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Invasive Urothelial Carcinoma of the Urinary Bladder in a 19-Year Old Boy with Urinary Schistosomiasis: A Case Report and Review of Literature

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***Abstract*: Background: Invasive urothelial carcinoma of the bladder is a malignant urothelial tumor seen mainly in the 6th and 7th decade of life, and extremely rare in the 1st and 2nd decade. The major predisposing factors include exposure to environmental carcinogens such as aniline dyes, rubber, cigarette smoking, and chronic irritation such as those from long standing bladder stones and indwelling urethral catheters. Only a few cases resulting from *Schistosoma haematobium*-induced chronic inflammation have been reported. Here we report a 19-year old boy who presented to our facility with 3month history of recurrent, terminal, painless hematuria and lower dull aching abdominal pain with *Schistosoma* ova on urine microscopy and biopsy confirmed an invasive urothelial carcinoma.**

***Keywords*: Bladder, transitional cell carcinoma, Schistosoma haematobium, radical cystectomy.**

1. Introduction

Bladder cancers are not usually common before the second decade of life [1], [2] with benign causes of hematuria being more common among patients in this age group. This epidemiological characteristic may lead to a delay in making a diagnosis of bladder cancer in patients in this age group [1]. There has been documented delay of up to a year or more from initial onset of symptoms to diagnosis in many cases [1]. In a study of a ten-year review of gross hematuria among children by Greenfield et al., only 3 out of 342 had bladder tumors [3]. Therefore, the apparent low index of suspicion of bladder cancer among patients with hematuria in this age group was understandable. The majority of patients aged 18-40 years with bladder cancer present with low-grade, non-muscle-invasive disease associated with better survival. However, there is a subset of younger patients with a higher proportion of women who presents with aggressive bladder cancer which may be partly explained by a higher prevalence of variant histology [4].

Bladder cancer is one of the most common forms of malignancies involving the urinary system and multiple risk factors have been associated with its etiology [5], [6]. The commonest being cigarette smoking, various occupational and chemical exposure, dyes, arsenic etc.

It is the 5th most commonly diagnosed cancer in Europe and the 9th leading cause of cancer death [7]. Bladder cancer affects males more than females and its incidence increase with age and seldom seen before the age of 40-years, and usually seen arising most commonly in the seventh decade of life [8]-[10].

Haematuria, frequent urination and pain during urination, are the most common symptoms of bladder cancer. Although bladder cancer are not common in the young, the unpleasant and deleterious consequences associated with delayed diagnosis necessitate the need to raise clinicians' index of suspicion for bladder cancer among patients in this age group.

2. Case Report

We report a 19-year old boy who presented to our facility with 3month history of recurrent, terminal hematuria which eventually progressed to total hematuria 3days prior to presentation. The hematuria was initially painless; however, an insidious onset of dull aching lower abdominal pain subsequently developed and this persisted till presentation. There was no history of trauma to the abdomen, no history of urethral instrumentation or catheterization prior to the onset of hematuria, however patient has history of swimming in pond, patient has no history of cigarette smoking, no history of exposure to any chemical carcinogens. General physical and Abdomino-pelvic examination were unremarkable. Urine microscopy revealed ova of *Schistosoma haematobium* and urine cytology was positive for malignancy. He had urethrocystoscopy which shows studded sandy patches in the posterior wall of the urinary bladder, covering almost the whole of the posterior wall of the bladder. There were also multiple exophytic mass lesions, the largest measuring about 5-7cm on the posterior wall around the right ureteric orifice. Multiple biopsies were taken and histopathologic examination revealed features of an invasive urothelial carcinoma of the bladder with ova of *Schistosoma haematobium* noted. Computed tomography scan (CT scan) of the abdomen showed a mass in

