CASE REPORT

PROSTATIC *SCHISTOSOMA JAPONICUM* WITH ATYPICAL IMMUNOPHENOTYPING OF INDIVIDUAL GLANDULAR TUBES: A CASE REPORT AND REVIEW OF THE LITERATURE

Zuhu Yu[1,2,3], Can Wei[1,2,3], Yadong Wang[1,2,3], Zhichao Ye[1,3], Zihui Wang[4], Zebo Chen[1,3], Liangchao Ni[1,3], Shangqi Yang[1,3], Yaoting Gui[3], Zhichen Guan[1], Zhiming Cai[3] and Yongqing Lai[1,3]

[1]Department of Urology, Peking University Shenzhen Hospital, Shenzhen; [2]Anhui Medical University, Hefei; [3]The Key Laboratory of Stem Cell Biology, Guangdong and Shenzhen Key Laboratory of Male Reproductive Medicine and Genetics, Institute of Urology, Peking University Shenzhen Hospital, Shenzhen PKU-HKUST Medical Center, Shenzhen; [4]Department of Pathology, Peking University Shenzhen Hospital, Shenzhen, PR China

Abstract. There are few cases of prostatic schistosomiasis. Here we report a case of *Schistosoma japonicum* of the prostate, in which the immunophenotyping of individual glandular tubes was atypical. Whether the *S. japonicum* infection contributed to the lesion or not is unknown. We suspect the lesion was a sign of early precancerous hyperplasia. Follow-up of this patient may give clues about the relationship between schistosomiasis and prostate cancer. This is the first case report of prostatic *S. japonicum* in the English literatures. A review of the literature is carried out.

Keywords: *Schistosoma japonicum*, prostate, immunophenotyping, glandular tube

INTRODUCTION

Schistosomiasis is found in 75 countries worldwide including Asia, Africa and Latin America and is one of the most important tropical infectious diseases in the world (Yosry, 2006). Approximately 200 million people worldwide are believed to be infected, leading to the loss of 1.53 million disability-adjusted life years (Gryseels *et al,* 2006). The major species of *Schistosoma* infecting humans are *Schistosoma mansoni*, *S. haematobium* and *S. japonicum*. *S. haematobium* lives in the veins of the bladder and perivesical venous plexus (Fu *et al,* 2012). The adult worm spawns its eggs in the bladder wall, leading to chronic inflammation of the bladder, which is associated with hyperplasia of the bladder mucosa and squamous metaplasia (Von Lichtenberg *et al,* 1971). On rare occasions, it can be found in the uterus, vaginal wall, prostate

Correspondence: Yongqing Lai, Department of Urology, Peking University Shenzhen Hospital, Shenzhen 518036, PR China.
Tel: +86 0755 83923333 5862
E-mail: yqlord@163.com

and other genitourinary organs (Cheever, 1978). To our knowledge, there are no case reports in the English literature of *S. japonicum* infecting the prostate. This is the first case report of prostatic *S. japonicum*.

CASE REPORT

A 66-year-old man came to the outpatient department with a complaint of frequent micturition. He denied a past medical history of diabetes, heart disease, hepatitis or tuberculosis. He did have a history of hypertension for several years. The patient had grown up in Honghu, a city along the bank of the Yangtze River, a place where *S. japonicum* is prevalent. He had no complaints of dysuria, hematuria, fever, diarrhea, vomiting or other symptoms. General physical examination was unremarkable. Rectal examination revealed an enlarged, firm prostate with no nodes. Laboratory investigations showed a total prostatic specific antigen (TPSA) of 5.7 ng/ml and a free prostatic specific antigen (FPSA) of 0.949 ng/ml (reference values: TPSA <4 ng/ml, FPSA <0.934 ng/ml). Ultrasound examination of the urinary system revealed an enlarged prostate. Ultrasound guided transrectal biopsy of the prostate was performed. Twelve specimens were obtained from the four zones of the prostate and sent for histopathological and immunohistochemical examinations. The results revealed hyperplasia of both the stromal cells and gland of the prostate. Additionally, scattered eggs of *S. japonicum* were found in the middle section of the left lateral side of the prostate (Fig 1A). Immunohistochemical examination (examining antibodies to p504S, 34βE12 and P63) revealed benign hyperplasia of the prostate. However, immunophenotyping of the individual glandular tubes was atypical (Fig 1B). A diagnosis of prostate cancer could not be ruled out completely. A serum examination revealed IgG against *S. japonicum* was positive (+++). The patient was treated with praziquantel for prostatic schistosomiasis. At present, the patient is undergoing close follow-up.

