Parasitol Res (2015) 114:351–358
DOI 10.1007/s00436-014-4250-9

REVIEW

Prostate adenocarcinoma associated with prostatic infection due to *Schistosoma haematobium*. Case report and systematic review

Jacinta Chaves Figueiredo · Joachim Richter · Nilo Borja · Antonino Balaca · Sandra Costa · Silvana Belo · Maria Amélia Grácio

Received: 29 October 2014 / Accepted: 26 November 2014 / Published online: 30 December 2014
© Springer-Verlag Berlin Heidelberg 2014

Abstract Schistosomiasis affects more than 240 million people worldwide, an infection which may cause urogenital manifestations including, among others, squamous bladder cancer and prostate involvement. We describe the first case of a prostate adenocarcinoma associated with prostatic *Schistosoma haematobium* infection occurring in Angola. Prostate carcinoma was suspected because of high levels of prostate-specific antigen. This observation prompted us to review the literature on schistosomiaisis with respect to genital pathology and prostate cancer. Described genital manifestations in men include funiculitis, epididymitis, granulomata of the seminal vesicles, testicular masses, and prostate lesions which may cause haematospermia and infertility. In contrast to bladder cancer, only 12 reports including the present case on 17 cases on prostate carcinoma associated with schistosomiasis have been published worldwide. The rarity of reports on prostate carcinoma associated with schistosomiasis is partly due to diagnostic constraints, and its incidence is underestimated. However, in emerging countries, the incidence of prostate cancer appears to increase mainly as a result of urbanization and improved access to health care where schistosomiasis prevalence is decreasing.

Keywords Schistosomiasis · *Schistosoma haematobium* · Prostate · Cancer · Prostate adenocarcinoma · Angola · Africa

J. C. Figueiredo · N. Borja · A. Balaca
Urology Service, Hospital Américo Boavida, Avenida Hoji Ya Henda, Luanda, Angola

J. Richter (✉)
Tropical Medicine Unit, Department for Gastroenterology, Hepatology and Infectious Diseases, University Hospitals, Faculty of Medicine, Heinrich-University Düsseldorf, Düsseldorf, FR, Germany
e-mail: Joachim.Richter@med.uni-duesseldorf.de

S. Costa
Serviço de Anatomia Patológica, Hospital Américo Boavida, Universidade Agostinho Neto, Avenida Hoji Ya Henda, Luanda, Angola

S. Belo · M. A. Grácio
Medical Parasitology Unit/Medical Helminthology and Malacology Group, Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, Rua da Junqueira 100, 1349-008 Lisbon, Portugal

Introduction

Human schistosomiasis *syn.* bilharziasis is a parasitic disease caused by trematode flukes of the genus *Schistosoma*. The World Health Organization conservatively estimates at least 240 million people worldwide who are infected with *Schistosoma* spp. with severe disease manifestations in estimated 20 million people and an incidence of 280,000 deaths yearly (WHO 2014; Colley et al. 2014). Mobile larvae called cercariae penetrate the skin when the individuals are in contact with contaminated freshwater about two months later the larvae have matured into the adult worms which descend the mesenterial vessels for reaching small peripheral vessels of the intestine, the bladder and/or reproductive organs. Adult schistosome worms colonize the blood vessels for years, successfully evading the immune system while excreting hundreds to thousands of ova daily, which must either leave the body in excreta or become trapped in nearby tissues. Trapped ova induce a chronic granulomatous response that causes local and systemic pathological effects ranging from anaemia, growth stunting, impaired cognition and decreased physical fitness, with largely unknown effects on endocrinologic hormones and their receptors to organ-specific effects such as severe hepatosplenism, portal fibrosis with portal hypertension (Colley et al. 2014). Urogenital involvement may cause

in women stigmatization, infertility, vagino-vesical fistulae and negative pregnancy outcomes, and in men infertility and scrotal swellings (Leutscher et al. 2000; Richter 2000; Richter et al. 2002, 2008; Kjetland et al. 2012). Schistosomiasis of the lower reproductive tract seems to constitute a risk factor for transmission of sexually transmitted diseases including HIV (Feldmeier et al. 1994; Kjetland et al. 2012; Ndeffo Mbah et al. 2013, 2014). Of the six species pathogenic to humans, two are endemic in Angola, *Schistosoma (S.) mansoni* and *Schistosoma haematobium* (Ministry of Health of Angola 2005; WHO 2014).

Materials and methods

A 56-year-old black man living in Malanje (Angola) was admitted to the Service of External Urology Consultation of the Américo Boavida Hospital in Luanda (Angola) because of diminution of the urinary jet, urine dripping, dysuria, pollakisura, nycturia, urgency for urination and with antecedent episodes of total haematuria and terminal haematuria, as well as haematospermia in adolescence. He recalled his actual urinary symptoms to having been present for at least 3 years. Medical history otherwise was not indicative, including treatments for arterial hypertension, but he did not recall any sexually transmitted infection (STI), trauma of the urethra, previous surgery. The patient admitted moderate consumption of alcohol and did not smoke. He did not know of any significant family antecedents.

Ethical considerations

Before the investigations, the patient was informed in detail on all investigations planned and provided written informed consent according to the protocol approved by the Ethics Committee of the Américo Boavida Hospital of Luanda and the Health Minister of Angola.

Literature research

To know about the frequency of the association of prostate cancer and schistosomiasis, a systematic MEDLINE research was performed with the search term association of "prostate cancer AND schistosomiasis". Other sources were retrieved from other published articles investigated not listed in these databases or via internet research. MEDLINE data were compared with other arguments to obtain a still approximative but better idea of the relative frequency of hits obtained. These terms included "prostate cancer", "adenocarcinoma of the prostate", "squamous prostate cancer", "schistosomiasis", "genitourinary schistosomiasis", "bladder cancer", "transitional bladder cancer", "squamous bladder cancer", "schistosomiasis AND bladder cancer", "genital schistosomiasis", "colon cancer AND schistosomiasis", "uterine cancer AND schistosomiasis", "uterus cancer AND schistosomiasis", "cervical cancer AND schistosomiasis". Although the case series was small and not comparable with other meta-analysis on a large number of trials, transparent data analysis is presented adhering to the spirit of the PRISMA declaration (Moher et al. 2009).

