

Association Between Prostate Cancer and Schistosomiasis in Young Patients: A Case Report and Literature Review

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This case report refers to a 47-year old patient with prostate cancer associated with schistosomiasis mansoni, who was submitted to radical prostatectomy. This is the third report published in the literature with respect to this association, and up to the present time it is still not known whether a cause and effect relationship exists between the two pathologies. The association between schistosomiasis and cancer has been well-documented in bladder cancer; however, there are no data yet proving the association of this disease with prostatic neoplasia. In this report, a third documented case of prostatic adenocarcinoma and schistosomiasis mansoni is described and a literature review is performed.

Key-Words: Prostate cancer, schistosomiasis, prostatectomy, pathology.

Schistosomiasis is one of the most important tropical infectious diseases in the world. Around 200-300 million people are estimated to be infected and 600 million to 1 billion individuals are at risk of acquiring the infection [1].

In 1991, Ferguson raised the hypothesis of a causal relationship between schistosomiasis and carcinoma of the bladder [2], later found to be caused by *Schistosoma haematobium* infection in geographical locations in which the prevalence of this parasite is high [3,4]. Subsequently, a relationship was found between schistosomiasis and other malignant tumors such as colorectal and kidney carcinomas associated with *S. japonicum* [5-8].

The concomitant presence of adenocarcinoma of the prostate and schistosomiasis is very rare. Up to the present time, only 7 cases of prostatic schistosomiasis associated with adenocarcinoma of the prostate have been reported, 3 of which were associated with *S. haematobium*, 2 with *S. mansoni* and in 2 cases the species of parasite was not specified [9-13]. The present report documents the third case of adenocarcinoma of the prostate and schistosomiasis mansoni found in the same surgical sample of a patient submitted to radical prostatectomy.

Case Report

IGB, 47 years of age, had a preoperative diagnosis of adenocarcinoma of the prostate, Gleason score 3+3, PSA 9.4 ng/mL and a 1.0 cm nodule on the left lobe of the prostate (cT2a). Transrectal biopsy revealed that 6 of the 6 fragments obtained (100% of the fragments) were positive, 10%-70% of each of the fragments containing tumor cells. Preoperative staging was negative for extraprostatic disease and in March 2006 the patient was submitted to radical, retropublic

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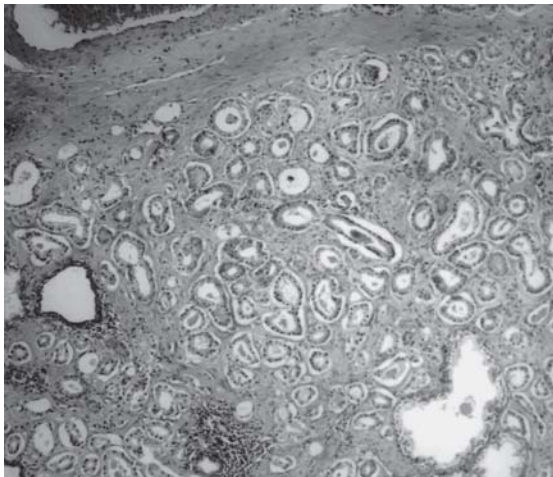
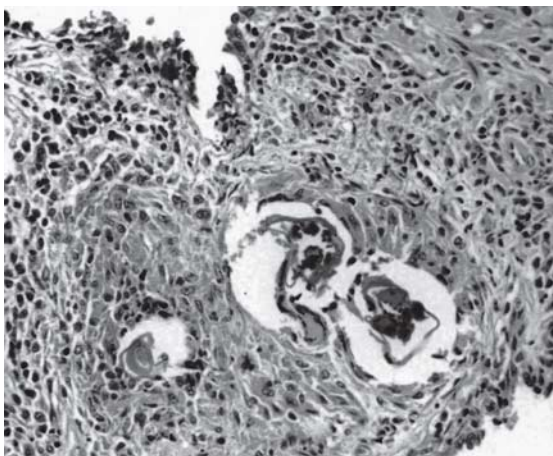
prostatectomy. Analysis of the surgical sample revealed adenocarcinoma of the prostate, Gleason score 3+3, affecting the left and right lobes, with extracapsular extension on the left, and a confined tumor associated with schistosomiasis mansoni (pT3aNOMx of the TNM classification) on the right. At the 3-month postoperative follow-up visit, the patient was continent and impotent with PSA < 0.02 ng/mL.

