

# Clinical and Histopathological Correlation of Different Bladder Schistosomiasis Lesions

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## Article Information

Received date: Jul 30, 2017

Accepted date: Aug 21, 2017

Published date: Aug 25, 2017

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**Keywords** Schistosomiasis; Lesions; Hematuria

## Abstract

**Objective:** To describe a case of a patient with bladder schistosomiasis, assessing the relationship between macroscopic and microscopic bladder schistosomiasis lesions.

**Methods:** We report the case of a 26 years old male patient with diagnosis of bladder schistosomiasis. We describe the clinical features, diagnosis, treatment and follow-up. We study and take separately biopsies of the macroscopic bladder lesions to further histopathological analysis.

**Main results:** The patient suffered hematuria and the diagnosis was confirmed by microbiological and histopathological studies. A course of Praziquantel was prescribed. After the diagnosis of schistosomiasis and transurethral resection of bladder, the patient is still undergoing controls because of the associated risks of the disease. The histological analysis showed modifications from normality but neither differences between the different lesions nor cancer specific pre-malignant lesions.

**Conclusions:** The patients who have suffered severe urinary schistosomiasis must complete long-term follow-up. The endoscopic and histological correlation doesn't show different patterns of aggressiveness.

## Introduction

*Schistosoma haematobium* is one of the parasitic infections with highest prevalence across Africa and Middle East. In 2006 it was estimated that more than 200 million people are infected across Africa, Asia, and South America, and close to 800 million are at risk of infection. The predominant self-reported symptoms are dysuria (91.2%), hypogastralgia (88.7%) or hematuria (87.1%); and these symptoms are characterized by serious and irreversible lesions in the urogenital tract induced by chronic infection that can eventually lead to squamous cell carcinoma of the bladder [1,2].

## Materials and Methods

26 years old male from Senegal with intermittent hematuria for the last 7 years. No other accompanying symptoms excepting a maculopapular eruption in arms when first hematuria signs appeared. The physical examination and blood analysis were within normal limits. Urine analysis showed macroscopic hematuria and leukocyturia and the microscopic examination of fresh urine showed *Schistosoma haematobium* eggs (Figure 1). Several urine cytologies were negative for malignancy.

Intravenous urography was first requested to study the urinary tract and presented normal upper urinary tract, normal function of both kidneys with tight suspicion of bladder defects. Consequently, flexible cystoscopy was requested, with occupation of almost the entire bladder mucosa by advanced exophytic and plane lesions of bladder schistosomiasis, described as polypoid solid lesions, cottony calcified lesions and sandy patches (Figure 2).

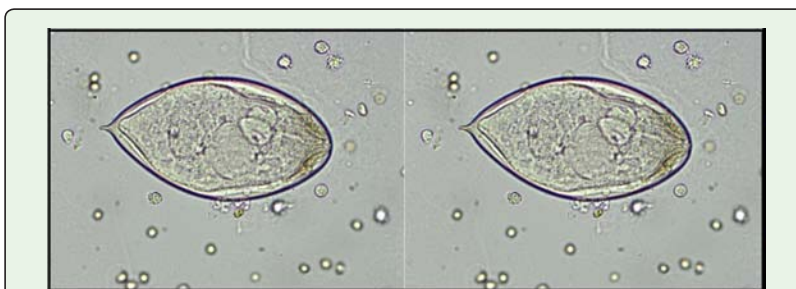
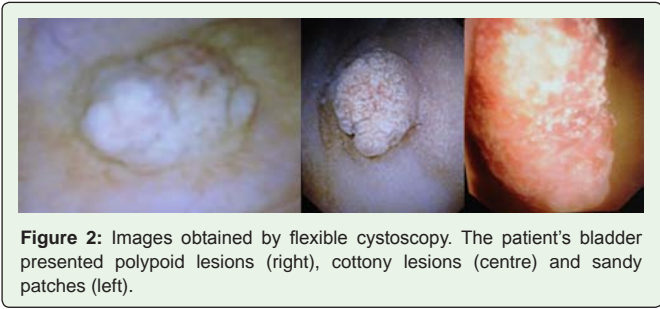
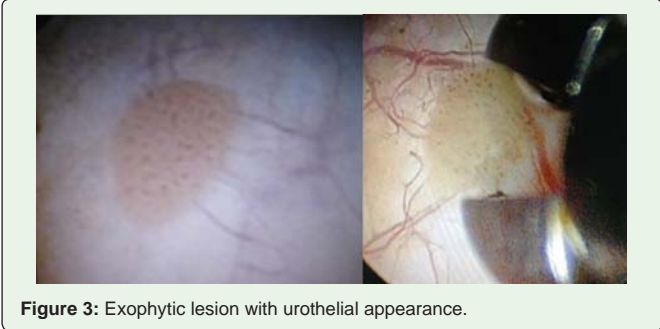


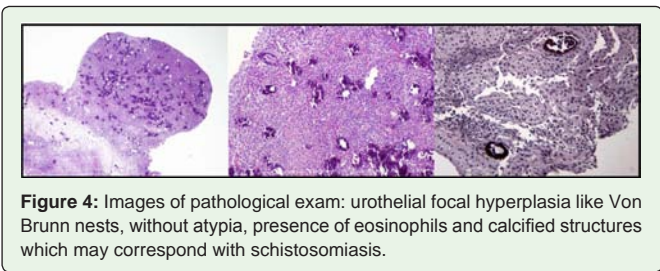
Figure 1: (right and left). This micrograph depicts an egg from a *Schistosoma haematobium* trematode parasite; magnified 500x.