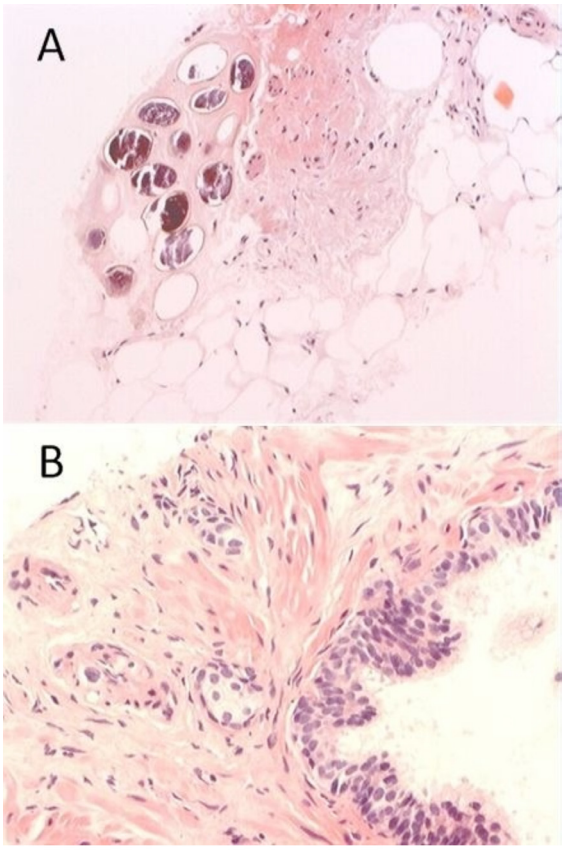

Fig 1–Photomicrograph of prostatic tissue. (A): Prostatic tissue with scattered *Schistosoma japonicum* eggs (x100). (B): Benign hyperplasia of prostate (x200).

DISCUSSION

Schistosomiasis of the prostate is uncommon. We searched PubMed for reports and found case reports of concomitant prostatic schistosomiasis and

Table 1
Published literature of patients with prostatic schistosomiasis.

Author	Year	Country of patient	Patient age (years)	Signs and symptoms	Medical history	Laboratory results	Pathological diagnosis	*Schistosoma* species
Al Adnani	1985	Iraq	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Squamous carcinoma of prostate	Not mentioned
Alexis and Domingo	1986	Puerto Rico	49	Urinary tract obstruction	Unremarkable	Alkaline phosphatase (↑), Acid phosphatase (↑)	PAC	*S. mansoni*
Cohen *et al*	1995	South Africa	27, 29, 29	Weight loss, malaise, back pain, urinary symptoms	Not mentioned	PSA (↑)	PAC	*S. haematobium*
Basilio-de-Oliveira *et al*	2002	Brazil	68	Routine examination	Unremarkable	PSA (↑)	PAC	*S.mansoni*
Lambertucci *et al*	2006	Brazil	56	Routine examination	Unremarkable	PSA (↑)	PAC has not been discarded.	*S.mansoni*
Bacelar *et al*	2007	Brazil	47	Diagnosis of PAC (Gleason score 3+3, cT2a)	PAC	PSA (↑)	PAC	*S.mansoni*
Mazigo *et al*	2010	Tanzania	50	Chronic hematuria and suprapubic pain	Unremarkable	Hemoglobin (↓)	PAC	*S. haematobium*
			75	Frequent micturition	Unremarkable	Urea (↑), Hemoglobin (↓)	PAC	*S. haematobium*
			41	Suprapubic mass, frequent micturition	Unremarkable	Hemoglobin (↓), Urine creatinine (↓)	PAC	*S. haematobium*