Results

Case report

At physical examination, the patient reported bilateral loin pain. Digital examination of the rectum revealed an enlarged prostate that was hard, irregular in shape, without a groove and with a peripheral nodule. Haematology tests revealed anaemia (7 g/dl) (normal value [*n*]=14.0/18.0), with relative eosinophilia 10 % ($n \leq 5$ %), serum urea 59 mg/dl ($n < 55$), serum creatinine 1.4 mg/dl ($n \leq 1.0$), urine with leucocytes 20/μl ($n \leq 10$) and numerous bacteria. Urine culture revealed a superinfection by *Escherichia coli*, 10^6/ml which was cured with ciprofloxacine. HIV serology was negative, prostatic specific antigen (PSA) was elevated to >100 ng/ml (n=0.02-4.0) and chest X-ray was normal.

At abdominal ultrasonography, the bladder neck was hyperechogenic, the urinary tract being otherwise normal. Prostate ultrasonography showed a heterogenous structure with an irregular and nodular capsule weighing 75 g by ultrasonographic volumetry (Sukov et al. 1977). Radiography of the pelvis and lumbosacral column showed foci suspicious of bone metastases. A sextant biopsy was made that histologically showed glands covered in epithelial cells showing signs of malignancy indicating a well-differentiated adenocarcinoma. Gleason score was (3+3) 6, with presence of *S. haematobium* ova (Fig. 1).

A combined treatment was initiated with s.c. injections of a luteinising hormone-releasing hormone (LHRH) agonist (goserelin acetate, Zoladex®, AstraZeneca, London, UK), and radiotherapy was foreseen. Unfortunately, the patient, who originated from a place 400 km distant from Luanda, did not come back for follow-up examinations.

Database research

The MEDLINE research with the term association "prostate cancer AND schistosomiasis" yielded 39 results of which 9 were case or small case series reports comprising 14 patients. Two other Nigerian publications were retrieved via the Internet (Al Adnani 1985; Tungekar and Al Adnani 1986; Alexis and Domingo 1986; Godec et al. 1992; Cohen et al. 1995; Ma and Srigley 1995; Basílio de Oliveira et al. 2002; Bacelar et al. 2007; Manasseh et al. 2009; Mazigo et al. 2010;

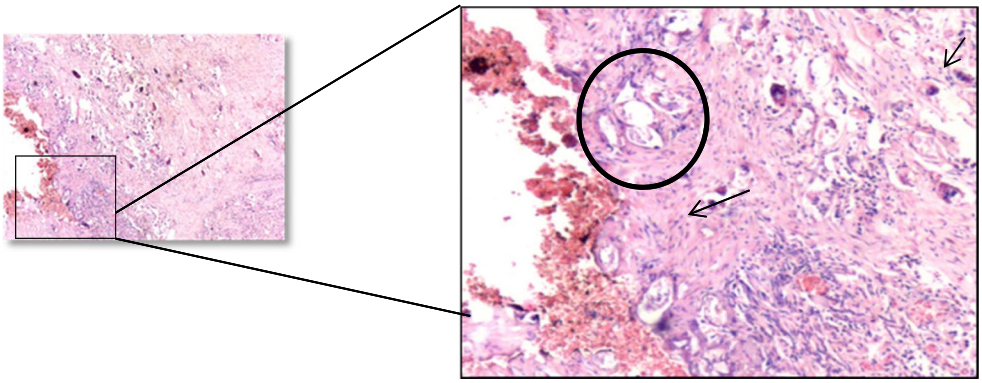

Fig. 1 Histological result of prostatic gland with adenocarcinoma (arrow) with Gleason of 3+3 and calcified eggs of *Schistosoma haematobium* (*inside the circle*). Haemotoxylin and eosin (H and E) stains. ×40 objective

Okani et al. 2013) The research process is described in detail in Table 1. Taken all together including our patient, only 17 cases have been described worldwide (Table 2). The median age of the patients including the patient presented was 50 years (range 27–75). In four studies, patient age was not reported. It was lower in patients with prostate cancer associated with *S. haematobium* infection (27, 29, 29, 41, 50, 56, 63, 75 years) as compared to patients with *S. mansoni* infection (47, 49, 68, 70 years). In three of the studies retrieved by the research "prostate cancer AND schistosomiasis", the low frequency of prostate cancer in case series was mentioned; in further 7/13 studies on "bladder cancer AND schistosomiasis", the absence of prostate involvement was specifically reported (Houston 1968; Powell et al. 1968; Sherif et al. 1980; Osegbe and Amaku 1984; Al Adnani 1986; Ebert 1987; Sharfi and Hassan 1994; Nabeeh et al. 1995; Dawam et al. 2001; Mohammed et al. 2003). For a rough comparison of the perceived importance of the medical problem, other MEDLINE research gave the following figures: the research term "prostate cancer" yielded 118.856, "bladder cancer" 60.888, "schistosomiasis" 22.832, "transitional bladder cancer" 14.945, "adenocarcinoma of the prostate" 13.568, "squamous bladder cancer 3.036, "genitourinary schistosomiasis" 1.642, "squamous prostate cancer" 1.237, "schistosomiaisis AND squamous bladder cancer" 594, "prostatete cancer AND Africa" 442, "schistosomiasis AND HIV" 269, "genital schistosomiasis" 257, "male genital schistosomiasis" 212, "colon cancer AND schistosomiasis" 113, "rectum cancer AND schistosomiasis" 84, "uterine cancer AND schistosomiasis" 60, "uterus cancer AND schistosomiasis" 60, and "cervical cancer AND schistosomiasis" 56, "prostate malignancy AND schistosomiasis" 26, "scrotal schistosomiasis" 17, "testicular carcinoma AND schistosomiasis" 15, and "hydrocele AND schistosomiasis" 7 hits, respectively.