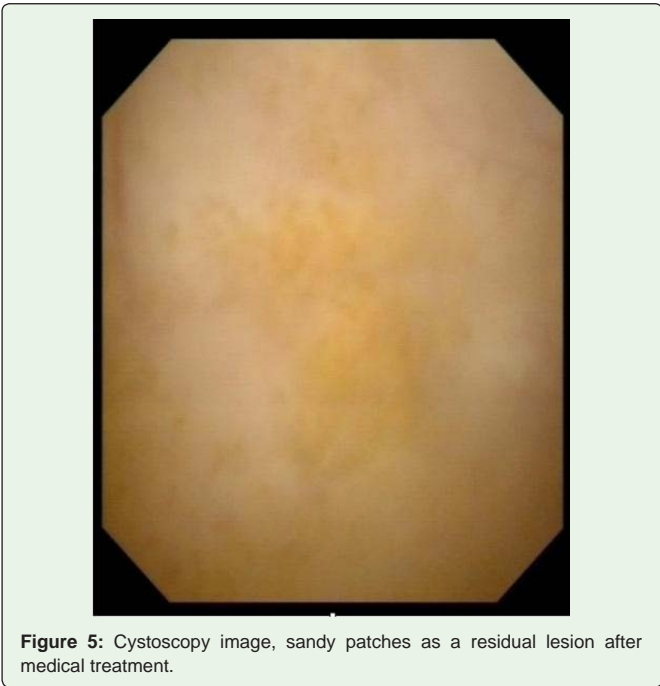
**Figure 2:** Images obtained by flexible cystoscopy. The patient's bladder presented polypoid lesions (right), cottony lesions (centre) and sandy patches (left).



**Figure 3:** Exophytic lesion with urothelial appearance.



**Figure 4:** Images of pathological exam: urothelial focal hyperplasia like Von Brunn nests, without atypia, presence of eosinophils and calcified structures which may correspond with schistosomiasis.



**Figure 5:** Cystoscopy image, sandy patches as a residual lesion after medical treatment.

Accordingly, medical treatment with Praziquantel was initiated (40 mg/kg/ day or 2400 mg/day), orally and single dose. No treatment-related adverse events were described during the follow up.

After 4 weeks of Praziquantel oral treatment, a cystoscopy was requested and showed a pale clinical improvement with those lesions previously described. However, a small exophytic lesion with non-muscle invasive urothelial tumour appearance was found on the posterior wall of the bladder, which led to transurethral bladder resection (TURB) (Figure 3). Additionally and during the procedure, a TURB-biopsy of each macroscopic lesion (polypoid solid lesions, cottony calcified lesions and sandy patches) was conducted in order to analyse any malignant or pre-malignant pathology features.

The histopathological examination of the different structures observed during the TURB showed the same tissue pattern: urothelial focal hyperplasia without atypia, presence of eosinophils and calcified structures. Those findings may confirm bladder schistosomiasis; however none of them are specific of schistosomiasis disease. Neither signs of malignancy Nor pre-malignancy at tissue examination.

A bladder examination and TURB of residual lesions were performed 10 months later. The previously described erythematous lesions, sandy patches; polypoid lesions and nodular lesions had turned on ovoid, plane and calcified structures at macroscopic view. The pathologist analysis described residual *Schistosoma* eggs, erosion, inflammation, eosinophils and focal hyperplasia with Brunnnests, with no evidence of malignancy (Figure 4).

A new cystoscopy was performed 24 months after the initial treatment, revealing a remarkable macroscopic improvement. The only remnant lesions seen were sandy patches with healthy bladder mucosa and good bladder capacity (Figure 5).

The patient is currently asymptomatic and without hematuria after 4 years of follow up with annual endoscopic bladder examination. The cystoscopy controls are almost normal with exception of residual sandy patches, no other suspicious endoscopic lesions on scheduled follow up.

### Discussion

Five *Schistosoma* species can cause infection in humans; *Schistosoma mansoni* (Africa and South America), *Schistosoma japonicum* (East Asia) and *Schistosoma haematobium* (Africa and Middle East) are the most frequent subtypes. Usually, *S. mansoni* and *S. japonicum* cause intestinal tract disease, while *S. haematobium* causes genitourinary tract disease [1,2].