PAC, prostatic adenocarcinoma; PSA, prostatic specific antigen; ↑, elevated; ↓, decreased.

adenocarcinoma. Schistosomiasis has long been associated with malignant disease. In 1911, Ferguson published a case series of 40 Egyptian patients with simultaneous bladder cancer and *S. haematobium* infection and proposed a relationship between schistosomiasis and bladder cancer. Some studies have reported a link between *S. japonicum* infection and carcinoma of the colon and rectum (Ch'en *et al,* 1965; Ming-Chai e*t al,* 1980). However, case reports of schistosoma infection and prostate cancer are rare (Table 1).

Al Adnani (1985) reported two Iraqi patients with schistosomiasis and prostatic carcinoma, squamous cell carcinoma of the prostate and calcified eggs in the seminal vesicles were found. Using immunohistochemistry, the author confirmed the tumor was a primary tumor of the prostate in both cases, rather than infiltration of bladder cancer (Bacelar *et al,* 2007).

Prostatic cancer and schistosomiasis of the prostate have also been reported in younger patients: a 49-year-old patient was diagnosed with simultaneous prostate cancer and *S. mansoni* (Alexis and Domingo, 1986), and another case was reported in 1992 (Godec *et al,* 1992). At the time of diagnosis, the patient already had spread of the cancer to his lumbar spine. Pathology showed a diffusely infiltrating adenocarcinoma with *S. mansoni* eggs surrounded by inflammatory cells. The authors suggested severe infection of the prostatic gland with *S. mansoni* eggs may be associated with the development of cancer in young patients. Cohen *et al* (1995) reported a case series of patients with simultaneous advanced prostate cancer and infection with *S. haematobium* in South Africa. The patients were diagnosed with advanced cancer at an unusually young age without a family history of malignancy. One patient was 27 years old and the other two were 29 years old. The young patients with simultaneous advanced prostate cancer and *S. haematobium* infection raise the possibility of a relationship between neoplasia of the prostate and schistosomiasis. The authors proposed infection with schistosoma could have been a causal factor for the development of prostate cancer at a young age.

The species of schistosoma in the case reports were *S. mansoni* and *S. haematobium*. As far as we know, there have been no case reports of *S. japonicum* of the prostate in the English literature; this is the first one. As to the possible relationship between schistosomiasis and carcinoma of the prostate, many authors have proposed the hypothesis that glandular atrophy associated with focal fibrosis of the prostate may lead to precancerous hyperplasia (Moore, 1936; Franks, 1973). Other authors have suggested the presence of carcinogens in the parasite and the enzyme beta-glucuronidase tends to act as cofactors for inducing cancer (Khalafallah and Abul-Fadl, 1964; Mazigo *et al,* 2010). In our case, fibrosis of the prostate was not clearly present, but the immunophenotying of individual glandular tubes was atypical. Studies of animal models with prostatic schistosomiasis may provide clues to the mechanisms involved.

Even though there are several case reports of schistosoma infection of the prostate in prostate cancer patients, the causal relationship between adenocarcinoma of prostate and schistosoma infection is unclear. In our case, the immunohistochemical examination revealed immunophenotying of individual glandular tubes was atypical. Whether schistosoma infection contributed to the atypical immunophenotying of the glandular tubes is unknown. We suspect precancerous hyperplasia is the cause of the elevated

PSA level, even though the diagnosis of precancerous lesions lacks sufficient evidence because of the limited pathologic findings. The patient is undergoing close follow-up. Follow-up may give a clue to the relationship between schistosomiasis and prostate cancer. If the patient develops precancerous lesions or adenocarcinoma, our suspicions will be supported by the findings. The possibility of a causal relationship between schistosomiasis and prostatic cancer will be further supported.