Table 1 Result of MEDLINE search on publications (search term "prostate cancer AND schistosomiasis")

Number of hits	39
Urologic reviews, management of urologic problems	3
Reviews on schistosomiasis	3
Schistosomiasis related bladder cancer	13
Tumour marker studies including schistosomiasis patients	3
Schistosomiasis of the seminal vesicles	3
Epidemiological studies reporting a low particularly low prevalence of prostate cancer	3
Schistosomal prostate lesions without malignancy	2
Prostate malignancy associated with schistosomiasis	9

Discussion

Schistosomal involvement of the genital organs has been reported mainly in infections due to *S. haematobium* but may occur also in relation to infections by the other species *S. mansoni*, *S. intercalatum*, *S. japonicum*. In men involvement of testicles, seminal vesicles, epididimus, funiculus spermaticus, testicular, scrotum and the gland have been reported (Oliveira 1951; Chaves and Figueiredo 1965; Zaher and El-Deeb 1971; Abul-Khair et al. 1980; Malik and Ibrahim 1982; Fievet et al. 1985; Omer 1985; Bambirra et al. 1986; Mikhail et al. 1988; Lukács et al. 1989; Elem et al. 1989; Wedel and Jess 1991; Githae 1992; Ihekwaba 1992; Khinev and Ralichkova 1993; Corachan et al. 1994; McKenna et al. 1997; Torresi et al. 1997; Vilana et al. 1997; Whitty et al. 2000; Schwartz et al. 2002; Richter et al. 2002; Al-Saeed et al. 2003; Alves et al. 2004; de Cassio Saito et al. 2004; Mortati Neto et al. 2004; Durand et al. 2004; Leutscher et al. 2005; Dauda and Rafindadi 2006; Pérignon et al. 2007; Lambertucci et al. 2007; Ramarokoto et al. 2008; Pawel et al. 2008; Rambau et al. 2009; Leutscher et al. 2009; Al-Qahtani and Droupy 2010; Hassan et al. 2011; Lopes et al. 2011; Periyasamy et al. 2011; Xue et al. 2011; Badmus et al. 2012; Shebel et al. 2012; Ehsani and Osunkoya 2013; Okani et al. 2013; Yu et al. 2013). Little is known on genital infections due to the less frequent species *S. mekongi*, *S. malayensis* and to infection by hybrids between human and zoonotic schistosomes, as well as *S. guineensis* (Moné et al. 2012). The association between urinary schistosomiasis and squamous bladder cancer is well-

Table 2 Cases of prostate carcinoma associated with schistosomiasis published

	S.h.	*S.m.*	*n.r.*	Reference (1st author)	Country of patients' origin
Adeno-Ca	3			Cohen	South Africa
	3			Mazigo	Tanzania
	1			Okani	Nigeria
	1			Figueiredo*	Angola*
		1		Godec	USA (imported)
		3		Alexis, Basilio, Bacelar	Brazil
		1		Manasseh	Nigeria
			1	Ma	Canada (Ghanaian immigrant)
Squamous	2			Adnani	Iraq
Sarcoma	1			Tungekar	Kuwait (imported)
Total	11	5	1		

S.h. Schistosoma haematobium, *S.m. Schistosoma mansoni*, *n.r.* not reported nor identifiable from epidemiology (Al Adnani 1985; Tungekar and Al Adnani 1986; Alexis and Domingo 1986; Godec et al. 1992; Cohen et al. 1995; Ma and Srigley 1995; Basílio de Oliveira et al. 2002; Bacelar et al. 2007; Manasseh et al. 2009; Mazigo et al. 2010; Okani et al. 2013; Figueiredo et al. 2014* is the present report)

documented especially in Egypt although geographic differences and co-factors are not sufficiently elucidated (Honeycutt et al. 2014). Not only chronic inflammation would play a role in the development of bladder cancer but also hormonal factors which may act without the necessity that worm ova are exactly localised in the place where cancer develops (Botelho et al. 2010a, b). The association between other malignancies and schistosomiasis is by far less evident, having been postulated associations between schistosomiasis and colonic or cervical cancer (Richter 2000). Histologically, schistosomiasis-associated bladder cancer is squamous (Botelho et al. 2010a; Honeycutt et al. 2014). In Angola, schistosomiasis-associated squamous bladder cancers have been a frequent cause of death (Lopes 1983; Leitão 1989; Botelho et al. 2010a).

The frequency of schistosomal prostate infections as resulting from post-mortem studies exceeds that of diagnosis in vivo by far. In a Zimbabwen study carried out in 1970, seminal vesicles were affected in 70 %, urinary bladder in 65 %, the vas deferens in 42 % and prostate in 21 % of male corpses (Gelfand et al. 1970). In a necropsy study in Zambia on 50 cadavers, the bladder was involved by *S. haematobium* in 62 %, seminal vesicles in 58 % and the prostate in 50 % of cases (Patil and Elem 1988). In a recent prospective study of prostate glands from 79 post-mortem cases of Nigerian adults who died of non-prostate-related illnesses, three patients (3.8 %) had schistosomiasis with ova of *S. haematobium* in the prostate. In these three cases, one case of schistosomiasis was associated with adenocarcinoma, one with nodular hyperplasia of the prostate and one was pure schistosomiasis (Okani et al. 2013). An inconstant key symptom for the involvement of the male genital organs is haematospermia (Omer 1985; Corachan et al. 1994; McKenna et al. 1997; Torresi et al. 1997; Whitty et al. 2000; Schwartz et al. 2002; Durand et al. 2004; Leutscher et al. 2005, 2009; Pérignon et al. 2007; Yu et al. 2013). Abnormal semen quality may contribute to infertility, and probably partly because male genital schistosomiasis is associated with haematospermia, it may constitute a factor for the transmission of sexually transmitted diseases (Feldmeier et al. 1994; Ndeffo Mbah et al. 2013, Ndeffo Mbah et al. 2014). The suspicion of genital schistosimiasis is confirmed by microscopy of the ejaculate confirming the presence of schistosome ova. Genital schistosomiasis may cause infertility and endocrine insufficiency in women and men (Rambau et al. 2009; Leutscher et al. 2009; Kjetland et al. 2012; Schanz et al. 2010; Santos et al. 2014). The prostate gland is not seldomly involved where echogenic and calcified foci may be detected (Vilana et al. 1997; Ramarokoto et al. 2008). Since ova are not always excreted in urine, multiple stool examinations are also required. In travelers from non-endemic areas, serology may be also useful (Corachan et al. 1994; McKenna et al. 1997; Torresi et al. 1997; Whitty et al. 2000; Schwartz et al. 2002; Durand et al. 2004; Pérignon et al. 2007). Prostatic lesions are seen most frequently in *S. haematobium* infections but have also been reported in infections by *S. mansoni*, *S. intercalatum*, and *S. japonicum* (Corachan et al. 1994; Lambertucci et al. 2007; Yu et al. 2013). Increased prevalence of leukocytes and elevated cytokine levels in semen from *S. haematobium*-infected Madagascan men (Leutscher et al. 2005) and premalignant abnormalities have been described in a prostatic *S. japonicum* infection (Yu et al. 2013). Considering the high prevalence of schistosomal prostate infections and the chronic inflammatory stimulus produced as well as the well-recognised oncogenicity of *S. haematobium* regarding squamous bladder cancer, one would expect to find more reports on the association between schistosomiasis and prostate cancer. Looking through the literature, it is striking that, as compared to the literature on schistosomiasis-associated bladder cancer, that there are so few reports on

