. In the periphery of the granuloma one of the schistosomal eggs (ovum) eliciting this granulomatous process is present (arrowhead + inset). (Haematoxylin-Eosin stain, original magnification 100X and 400x respectively)

light infections are more common among adults, making the detection of their active infections more difficult. Thus, adults who score as "egg-negative" in urine filtrations may be minimally infected with S. haematobium, with ongoing tissue injury and inflammation.[3]

Cystoscopy is indicated in cases where non-invasive semiological evaluation does not lead to a diagnosis.[12] Thus, patients with negative egg-counts require a cystoscopy, which can show very characteristic laesions and generally is followed by transurethral biopsy of the bladders laesions and histopathological examination of the resected tissue. Cystoscopy may also be used to evaluate bladder-neck stenosis, bladder calcification, and ureteral orifices stenosis. Again, when these results are positive, medical treatment should be started.[1,12]

Other diagnostic tests for urinary tract sequelae include ultrasonography for ureteral obstruction or to detect hydronephrosis, urography to evaluate bladder morphology and ureteral stenosis and CT in suspected cases of kidney tumour.

As medical treatment the two drugs proven to be active against S. haematobium are praziquantel and metrifonate. They are both effective treatments and

Key messages for clinical practice

1. Thorough patient history and specifically inquiries into travel history are important before diagnosing a patient with Chronic Pelvic Pain Syndrome.
2. When patient history reveals travelling in a schistosomiasis endemic area, always consider schistosomiasis as a differential diagnosis, especially when the classic therapy for his symptoms fails.
3. The presentation of schistosomiasis may differ greatly depending on the stage, the severity of the infection and on the localisation of the eggs of the parasite.
4. Diagnosis is based on urine-analysis and egg count, but a negative egg count does not exclude the disease. Cystoscopic findings and biopsies are very characteristic.
5. Early ultrasound findings can be atypical. Therefore, a repeat ultrasound is suggested in case of remaining complaints. A submucosal mass protruding in the bladder is suggestive.
6. An important association with late presenting non-transitional cell bladder carcinoma (SCC) exists, requiring cystoscopy with biopsies and cytology for diagnosis.
7. Effective pharmacologic treatments are available, but none of these prevents reinfection nor can they reverse the damage done by the infection. Follow-up is essential.

have few adverse effects.[1,11] Our patient was given praziquantel. Surgical treatments are only necessary when complications or bladder cancer occur and are not further discussed here.

Epidemiological studies carried out in Ghana showed that bladder damage seen on ultrasound is common in young adults as well as in older people, but it is not clear when cancer starts to develop. Also, it is not clear whether medical treatment of schistosomiasis can interrupt or prevent cancer development.[8,10] The medical treatment is efficient, but therapeutic failure (with complications) is possible. Therefore, yearly follow-up with cystoscopy, cytology, medical imaging of the higher urinary tracts and eosinophil count is required, next to lifelong awareness because of the possible late development of SCC.

References

1. Bichler KH, Savatovsky I; Urinary Tract Infection, European Association of Urology; Naber KG, Bischop MC, et al. EAU Guidelines for the Management of Urogenital Schistosomiasis. Eur Urol 2006;49(6):998-1003.
2. Cetron MS, Chitsulo L, Sullivan JJ et al. Schistosomiasis in Lake Malawi. Lancet 1996;348(9037):1274-8.
3. Hodder SL, Mahmoud AAF, Sorenson K et al. Predisposition to urinary tract epithelial metaplasia in schistosoma haematobium infection. Am J Trop Med Hyg 2000;63(3-4):133-8.
4. Neal PM. Schistosomiasis - an unusual cause of ureteral obstruction. Clin Med Res 2004;2(4):216-27.
5. El-Sebaie M, Zaghloul MS, Howard G et al. Squamous cell carcinoma of the bilharzial and non-bilharzial urinary bladder: a review of etiological features, natural history, and management. Int J Clin Oncol 2005;10(1):20-5.
6. Manunta A, Vincendeau S, Kiriakou G et al. Non-transitional cell bladder carcinomas. BJU Int 2005;95(4):497-502.
7. Abol-Enein H, Kava BR, Carmack AJK. Nonurothelial cancer of the blad-

der. Urology 2007;69 Suppl 1:93-104.

8. Shiff C, Naples JM, Isharwal S et al. Non-invasive methods to detect schistosome-based bladder cancer: is the association sufficient for epidemiological use? Trans R Soc Trop Med Hyg 2010;104(1):3-5.

9. Gabbi C, Bertolotti M, Iori R et al. Acute abdomen associated with schistosomiasis of the appendix. Dig Dis Sci 2006;51(1):215-7.

10. Wagatsuma Y, Aryeetey ME, Sack DA et al. Resolution and resurgence of schistosoma haematobium-induced pathology after community-based chemotherapy in Ghana, as detected by ultrasound. J Infect Dis 1999;179(6):1515-22.

11. Danso-Appiah A, Utzinger J, Liu J et al. Drugs for treating urinary schistosomiasis. Cochrane Database of Systematic Reviews 2008, Issue 3. Art. No.: CD000053. DOI: 10.1002/14651858.CD000053.pub2.

12. Silva IM, Thiengo R, Conceição MJ et al. Cystoscopy in the diagnosis and follow-up of urinary schistosomiasis in Brazilian soldiers returning from Mozambique, Africa. Rev Inst Med Trop Sao Paulo 2006;48(1):39-42.

13. Salem S, Mitchell RE, El-Alim El-Dorey A et al. Successful control of schistosomiasis and the changing epidemiology of bladder cancer in Egypt. BJU Int 2011;107(2):206-11.

14. el-Mawla NG, el-Bolkainy MN, Khaled HM. Bladder cancer in Africa: update. Semin Oncol 2001;28(2):174-8.