In conclusion, the relationship between schistosomiasis and prostate cancer remains unclear. We report a case of *S. japonicum* of the prostate in which the immunohistochemistry findings showed atypical individual glandular tubes. We suspect the lesion is an early stage of precancerous hyperplasia. Follow-up will help us better understand the relationship between schistosomiasis and prostate cancer.

ACKNOWLEDGEMENTS

This work was supported by the National Natural Science Foundation of China (No. 81101922).

REFERENCES

Al Adnani MS. Schistosomiasis, metaplasia and squamous cell carcinoma of the prostate: histogenesis of the squamous cancer cells determined by localization of specific markers. *Neoplasma* 1985; 32: 613-22.

Alexis R, Domingo J. Schistosomiasis and adenocarcinoma of prostate: a morphologic study. *Hum Pathol* 1986; 17: 757-60.

Bacelar A, Castro LG, De Queiroz AC, Cafe E. Association between prostate cancer and schistosomiasis in young patients: a case report and literature review. *Braz J Infect Dis* 2007; 11: 520-2.

Basilio-de-Oliveira CA, Aquino A, Simon EF, Eyer-Silva WA.Concomitant prostatic schistosomiasis and adenocarcinoma: case report and review. *Braz J Infect Dis* 2002; 6: 45-9.

Ch'en MC, Hu JC, Chang PY, *et al.* Pathogenesis of carcinoma of the colon and rectum in schistosomiasis japonica: a study on 90 cases. *Chin Med J* 1965; 84: 513-25.

Cheever AW. Schistosomiasis and neoplasia. *J Natl Cancer Inst* 1978; 61: 13-8.

Cohen RJ, Edgar SG, Cooper K. Schistosomiasis and prostate cancer. *Pathology* 1995; 27: 115-6.

Ferguson AR. Associated bilharziosis and primary malignant disease of the urinary bladder, with observations on a series of forty cases. *J Pathol Bacteriol* 1911; 16: 76-94.

Franks LM. Proceedings: etiology, epidemiology, and pathology of prostatic cancer. *Cancer* 1973; 32: 1092-5.

Fu CL, Odegaard JI, Herbert DR,Hsieh MH. A novel mouse model of *Schistosoma haematobium* egg-induced immunopathology. *PLoS Pathog* 2012; 8: e1002605.

Godec CJ, Grunberger I, Carr GA. Simultaneous presence of schistosomiasis and advanced cancer in prostate. *Urology* 1992; 39: 547-9.

Gryseels B, Polman K, Clerinx J, Kestens L. Human schistosomiasis. *Lancet* 2006; 368: 1106-18.

Khalafallah AS, Abul-Fadl MA. Studies on the urinary excretion of certain tryptophan metabolites before and after tryptophan loading dose in bilharziasis, bilharzial bladder cancer and certain other types of malignancies in Egypt. *Br J Cancer* 1964; 13: 592-604.

Lambertucci JR, Voieta I, Barbosa AJ. Schistosomiasis mansoni of the prostate. *Rev Soc Bras Med Trop* 2006; 39: 233-4.

Mazigo HD, Zinga M, Heukelbach J, Rambau P. Case series of adenocarcinoma of the prostate associated with *Schistosoma haematobium* infection in Tanzania. *J Glob Infect Dis* 2010; 2: 307-9.

Ming-Chai C, Chi-Yuan C, Pei-Yu C, Jen-Chun H. Evolution of colorectal cancer in schistosomiasis: transitional mucosal changes adjacent to large intestinal carcinoma in colectomy specimens. *Cancer* 1980; 46: 1661-75.

Moore RA.The Evolution and involution of the prostate gland. *Am J Pathol* 1936; 12: 599-624.

Von Lichtenberg F, Edington GM, Nwabuebo I, Taylor JR, Smith JH. Pathologic effects of schistomiasis in Ibadan Western State of Nigeria. II. Pathogenesis of lesions of the bladder and ureters. *Am J Trop Med Hyg* 1971; 20: 244-54.

Yosry A. Schistosomiasis and neoplasia. *Contrib Microbiol* 2006; 13: 81-100.