prostate carcinoma associated with schistosomiasis and, interstingly, no report on schistosomaisis associated with testicular carcinoma (in all 15 references found in MEDLINE on testicular malignancy AND schistosomiasis, malignancy was excluded, 12 references indicated schistosomiasis mimicking a testicular malignancy [Elem et al. 1989; Wedel and Jess 1991; Githae 1992; Ihekwaba 1992; Khinev and Ralichkova 1993; de Cassio Saito et al. 2004; Mortati Neto et al. 2004; Dauda and Rafindadi 2006; Rambau et al. 2009; Al-Qahtani and Droupy 2010; Hassan et al. 2011; Periyasamy et al. 2011]).

One hypothesis that one could put forward is that the large majority of schistosomiasis-associated prostate cancers are missed by figures regarding the health care systems in schistosomiasis endemic areas. Usually, these rural areas characterized by poverty and very little access to appropriate health care. Furthermore, people from highly endemic areas who live since generations exposed to *S. haematobium* may interpret haematuria and hematospermia as signs which are not life-menacing or even as a parallel for sexual maturity similar to menarche in adolescent girls (Amazigo et al. 1997). Men with prostate cancer may not go to seek health care, a way which may take hours or even days of walk. When they die, this may be perceived as "slim disease", or when a febrile bacterial superinfection occurs, death may be interpreted as a febrile malaria attack. In fact, autopsies are rarely performed in this setting. Where health care centres are available, it is extremely difficult to have histopathology examinations performed (Okesina 2009). Test methods which rose the suspicion of prostate cancer in our patient such as PSA increase or its velocity are even more seldomly available (Bolarin and Badejo 1985; Cohen et al. 1995; Thompson and Ankerst 2007; Ehsani and Osunkoya 2013). Since the advent of less invasive tools namely ultrasonography, schistosomal lesions of the genital tract as well as prostate abnormalities may be more frequently recognised in vivo (Vilana et al. 1997; Richter 2000; Richter et al. 2003; Ramarokoto et al. 2008). But, even ultrasonography is still mostly not available for the poor people of rural environments.

An alternative hypothesis to explain the rarity of prostate cancer associated with schistosomiasis might be that this association is in fact very rare and is even more rare than the one to be expected by the mere coincidence of two frequent disease conditions. Interestingly, prostate cancer was deemed to be rare in Africa, an argument which was put forward against a genetic predisposition for prostate cancer in Africans and African descendents (Houston 1968; Sherif et al. 1980; Peters and Armstrong 2005). Many reports on haematuria in endemic areas report squamous bladder cancer and specifically mention that the prostate was not involved (Powell et al. 1968; Osegbe and Amaku 1984; Al Adnani 1986; Ebert 1987; Sharfi and Hassan 1994; Nabeeh et al. 1995; Dawam et al. 2001; Mohammed et al. 2003). Moreover, in emerging countries, the decrease of schistosomiasis infections seems to be paralleled by an increase of prostate carcinoma (Magoha 2007; Parkin et al. 2008; Tindall et al. 2013). A meta-analysis of studies performed worldwide showed significant differences of incidence and outcomes of prostate cancers between rural and urban settings (Obertova et al. 2012). Former Egyptian studies indicated that although schistosomiasis was highly prevalent and incidence of squamous bladder cancer was high, prostate cancer was rare (Sherif et al. 1980). In a recent Egyptian study, i.e. a study performed in a country of high prevalence of schistosomiasis in rural settings, the incidence of prostate cancer was found to be almost five times higher in men living in urban settings which are usually free of schistosomiasis (Dey et al. 2011). Epidemiological studies have yielded evidence that actually prostate cancer is frequent in Africa (Magoha 2007; Parkin et al. 2008; Ogunbiyi 2011; Tindall et al. 2013; Laryea et al. 2014; Hsing et al. 2014; Wabinga et al. 2014; Saeed et al. 2014). Especially in emerging nations such as Egypt, Ghana, Nigeria or Brazil, increase of life expectancy and improvement of health care is to be expected to coincide with an increase of the diagnosis of prostate cancer, as it has already been observed in cancer registries of Nigeria, Ghana, Sudan and Uganda which cover mainly urban populations (Ogunbiyi 2011; Hsing et al. 2014; Laryea et al. 2014; Wabinga et al. 2014; Saeed et al. 2014). Risk factors suspected in the Western world such as sedentary life and fatty food would also affect these populations. These observations must be taken into account when interpreting statistics on the incidence of prostate cancer in schistosomiasis endemic countries.