Pathology

The surgical sample weighed 45 grams, and had seminal vesicles of normal appearance. Histological evaluation was carried out on sections of paraffin blocks using the usual hematoxylin and eosin staining technique. The microscopic study confirmed adenocarcinoma of the prostate (Figure 1), Gleason score 6 (3+3), the principal area affected being the base of the left lobe, with extracapsular extension and no invasion of the seminal vesicles. The sections of the right lobe of the gland were found to contain isolated and confluent granulomatous lesions and *S. mansoni* eggs, which were mostly viable and with recent granulomas (Figures 2 and 3). This type of abnormality was not found in the sections from the left lobe, in the seminal vesicles or in the periprostatic tissue.

Discussion

Schistosomiasis has long been associated with certain types of neoplasia. The association of *S. haematobium* with bladder cancer in patients from regions in which the disease is endemic (part of Africa, particularly along the River Nile, and in the Middle East) is a frequent and well-known fact [3,10]. *S. haematobium* lives in the perivesical venous plexus and in the veins of the bladder. It deposits its eggs in the bladder wall, provoking untreatable chronic cystitis associated with hyperplasia of the bladder mucosa and squamous metaplasia [14]. Less frequently, it is found in the uterus, vaginal wall, prostate and other organs [13]. High levels of beta-glucuronidase have been found in patients with schistosomiasis, this enzyme being known to produce carcinogenic agents [9]. One important aspect observed in several studies concerns the age of the patients in whom

Figure 1. Adenocarcinoma of the prostate (100x).**Figure 2.** Various viable *S. mansoni* eggs with granulomatous lesions (100x).**Figure 3.** *S. mansoni* eggs (400x).

schistosomiasis is associated with cancer. In one study carried out in 1,095 patients with bladder cancer in India, the mean age of patients was lower (46.7 versus 53.2 years, $p < 0.05$) in the egg-positive cases (82.4% of surgical samples taken during cystectomy) compared to the egg-negative cases [4]. Likewise, rates of colorectal cancer are high in China in regions that are endemic for *S. japonicum* compared to non-endemic areas. In one study involving 454 patients, mean age was only 36.9 years, 6.5 years younger in the 288 patients of the group in whom cancer was associated with schistosomiasis ($p < 0.05$) [7].

S. mansoni affecting the urological organs has been well-documented [10]. Radstake et al. found *S. mansoni* eggs in the bladder wall of 22.5% of autopsied patients with bladder cancer [15]. *S. mansoni* eggs are found in the prostate of 7% of patients with schistosomiasis. In one study carried out in autopsied patients with schistosomiasis, the prostate and bladder were affected in 6.5% and 22% of cases, respectively [10]. Moreover, in 73.7% of cases of patients with

schistosomiasis in which the prostate was affected, age varied between 14 and 40 years. Further studies carried out in areas that are endemic for *S. mansoni*, such as South America, may provide further information with respect to this parasite and may confirm a possible association between schistosomiasis and prostate cancer, since the habitat of this parasite is known to be close to the prostate [16]. Despite the relative frequency of infestation of the prostate in endemic areas, the association of schistosomiasis and prostate cancer has rarely been reported.

The hypothesis has been proposed that glandular atrophy associated with focal fibrosis of the prostate, as seen during the aging process, may lead to precancerous hyperplasia [17,18]. The fibrosis in the stroma and the possible secondary glandular atrophy observed in schistosomiasis of the prostate may likewise act to induce preneoplastic glandular changes. In addition, the presence of carcinogens in the parasite may act as a cofactor responsible for inducing neoplasia, as previously suggested by various authors [9,19,20].

Our patient is the third reported case of prostatic schistosomiasis mansoni associated with prostate cancer. The first two cases describing this association were reported by Al Adnani in 1985 [9]. In that study, carried out in Kuwait, the authors reported on a histological study of surgical samples taken from two Iraqi patients submitted to prostatectomy in which various schistosoma eggs associated with squamous carcinoma cells of the prostate were found together with calcified eggs in the seminal vesicles. The author questioned whether this might be the case of a bladder tumor invading the prostate; however, the tumor was confirmed to be primary of the prostate in both cases. This author omitted, however to describe the species of parasite and the clinical history of the patients. In another two reports on one single patient, *S. mansoni* eggs were found in the prostate of a 49-year old patient with metastasized prostate cancer, treated with bilateral orchiectomy and radiotherapy. The authors suggested that a

large number of eggs may be related to the development of cancer in young patients [10,11].

Cohen et al. reported on three patients in South Africa, one of 27 years of age and the other two of 29 years of age, with advanced prostate cancer and no family history of the disease [12]. In all three patients, prostate cancer was associated with the presence of multiple eggs of *S. haematobium* (some viable and others calcified). In these cases, the young age of the patients affected once again emphasizes the possibility of a causal relationship between the diseases.

