

Case Report

Bilharzial-associated Squamous Cell Carcinoma of the Bladder in Pregnancy: A Case Report from the Women and Newborn Hospital in Lusaka, Zambia

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ABSTRACT

Squamous cell carcinoma (SCC) of the bladder is a rare and devastating malignancy, usually associated with *Schistosoma haematobium*, particularly in bilharzia-endemic regions of sub-Saharan Africa. Little is written about the condition in pregnancy.

A 21-year-old Gravida 2 Para 1 at 28 weeks gestation presented with worsening symptoms of dysuria, increased frequency of micturition, backache, a painful suprapubic mass and haematuria of over a period of 3 weeks. On examination, vital signs were normal, height of fundus 26cm, with a tender suprapubic mass. Extra peritoneal laparotomy revealed multiple signs of a bladder malignancy which were confirmed by histopathology as *Schistosoma haematobium* ova and invasive keratinising SCC of the bladder, grade 1. Intraoperatively, T4 carcinoma staging was confirmed. Patient was delivered prematurely by caesarean section due to worsening symptoms. Palliative care was instituted as the functional status of the patient did not allow for definitive

management.

Subclinical urinary schistosomiasis can progress to a SCC of the bladder, presenting with symptoms implicated in conditions such as bladder lithiasis, Urinary tract infections and pregnancy. Urine cytology and mass drug administration should be enforced as means of early detection and prevention, respectively in endemic regions.

INTRODUCTION

Squamous cell carcinomas of the bladder are a rare and devastating malignancy usually associated with a *Schistosoma haematobium* aetiology in bilharzia-endemic regions. About 65% of all bladder tumours in regions where bilharziasis is endemic are squamous cell carcinomas and more than 90% of bilharzial squamous cell carcinomas present in T3 and T4 stages¹. Squamous cell carcinomas of the bladder in pregnancy are scarcely represented in the literature and management thereof is made difficult by the fate of the foetus².

We discuss the management of a case of bilharzial associated bladder SCC in pregnancy recorded at the Women and Newborn Hospital (WNH) in Lusaka, Zambia.

Keywords: *Schistosoma haematobium*, pregnancy, squamous cell carcinoma, bladder cancer, Bilharzia, sub-Sahara Africa

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Case Description

A 21-year-old Gravida 2, Para 1, at 28⁺/40 weeks gestation by dates, referred to WNH from a mission hospital with suspicion of hydronephrosis in pregnancy based on a pelvic ultra sound scan findings. She presented with dysuria, increased frequency of micturition, backache, painful suprapubic mass, and haematuria.

Prior to her admission, she consulted spiritual healers and was given an unknown liquid to imbibe. This was ensued by worsening haematuria, which she momentarily ignored as it was described as evidence of cleansing by her spiritual healers.

On hospital admission, examination findings were as follows, blood pressure, respiratory rate, temperature and pulse rate were normal. Obstetric examination revealed a symphysial fundal height of 26cm, and a tender suprapubic mass. A clinical diagnosis of bladder lithiasis in pregnancy was made backed by a pelvic abdominal ultra sound scan which showed hydronephrosis. Her full blood count result showed a moderate anaemia, HIV test was negative. Antibiotics, analgesia, corticosteroids and haematinics were administered to her.

An extraperitoneal laparotomy and a cystotomy was conducted five days after admission which revealed an intensified vascular network in a grossly thickened bladder wall whose mucosa had been completely replaced by nodular lesions which were friable and had a bleeding tendency. No lithiasis was found. Histopathology revealed ova of *Schistosoma haematobium* and an invasive squamous cell carcinoma keratinizing type, grade 1 (figure 1). Delivery was planned for at 34 weeks to enhance foetal lung maturity, after which definitive management was to be instituted.

Eight days postoperative as the patient felt better and awaiting delivery, the patient requested permission to attend a funeral for her late child which was granted, and a request was made to a hospital in her local area to take care of her in case of any emergency. She returned five days later with an infected surgical wound and a vesicocutaneous fistula.