The development of malignancies is multifactorial, and the identification of risk factors is difficult. Furthermore, not necessarily all histologic types of prostate cancer are due to the same factors. In analogy with bladder cancer, one would expect that especially squamous prostate cancer is related to schistosomiasis, whereas the most frequent type of prostate cancer described in association with schistosomiasis is adenocarcinoma (see Table 2). Interestingly, an Egyptian study observed that carcinoembryonic antigen was increased in patients with *S. haematobium* infection whether associated with squamous bladder carcinoma or not but not in patients with prostate cancer (Alsabti and Kamel 1979). The species most frequently described in association with prostate cancer is *S. haematobium*. Models to explain carcinogenesis in bladder cancer may possibly be applicable only to squamous prostate carcinoma but not to adenocarcinoma. For example, in Egypt, transitional cell bladder carcinoma has supplanted squamous cell bladder carcinoma following the decline in the prevalence of *S. haematobium* infection (Felix et al. 2008). It is also conceivable that human populations in co-evolution for hundreds to thousands of years with *S. haematobium* involving frequently the prostate gland have developed a certain immune tolerance. Individually, the severity of organ pathology is not strictly correlated to the worm burden, which means that

individual genetic factors influence the inflammatory and immune response phaenotype and thus the outcome of the infection as it has been shown in *S. mansoni*-related liver fibrosis (King et al. 2004; Chevillard et al. 2003). Therefore, it is possible that the immune response to schistosome antigens in single patients triggers carcinogenesis, an observation that explains why some of the patients described develop their prostate cancer at a very young age below 30 years.

Conclusions

There are only very few reports on the association between schistosomiasis and prostate cancer, mainly case reports, if one considers the high prevalence of schistosomiasis in endemic areas and the high incidence of prostate cancer worldwide. The total number of patients with such a disease association published amounts to 17 cases. This scarcity of reports is partly due to the diagnostic difficulties in patients of rural endemic areas with limited access to health care and financial constraints. However, since other conditions affecting the same patient groups such as squamous bladder cancer and genital schistosomiasis are much better documented, prostate cancer related to schistosomiasis is probably rare. In individual patients with a particular genetic background and immunological phenotype schistosomiasis may contribute to the development of prostate cancer at a young age. In future, the incidence or prostate cancer must be expected to increase in Africa. The decrease of the prevalence of schistosomiasis will be statistically more than counterbalanced by the increased chance of reaching a higher age, of being diagnosed in a less resource-poor environment and by the increasing risk associated with an urban lifestyle.

References

Abul-Khair MH, Arafa NM, Sobeih AM, Taalab AA (1980) Sonography of bilharzial masses of the scrotum. J Clin Ultrasound 8(3):239–240

Al Adnani MS (1985) Schistosomiasis, metaplasia and squamous cell carcinoma of the prostate: histogenesis of the squamous cancer cells determined by localization of specific markers. Neoplasma 32(5): 613–622

Al Adnani MS (1986) Origin of carcinomas causing bladder neck obstruction demonstrated by immunoperoxidase localisation of specific antigens. Br J Urol 58(3):283–286

Alexis R, Domingo J (1986) Schistosomiasis and adenocarcinoma of prostate: a morphologic study. A case of prostatic adenocarcinoma coincident with *Schistosoma mansoni*. Hum Pathol 17(7):757–760

Al-Qahtani SM, Droupy SJ (2010) Testicular schistosomiasis. Saudi Med J 31(3):325–327

Alsabti EA, Kamel A (1979) Carcinoembryonic antigen (CEA) in patients with malignant and non-malignant diseases. Neoplasma 26(5): 603–609

Al-Saeed O, Sheikh M, Kehinde EO, Makar R (2003) Seminal vesicle masses detected incidentally during transrectal sonographic examination of the prostate. J Clin Ultrasound 31(4):201–206

Alves LS, Assis BP, Rezende MM (2004) Schistosomal epididymitis. Int Braz J Urol 30(5):413–415

Amazigo UO, Anago-Amanze CI, Okeibunor JC (1997) Urinary schistosomiasis among school children in Nigeria: consequences of indigenous beliefs and water contact activities. J Biosoc Sci 29(1):9–18

Bacelar A, Castro LG, de Queiroz AC, Café E, Braz J (2007) Association between prostate cancer and schistosomiasis in young patients: a case report and literature review. Infect Dis 11(5):520–522

Badmus TA, Takure AO, Osasan SA, Olajide AO, Sabageh DO (2012) Testicular schistosomiasis: a case report. Niger Postgrad Med J 19(1):50–51

Bambirra EA, Andrade Jde S, Bamberg A, de Souza EA, Mitidiero CE, de Souza AF (1986) Testicular schistosomiasis mansoni: a differential diagnostic problem with testicular neoplasias. Am J Trop Med Hyg 35(4):791–792

Basílio de Oliveira CA, Aquino A, Simon EF, Eyer-Silva WA (2002) Concomitant prostatic schistosomiasis and adenocarcinoma: case report and review. Braz J Infect Dis 6(1):45–49

Bolarin DM, Badejo OA (1985) Prostate-specific aci phosphatase in Nigerian patients with prostate carcinoma. East Afr Med J 62(5): 332–337

Botelho MC, Machado JC, da Costa JM (2010a) *Schistosoma haematobium* and bladder cancer: what lies beneath? Virulence 1: 84–87

Botelho MC, Soares R, Vale N, Ribeiro R, Camilo V, Almeida R, Medeiros R, Gomes P, Machado JC, Correia da Costa JM (2010b) *Schistosoma haematobium*: identification of new estrogenic molecules with estradiol antagonistic activity and ability to inactivate estrogen receptor in mammalian cells. Exp Parasitol 126:526–535

Chaves E, Figueiredo JN (1965) Schistosomiasis of the scrotum. Rev Inst Med Trop Sao Paulo 7(6):343–345

Chevillard C, Moukoko CE, Elwali NE, Bream JH, Kouriba B, Argiro L, Rahoud S, Mergani A, Henri S, Gaudart J, Mohamed-Ali Q, Young HA, Dessein AJ (2003) IFN-gamma polymorphisms (IFN-gamma + 2109 and IFN-gamma +3810) are associated with severe hepatic fibrosis in human hepatic schistosomiasis (*Schistosoma mansoni*). J Immunol 171(10):5596–5601