Basilio-de-Oliveira et al. reported the case of a 68 year old Brazilian patient submitted to prostatic biopsy in which adenocarcinoma of the prostate and various *S. mansoni* eggs were found [13]. In the investigation for metastases, a mass was found on the right kidney, later identified as a renal carcinoma; however, no association was found between schistosomiasis and the renal lesion. Radical prostatectomy was carried out and schistosomiasis was treated with oxamniquine.

The age at the time of diagnosis of prostate cancer of the patient in the present case report and of four of the five patients for whom age was provided, was under 50 years (mean 36 years), compatible with the age of patients in the autopsy studies discussed previously and well below the mean age at diagnosis of patients with prostate cancer. Cohen et al. believes that these tumors develop years earlier, possibly when patients are around 20 years of age, at which age infestation by schistosomiasis tends to occur in endemic regions [12].

Conclusion

The association of prostate cancer and schistosomiasis is rare and may be related to the early development of prostate cancer in endemic regions. Investigation of the possible carcinogenic agents in experimental models of prostatic schistosomiasis may lead to greater understanding of the physiopathology of this association.

References

- King C.H., Mahmoud A.A.F. *Schistosoma* and other trematodes. In: Gorbarch S.L., Bartlett J.G., Lacklow N.R. eds. Infectious Diseases. Philadelphia: W.B. Saunders Company, 1998.
- Ferguson A.R. Associated bilharziosis and primary malignant disease of the urinary bladder, with observations on a series of forty cases. *Journal of Pathology and Bacteriology* 1991;16:76-94.
- Malik M.O., Veress B., Daoud E.H., el Hassan A.M. Pattern of bladder cancer in the Sudan and its relation to schistosomiasis: a study of 255 vesical carcinomas. *J Trop Med Hyg* 1975;78:219-63.
- El-Bolkainy M.N., Mokhtar N.M., Ghoneim M.A., Hussein M.H. The impact of schistosomiasis on the pathobiology of bladder carcinoma. *Cancer* 1981;48:2643-8.
- Smith J.H., Kamel I.A., Elwi A., Von Lichtenberg F. A quantitative post mortem analysis of urinary schistosomiasis in Egypt. I. Pathology and pathogenesis. *Am J Trop Med Hyg* 1974;23:1054-71.
- Cheever A.W. Schistosomiasis and neoplasia. *J Natl Cancer Inst* 1978;61:13-8.
- Chen M.C., Chang P.Y., Chuang C.Y., et al. Colorectal cancer and schistosomiasis. *Lancet* 1981;1:971-3.
- Kuper H., Adami H.O., Trichopoulos D. Infections as a major preventable cause of human cancer. *J Intern Med* 2000;248:171-83.
- Al Adnani M.S. 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.
- Godec C.J., Grunberger I., Carr G.A. Simultaneous presence of schistosomiasis and advanced cancer in prostate. *Urology* 1992;39:547-9.
- Cohen R.J., Edgar S.G., Cooper K. Schistosomiasis and prostate cancer. *Pathology* 1995;27:115-6.
- Basilio-de-Oliveira C.A., Aquino A., Simon E.F., Eyer-Silva W.A. Concomitant Prostatic Schistosomiasis and Adenocarcinoma: Case Report and Review. *Braz J Infect Dis* 2002;6:45-9.
- Von Lichtenberg F., Edington G.M., Nwabuebo I., et al. Pathologic effects of schistosomiasis in Ibadan, Western State of Nigeria. II. Pathogenesis of lesions of the bladder and ureters. *Am J Trop Med Hyg* 1971;20:244-54.
- Radstake H.N., Collenteur J.C., Herderschee D., Smit A.M. Bladder involvement in schistosomiasis *Schistosoma mansoni*. *Trop Geogr Med* 1973;25:84-7.
- Gelfand M., Ross C.M.D., Blair D.M., et al. Schistosomiasis of the male pelvic organs. Severity of infection as determined by digestion of tissue and histologic methods in 300 cadavers. *Am J Trop Med Hyg* 1970;19:779-84.
- Moore R.A. The evolution and involution of the prostate gland. *Am J Pathol* 1936;12:599-624.
- Franks L.M. Proceedings: Etiology, epidemiology and pathology of prostatic cancer. *Cancer* 1973;32:1092-5.
- Khalafallah A.S., Abul-Fadl M.A. Studies on the urinary excretion of certain tryptophan metabolites before and after tryptophan loading dose in bilharziosis, bilharzial bladder cancer and certain other types of malignancies in Egypt. *Br J Cancer* 1964;13:592-604.
- Abdel-Tawab G.A., Kelada F.S., Kelada N.L. et al. Studies on the aetiology of bilharzial carcinoma of the urinary bladder. V. Excretion of tryptophan metabolites in urine. *Int J Cancer* 1966;1:377-82.