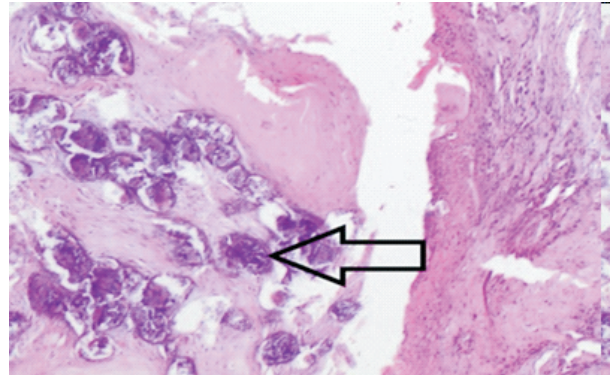


Figure 1. Micrograph showing *S. haematobium* ova adjacent to carcinoma in the bladder wall

The patient went into preterm labour at 32 weeks gestation, nine days after readmission, and delivered a 1.2kg male infant via classical caesarean section because vaginal delivery was considered unattainable due to her clinical condition. Intraoperatively, T4 cancer staging was confirmed. The neonate died 7 days later due to prematurity related complications.

Worsening symptoms of the patient warranted her prompt transfer to the Cancer Diseases Hospital of the University Teaching Hospitals, Lusaka, 14 days after the delivery. A computed tomography (CT) scan done without contrast due to the vesicocutaneous fistula, showed hydronephrosis, a heterogenous bladder mass with mass effect on the rectum, while the liver and lungs appeared normal (figure 2). The CT scan was paid for by social services as the patient could not afford it.

A radical cystectomy and urine by-pass surgery using an ileal conduit was proposed as main stay of treatment, but was found to be contraindicated due to the patient's inflamed surgical wound and general poor performance status including depression. Palliation was instigated and is currently underway, and the patient was discharged from the Cancer Diseases Hospital with ongoing care at home or nearest health facility. The management plan was discussed fully with the patient and her care givers. She awaits reassessment for surgery if and when the

inflammation subsides or further palliative intervention if need be.

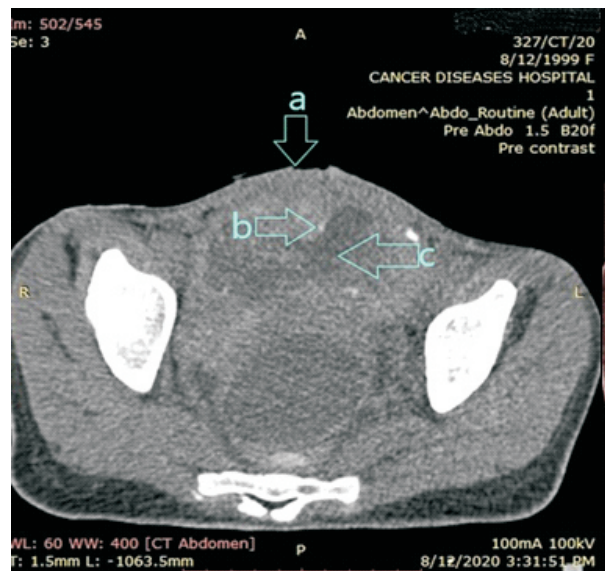


Figure 2. CT scan without contrast showing; A: anterior abdominal wall, B: calcifications, and C: heterogenous mass.

DISCUSSION

Urinary schistosomiasis, caused by the trematode *Schistosoma haematobium*, whose intermediate host is a mollusc and definitive host is man, is asymptomatic in the majority of people it affects³. Inflammatory cells associated with *Schistosoma haematobium* ova deposited in the walls of the urinary bladder and chronic cystitis in urinary schistosomiasis have been implicated in the production of carcinogenic radicals and genetic mutations which cause squamous cell carcinomas of the bladder⁴.

Clinical presentation of squamous cell carcinomas of the bladder includes primarily haematuria with other symptoms such as pain, frequency, urgency, recurring UTIs, chronic cystitis, and advanced stage and may also present with backache and hydronephrosis⁵. This symptomatology is consistent with the presentation of our patient. Conditions such as urinary bladder calculi and pregnancy may present with similar symptoms^{6,7}.

While the mainstay for definitive diagnosis of bladder squamous cell carcinomas remains, bladder wall biopsies for histopathological assays, urine cytology, and adjunct markers such as cytokeratin can provide accurate non-invasive diagnostic criteria, and can be a means of early detection thereof^{8,9}. Additionally, cystoscopy is an important and readily available diagnostic tool as an initial investigation before surgical interventions are instigated.

Radical cystectomy is the gold standard for the treatment of squamous cell carcinomas of the bladder with perioperative chemotherapy and radiation ostensibly being of little benefit¹⁰. However, the health status of our patient could not allow for such surgical interventions, instead palliative care was instituted to support the patients' wellbeing. Recent developments and studies around radiation warrant its re-evaluation as an adjuvant or neoadjuvant treatment⁵. Extensive inoperable squamous cell carcinomas of the bladder should be treated with a combination of chemotherapy and radiation¹¹, however this patient was not clinically fit to undergo this kind of treatment, moreover, she presented in the late second trimester and room was given to allow for foetal maturity. Because most treatment is potentially fetotoxic, termination of pregnancy is advised if the diagnosis of squamous cell carcinoma of the bladder in pregnancy is made before 18 weeks of gestation while administration of corticosteroids to improve neonatal lung function and delaying delivery until viability age are advised if the diagnosis is made after 18 weeks gestation².