Cohen RJ, Edgar SG, Cooper K (1995) Schistosomiasis and prostate cancer. Pathology 27(2):115–116

Colley D, Bustinduy AL, Secor WE, King C (2014) Human schistosomiasis. Lancet 383(9936):2253–2264

Corachan M, Valls ME, Gascon J, Almeda J, Vilana R (1994) Hematospermia: a new etiology of clinical interest. Am J Trop Med Hyg 50(5):580–584

Dauda MM, Rafindadi AH (2006) Testicular schistosomiasis simulating malignancy. Trop Dr 36:182–183

Dawam D, Kalayi GD, Osuide JA, Muhammad I, Garg SK (2001) Haematuria in Africa: is the pattern changing? BJU Int 87(4):326–330

de Cassio Saito O, de Barros N, Chammas MC, Oliveira IR, Cerri GG (2004) Ultrasound of tropical and infectious diseases that affect the scrotum. Ultrasound Q 20(1):12–18

Dey S, Zhang Z, Hablas A, Seifeldein IA, Ramadan M, El-Hamzawy H (2011) Geographic patterns of cancer in the population based. Cancer Epidemiol 35:254–264

Durand F, Brion JP, Terrier N, Pinel C, Pelloux H (2004) Funiculitis due to *Schistosoma haematobium*: uncommon diagnosis using parasitologic analysis of semen. Am J Trop Med Hyg 70(1):46–47

Ebert W (1987) Incidence and significance of bilharziasis in the Republic of Mozambique state Caique. Z Urol Nephrol 80(11):625–628, German

Ehsani L, Osunkoya AO (2013) Schistosomiasis of the prostate: a case report. Anal Quant Cytol Histol 35(3):178–180

Elem B, Patil PS, Lambert TK (1989) Giant fibrous pseudotumor of the testicular tunics in association with *Schistosoma haematobium* infection. J Urol 141(2):376–377

Feldmeier H, Krantz I, Poggensee G (1994) Female genital schistosomiasis as a risk-factor for the transmission of HIV. Int J STD AIDS 5(5):368–372

Felix AS, Soliman AS, Khaled H, Zaghloul MS, Banerjee M, El-Baradie M, El-Kalawy M, Abd-Elsayed AA, Ismail K, Hablas A, Seifeldin IA, Ramadan M, Wilson ML (2008) The changing patterns of bladder cancer in Egypt over the past 26 years. Cancer Causes Control 19(4):421–429

Fievet JP, Gras C, Floch JJ, Zimmermann JM, Cazenave JC, Barnaud P (1985) Genitourinary bilharzioma. Isolated cases of vesical bilharzioma and epididymal bilharzioma. Med Trop (Marseille) 45(3):313–317, French

Gelfand M, Ross CMD, Blar DM, Castle WM, Weber MC (1970) Schistosomiasis of the male pelvic organs severity of infection as determined by digestion of tissue and histologic methods in 300 cadavers. Am Trop Med Hyg 19(5):779–784

Githae GM (1992) Testicular schistosomiasis simulating a malignant tumour or tuberculosis. S Afr Med J 81(6):338

Godec CJ, Grunberger I, Carr GA (1992) Simultaneous presence of schistosomiasis and advanced cancer in prostate. Urology 39(6): 547–549

Hassan A, El-Mogy S, Zalata K, Mostafa T (2011) Testicular schistosomiasis: a case study. Fertil Steril 95(6):2124.e1–4

Honeycutt J, Hammam O, Fu CL, Hsieh MH (2014) Controversies and challenges in research on urogenital schistosomiasis-associated bladder cancer. Trends Parasitol. doi:10.1016/j.pt.2014.05.004 [Epub ahead of print]

Houston W (1968) The Bantu prostate: a study of prostatic disease in Central Africa. J Urol 99(3):316–320

Hsing AW, Yeboah E, Biritwum R, Tettey Y, De Marzo AM, Adjei A, Netto GJ, Yu K, Li Y, Chokkalingam AP, Chu LW, Chia D, Partin A, Thompson IM, Quraishi SM, Niwa S, Tarone R, Hoover RN (2014) High prevalence of screen detected prostate cancer in West Africans: implications for racial disparity of prostate cancer. J Urol 192(3): 730–735

Ihekwaba FN (1992) Schistosomiasis of the testis. Cent Afr J Med 38(3): 123–127

Khinev A, Ralichkova L (1993) A case of urogenital schistosomiasis–a mask of acute scrotum. Khirurgiia (Sofiia) 46(5):56–57, Bulgarian

King CH, Blanton RE, Muchiri EM, Ouma JH, Kariuki HC, Mungai P, Magak P, Kadzo H, Ireri E, Koech DK (2004) Low heritable component of risk for infection intensity and infection-associated disease in urinary schistosomiasis among Wadigo village populations in Coast Province, Kenya. Am J Trop Med Hyg 70(1):57–62

Kjetland EF, Leutscher PD, Ndhlovu PD (2012) A review of female genital schistosomiasis. Trends Parasitol 28(2):58–65

Lambertucci JR, Voieta I, Barbosa AJ (2007) Schistosomiasis mansoni of the prostate. [Article in English, Portuguese]. Rev Soc Bras Med Trop 40(3):341–342

Laryea DO, Awuah B, Amoako YA, Osei-Bonsu E, Dogbe J, Larsen-Reindorf R, Ansong D, Yeboah-Awudzi K, Oppong JK, Konney TO, Boadu KO, Nguah SB, Titiloye NA, Frimpong NO, Awittor FK, Martin IK (2014) Cancer incidence in Ghana, 2012: evidence from a population-based cancer registry. BMC Cancer 14(1):362

Leitão J (1989) Contribuição para o Estudo da Schistosomiase a *S haematobium* em Angola. Medical Thesis, Luanda University, Angola. Direcção Nacional de Controlo de Endemias. 47 pp. (Portuguese)

Leutscher P, Ramarokoto CE, Reimert C, Feldmeier H, Esterre P, Vennervald BJ (2000) Community-based study of genital schistosomiasis in men from Madagascar. Lancet 355(9198):117–118