The prevalence of urinary schistosomiasis is highest in sub-Saharan Africa. The infection tends to occur in rural areas. The children acquire the infection by bathing in fresh water ponds, lakes and rivers contaminated with larvae which enter in the body through skin defects on feet and leg. In *S. haematobium* infection there is no significant difference in prevalence or intensity between gender and age groups.

As a consequence, human contact with freshwater is required for transmission of schistosomiasis. The lifecycle begins with eggs seeding into fresh water through faeces (*S. mansoni* and *S. japonicum*) or urine (*S. haematobium*). The eggs hatch and release miracidio penetrate snails, which are the intermediate host. Cercariae, the infectious form, are produced inside the snail, and are then released from the

snail into the water. Cercariae penetrate in human skin and reach the liver, where they mature. The adult worms migrate to the mesenteric venous of the colon or the vesicle venous plexus (*S. haematobium*). After months the female worms deposit eggs that move towards the lumen of the intestine or bladder and ureters and are eliminated in faeces or urine [2].

Regarding clinical manifestations, dermatitis, abdominal pain, fever, hematuria and hemospermia can be observed during the acute *S. haematobium* infection [3].

*S. haematobium* typically involves the bladder, lower ureters, seminal vesicles [4,5]. The acute lesions are inflammatory: mucosal granulomas, nodules or masses which usually ulcerate and show hyperaemic surrounding mucosa. On the other hand, chronic lesions are fibrotic: pale mucosa with patches of granular floor, known as “sandy patches”. The patchy nature of the lesion may spare healthy mucosa that becomes encysted by the surrounding fibrosis, leading to a typical picture known as “cystic cystitis”. The bladder neck is one of the most frequent sites for oviposition which may induce a bladder neck obstruction. The same lesions have been described in the lower ureters with the same result.

In longstanding infection, dysuria, hesitancy and intermittent hematuria are common symptoms. At this stage the bladder wall is fibrotic and may present patches and calcifications. Bladder neck obstruction, hydro ureter and hydronephrosis can ensue, leading to obstructive renal failure and bacterial infection. Female genital manifestations may include hypertrophic and ulcerative lesions of the vulva, vagina and cervix, as well as affect ovaries and fallopian tubes leading to infertility. Male genital manifestations may involve of the epididymus, testicles, spermatic cord or prostate. Genital lesions can be reversible with treatment. Genital schistosomiasis infection is also described as a risk factor for VIH sexually transmitted infection [6].

To our knowledge the correlation between histopathological findings and each macroscopic image has not yet been described for urinary schistosomiasis. Regarding female genital schistosomiasis a histopathological findings of the different macroscopic lesions caused by *S. haematobium* where described. The authors reported 1) rubbery papules with showed *S. haematobium* ova by eosinophil response and epithelial erosion (Splendore-Hoeppli phenomenon); 2) sandy patches characterized by moderate immune reaction; and 3) a malignant-looking lesion without neoplastic cells detected. Neither dysplasia nor atypia were seen in the biopsy specimens [6].

Finally, longstanding infection may also be associated with bladder cancer [4]. In East Africa and Middle East, Schistosomiasis is, in part, responsible for the high incidence of bladder cancer; the median age at diagnosis of this cancer is in the fifth decade. Bladder cancer is approximately five fold higher in men than in women, probably due to men being more often employed in agricultural duties. Schistosomiasis is associated with all types of bladder cancer: squamous cell carcinoma (50%), transitional cell carcinoma (36%), adenocarcinoma (10%), and mixed or undifferentiated tumours (5%).

Our patient presented an extended and advanced bladder condition, according with a longstanding schistosomiasis disease. The macroscopic cystoscopy exploration described 1) inflammatory lesions as hyperaemic mucosa; 2) exophytic lesions as solid nodules or papillary tumours; 3) fibrotic and plane lesion as sandy patches or mucosal scars. The histopathological examination showed inflammatory response with erosion, inflammation, eosinophils and hyperplasia in the shape of “Brunnests”; however there is not a correlation between the grade of macroscopic damage and the grade of histopathological aggressiveness or malignancy, instead of the independent collection of bladder tissue samples during TURB. After treatment with Praziquantel these lesions developed a macroscopic and clinical improvement. The follow up consisted in an annual cystoscopy, which only showed “sandy patches”, described as fibrotic or residual lesions. After 4 years of annual follow up, there are no signs of bladder cancer.

## Conclusions

*Schistosomiasis* is one of the most ancient diseases known to affect humans on very large scale. Out of endemic areas a high degree of suspicion is needed in order to avoid diagnosis failures. Treat the infection and perform a long follow up to avoid the associated risks is mandatory.

The different bladder macroscopic lesions, independently of the grade of advancement, show the same histopathological pattern and none of them present neither atypia nor malignant fashion at any stage. In our case, there is not a relationship between the microscopic and macroscopic features of bladder schistosomiasis, in spite of the meticulous collection of each biopsy from each different macroscopic lesion.

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