Bilharzial infections sequelae such as bladder cancers are preventable primarily via mollusc control and mass anti-bilharzial drug administration in endemic areas¹², and secondarily via early detection using cytology and screening of high-risk groups, such as farmers older than 20 years, in endemic areas¹³. However, the use of anti-bilharzial drugs such as praziquantel in the control of schistosomiasis should be closely monitored to prevent the development of drug resistance¹⁴.

CONCLUSION

Subclinical urinary schistosomiasis can progress to a chronic phase characterised by squamous cell carcinomas of the bladder, which have been shown to present with symptoms also implicated in conditions such as bladder lithiasis, UTIs and pregnancy. Squamous cell carcinomas of the bladder in pregnancy, whose prognosis is poor, can therefore be easily misdiagnosed. Early detection through urine cytology, screening and mass drug administration should be utilised in tandem to prevent the condition.

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REFERENCES

1. El-Sebaie, M., Zaghoul, M. S., Howard, G., & Mokhtar, A., *Squamous cell carcinoma of the bilharzial and non-bilharzial urinary bladder: A review of etiological features, natural history, and management.* . International Journal of Clinical Oncology, 2005. **10**(1): p. 20-25.
2. Alleemudder, D.I., Alleemudder, A. I., Harry, D., & Fountain, S. , *Bladder squamous cell carcinoma in pregnancy.* Journal of Obstetrics and Gynaecology., 2016. **36**(3): p. 388-389.
3. Bamgbola, O.F., *Urinary schistosomiasis.* Pediatric Nephrology, 2014. **29**(11): p. 2113-2120.
4. Yosry, A., *Schistosomiasis and neoplasia.* Contrib Microbiol, 2006. **13**: p. 81-100.
5. Martin, J.W., Carballido, E. M., Ahmed, A., Farhan, B., Dutta, R., Smith, C., & Youssef, R. F. , *Squamous cell carcinoma of the urinary bladder: Systematic review of clinical characteristics and therapeutic approaches.* Arab Journal of Urology, 2016. **14**(3): p. 183-191.
6. Juan, H.-C., Tsia, Y.-F., Liu, C.-C., Pan, S.-C., Chang, P.-C., Huang, C.-H., & Huang, S.-P. , *A Giant Bladder Stone With Bilateral Hydronephrosis in a Young Male.* Urological Science, 2010. **21**(2): p. 103-106.
7. Simonsen, J.A., Graumann, O., Toft, A., Henriques, C. U., & Walter, S. , *Diagnosis and treatment of symptomatic hydronephrosis in pregnancy.* Ugeskrift for Laeger., 2015. **177**(38).
8. Attallah, A.M., El-Didi, M., Seif, F., El-Mohamady, H., & Dalbagni, G. , *Comparative Study Between Cytology and Dot-ELISA for Early Detection of Bladder Cancer.* American Journal of Clinical Pathology., 1996. **105**(1,): p. 109-114.
9. Sullivan, P.S., Chan, J. B., Levin, M. R., & Rao, J. , *Urine cytology and adjunct markers for detection and surveillance of bladder cancer.* American Journal of Translational Research., 2010. **2**(4): p. 412-440.
10. Stensland, K.D., Zaid, H., Broadwin, M., Sorcini, A., Canes, D., Galsky, M., & Moinzadeh, A. , *Comparative Effectiveness of Treatment Strategies for Squamous Cell Carcinoma of the Bladder.* European Urology Oncology, 2018.
11. Prempre, T., & Amornmarn, R. , *Radiation Management of Squamous Cell Carcinoma of the Bladder.* Acta Radiologica: Oncology., 1984. **23**(1): p. 37-42.
12. Lubeya, M., et al., *Hepatosplenic schistosomiasis.* The Lancet, 2010. **376**(9753): p. 1645.
13. Shokeir, A.A., *Squamous cell carcinoma of the bladder: Pathology, diagnosis and treatment.* BJU International., 2004. **93**(2): p. 216-220.
14. LoVerde, P.T., *Schistosomiasis,* in *Digenetic Trematodes,* R.T.B. Fried, Editor. 2019, Springer International Publishing. p. 45-70.