Leutscher PD, Pedersen M, Raharisolo C, Jensen JS, Hoffmann S, Lisse I, Ostrowski SR, Reimert CM, Mauclere P, Ullum H (2005) Increased prevalence of leukocytes and elevated cytokine levels in semen from *Schistosoma haematobium*-infected individuals. J Infect Dis 191(10):11639–11647

Leutscher PD, Høst E, Reimert CM (2009) Semen quality in Schistosoma haematobium infected men in Madagascar. J Acta Trop 109(1):41–44

Lopes C (1983) A carcerização vesical na schistosomiase em Angola. Medical Thesis, Luanda Unversity, Angola: 125 pp. (Portuguese)

Lopes EJ, de Almeida CE, Jacobino M (2011) Schistosomiasis mansoni in the seminal vesicle. [Article in Portuguese]. Case Rep Infect Dis 2011:787961. doi:10.1155/2011/787961, Epub 2011 Jun 30

Lukács T, Pajor L, Hamza L, El-Seaghy AA (1989) Schistosomal granulation masquerading as testicular tumour. Acta Chir Hung 30(3): 187–191

Ma TK, Srigley JR (1995) Adenocarcinoma of prostate and schistosomiasis: a rare association. Histopathology 27(2):187–189

Magoha GA (2007) Overview of prostate cancer in indigenous black Africans and blacks of African ancestry in diaspora 1935–2007. East Afr Med J 84(9 Suppl):3–11

Malik MO, Ibrahim A (1982) Scrotal swellings in Sudanese patients: a surgical pathology study. Int Surg 67(4 Suppl):513–515

Manasseh AN, Echejoh GO, Tanko MN, Silas OO, Dakum NK, Mandong BM (2009) Prostatic adenocarcinoma coexisting with schistosomiasis. A case report and review of literature. Int J Med Med Sci 1(3):33–37

Mazigo HD, Zinga M, Heukelbach J, Rambau P (2010) Case series of adenocarcinoma of the prostate associated with Schistosoma haematobium infection in Tanzania. J Glob Infect Dis 2(3):307–309

McKenna G, Schousboe M, Paltridge G (1997) Subjective change in ejaculate as symptom of infection with *Schistosoma haematobium* in travellers. BMJ 315(7114):1000–1001

Mikhail NE, Tawfic MI, Hadi AA, Akl M (1988) Schistosomal orchitis simulating malignancy. J Urol 140(1):147–148

Ministry of Health of Angola (2005) Ministerio de Ministério da Saúde de Angola (MINSA). Inquérito Nacional sobre prevalência de helmintíases intestinais e das schistosomíases en crianças em idade escolar. Ministério da Saúde de Angola pp. 1–23. In Portuguese

Mohammed AZ, Alhassan SU, Edino ST, Ochicha (2003) Histopathological review of prostatic diseases in Kano, Nigeria. Niger Postgrad Med J 10(1):1–5

Moher D, Liberati A, Tetzlaff J, Altman DG (2009) PRISMA group preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 62(10):1006–1012

Moné H, Minguez S, Ibikounlé M, Allienne JF, Massougbodji A, Mouahid G (2012) Natural interactions between S. haematobium and S. guineensis in the Republic of Benin. Sci World J: e793420

Mortati Neto N, Grando JP, Moreira HA (2004) Testicular schistosomiasis mimicking tumour. Int Braz J Urol 30(6):502–503

Nabeeh A, Gomha M, Shaaban AA, El-Baz M, El-Dosoky I, Ashamallah A, Ghoneim MA (1995) Orthotopic bladder substitutes: histopathologic risk factors. Scand J Urol Nephrol 29(4):463–467

Ndeffo Mbah ML, Poolman EM, Drain PK, Coffee MP, van der Werf MJ, Galvani AP (2013) HIV and *Schistosoma haematobium* prevalences correlate in sub-Saharan Africa. Trop Med Int Health 18(10):1174–1179

Ndeffo Mbah ML, Gilbert JA, Galvani AP (2014) Evaluating the potential impact of mass praziquantel administration for HIV prevention in *Schistosoma haematobium* high-risk communities. Epidemics 7: 22–27

Obertova Z, Brown C, Holmes H, Lawrenson R (2012) Prostate cancer, incidence and mortality in rural men – a systematic review. Rural Remote Health 12:epub2039

Ogunbiyi OJ (2011) Impact of health system challenges on prostate cancer control: health care experiences in Nigeria. Infect Agent Cancer 6(Suppl 2):5

Okani C, Akang E, Ogunbiyi O (2013) Incidence of sub-clinical prostatic disease at autopsy in the University College Hospital, Ibadan. Open J Urol 3:80–86

Okesina AB (2009) Pathology in West Africa problems of training and practice. Bull R Soc Pathol 148:306–308

Oliveira ES (1951) Schistosomiasis and an elephantoid state; case of an elephantoid condition of the scrotum with the presence of Schistosoma ova. Folha Med 32(20):159–160, Portuguese

Omer EF (1985) Inflammatory conditions and semen quality among subfertile Sudanese males. Trop Dr 15(1):27–28

Osegbe DN, Amaku EO (1984) Haematuria in Nigerians: a prospective study. J Trop Med Hyg 87(3):115–117

Parkin DM, Sitas F, Chirenje M, Stein L, Abratt R, Wabinga H (2008) Part I: cancer in Indigenous Africans–burden, distribution, and trends. Lancet Oncol 9(7):683–692

Patil PS, Elem B (1988) Schistosomiasis of the prostate and the seminal vesicles: observations in Zambia. J Trop Med Hyg 91(5):245–248

Pawel BR, Osman J, Nance ML, McGowan KL (2008) Schistosomiasis: an unexpected finding in an inguinal hernia sac. Pediatr Dev Pathol 11(5):402–404

Pérignon A, Pelicot M, Consigny PH (2007) Genital schistosomiasis in a traveler coming back from Mali. J Travel Med 14(3):197–199

Periyasamy P, Subramaniam SR, Rajalingham S (2011) An increasingly notorious mimicker of testicular tumours; crossing borders. BMJ Case Rep. doi:10.1136/bcr.09.2011.4816

Peters N, Armstrong K (2005) Racial differences in prostate cancer treatment outcomes: a systematic review. Cancer Nurs 2:108–118

Powell SJ, Engelbrecht HE, Welchman JM (1968) Hydronephrosis and urinary tract bilharziasis. A radiological and necropsy survey. Trans R Soc Trop Med Hyg 62(2):231–237

Ramarokoto CE, Leutscher PD, van Dam G, Christensen NO (2008) Ultrasonographical findings in the urogenital organs in women and men infected with Schistosoma haematobium in northern Madagascar. Trans R Soc Trop Med Hyg 102(8):767–773

Rambau PF, Chandika A, Chalya PL, Jackson K (2009) Scrotal swelling and testicular atrophy due to schistosomiasis in a 9-year-old boy: a case report. Acta Trop 109(1):41–44

Richter J (2000) Evolution of schistosomiasis-induced pathology after therapy and interruption of exposure to schistosomes: a review of ultrasonographic studies. Acta Trop 77:111–131

Richter J, Stegemann U, Häussinger (2002) Hydrocele in a young boy with Schistosoma mansoni infection. Brit J Urol 89:1–2

Richter J, Hatz C, Häussinger D (2003) Ultrasound in tropical and parasitic diseases. Lancet 362:900–902

Richter J, Lux J, Reinecke P, Müller-Mattheis V (2008) Of flukes and fistulae. Lancet 371(9620):1308

Saeed IE, Weng HY, Mohamed KH, Mohammed SI (2014) Cancer incidence in Khartoum, Sudan: first results from the cancer registry, 2009–2010. Cancer Med Cancer Med 3(4):1075–1084

Santos J, Gouveia MJ, Vale N, Delgado Mde L, Gonçalves A, da Silva JM, Oliveira C, Xavier P, Gomes P, Santos LL, Lopes C, Barros A, Rinaldi G, Brindley PJ, da Costa JM, Sousa M, Botelho MC (2014) Urinary estrogen metabolites and self-reported infertility in women infected with *Schistosoma haematobium*. PLoS One 9(5):e96774. doi:10.1371/journal.pone.0096774, eCollection 2014

Schanz A, Richter J, Beyer I, Baldus SE, Hess AP, Kruessel JS (2010) Genital schistosomiasis as a cause of female sterility and acute abdomen. Fertil Steril 93(6):2075 e9

Schwartz E, Pick N, Shazberg G, Potasman I (2002) Hematospermia due to schistosome infection in travelers: diagnostic and treatment challenges. Clin Infect Dis 35(11):1420–1424

Sharfi AR, Hassan O (1994) Evaluation of haematuria in Khartoum. East Afr Med J 71(1):29–31

Shebel HM, Elsayes KM, Abou El Atta HM, Elguindy YM, El-Diasty TA (2012) Genitourinary schistosomiasis: life cycle and radiologic-pathologic findings. Radiographics 32(4):1031–1046

Sherif M, Ibrahim AS, El-Aaser AA (1980) Prostatic carcinoma in Egypt: epidemiology and etiology. Scand J Urol Nephrol Suppl 55: 25–26

Sukov RJ, Scardino PT, Sample WF, Winter J, Confer DJ (1977) Computed tomography and transabdominal ultrasound in the evaluation of the prostate. J Comput Assist Tomogr 1(3): 281–289

Thompson IM, Ankerst DP (2007) Prostate-specific antigen in the early detection of prostate cancer. CMAJ 176(13):1853–1858

Tindall EA, Bornman MS, van Zyl S, Segone AM, Monare LR, Venter PA, Hayes VM (2013) Addressing the contribution of previously described genetic and epidemiological risk factors associated with increased prostate cancer risk and aggressive disease within men from South Africa. BMC Urol 13:74. doi:10.1186/1471-2490-13-74

Torresi J, Sheori H, Ryan N, Yung A (1997) Usefulness of semen microscopy in the diagnosis of a difficult case of *Schistosoma haematobium* infection in a returned traveler. J Travel Med 4(1): 46–47

Tungekar MF, Al Adnani MS (1986) Sarcomas of the bladder and prostate: the role of immunohistochemistry and ultrastructure in diagnosis. Eur Urol 12(3):180–183

Vilana R, Corachan M, Gascon J, Valls E, Bru C (1997) Schistosomiasis of the male genital tract: transrectal sonographic findings. J Urol 4: 1491–1493

Wabinga HR, Nambooze S, Amulen PM, Okello C, Mbus L, Parkin DM (2014) Trends in the incidence of cancer in Kampala, Uganda 1991–2010. Int J Cancer 135(2):432–439

Wedel PG, Jess P (1991) Testicular schistosomiasis simulating malignancy. Case report. Scand J Urol Nephrol 25(3):237–238

Whitty CJ, Mabey DC, Armstrong M, Wright SG, Chiodini PL (2000) Presentation and outcome of 1107 cases of schistosomiasis from Africa diagnosed in a non-endemic country. Trans R Soc Trop Med Hyg 94:531–534

World Health Organization (WHO) (2014) Schistosomiasis, Fact sheet N°115. http://www.who.int/mediacentre/factsheets/fs115/en/. Last accessed Dec 17, 2014

Xue K, Pridgeon S, Gillibrand R, Sanchez de Crespo J, Godbole H, Fowlis G (2011) Clinical presentations of *Schistosoma hematobium:* three case reports and review. Can J Urol 18(3):5757–5762

Yu Z, Wei C, Wang Y, Ye Z, Wang Z, Chen Z, Ni L, Yang S, Gui Y, Guan Z, Cai Z, Lai Y (2013) Prostatic *Schistosoma japonicum* with atypical immunophenotyping of individual glandular tubes: a case report and review of the literature. Southeast Asian J Trop Med Public Health 44(4):568–573

Zaher MF, El-Deeb AA (1971) Bilharziasis of the prostate: its relation to bladder neck obstruction and its management. J Urol 106(2):257–261