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the bladder wall which has extended into the lower 3cm of the right ureter obstructing the ureteric orifice with dilatation of the ureter and right hydronephrosis. The clinical stage of the urinary bladder carcinoma was T4aN0M0. The patient had radical cystectomy with pelvic lymphadenectomy and ileal neo-bladder construction. He had a smooth recovery; results of histology confirmed a muscle invading urothelial carcinoma of the bladder with no malignant deposits seen in the surrounding fatty tissues excised or the lymph nodes. He did well post operatively with good continence and was rehabilitated back to school on outpatient follow up visits and scheduled to have adjuvant chemotherapy. Patient however could not go through with the chemotherapy due to financial issues, and he subsequently developed lung, liver and bone metastasis one year after the surgery, resulting in his demise from multiple organ failure.

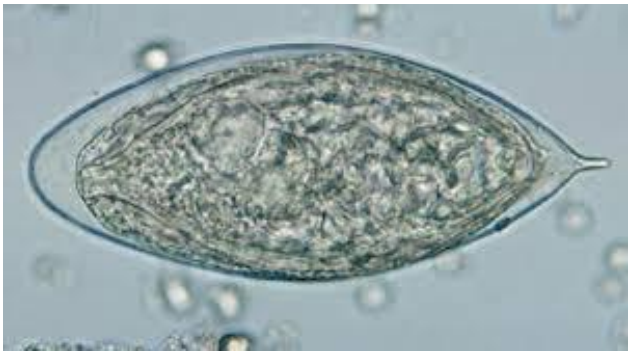

Fig. 1. Schistosoma haematobium ova in the urine microscopy of the patient

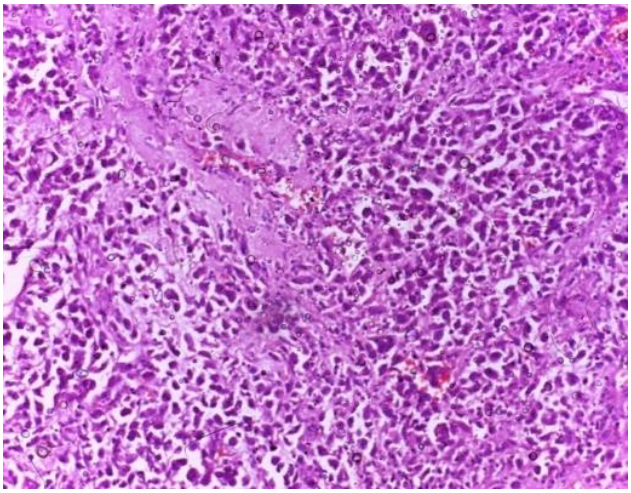

Fig. 2. Histologic sections of bladder tumour showing invasive malignant epithelial tumour disposed in solid sheets with areas of necrosis (arrow) (H&E x200)

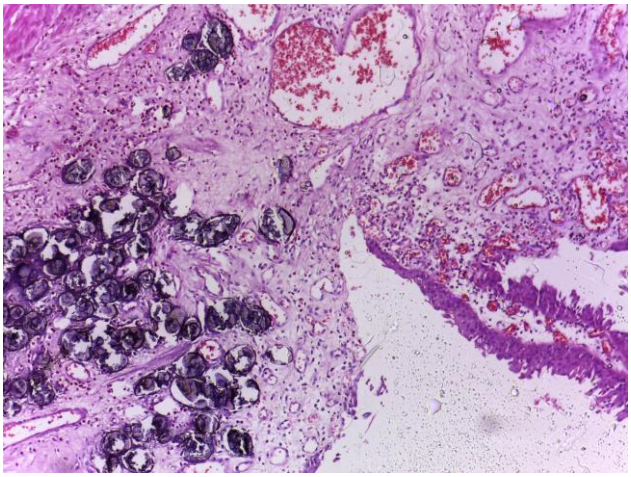

Fig. 3. Histologic sections of the bladder of same patient showing a solitary papillary urothelial lesion (lower right corner) and numerous calcified Schistosome ova (arrows) H&E x100

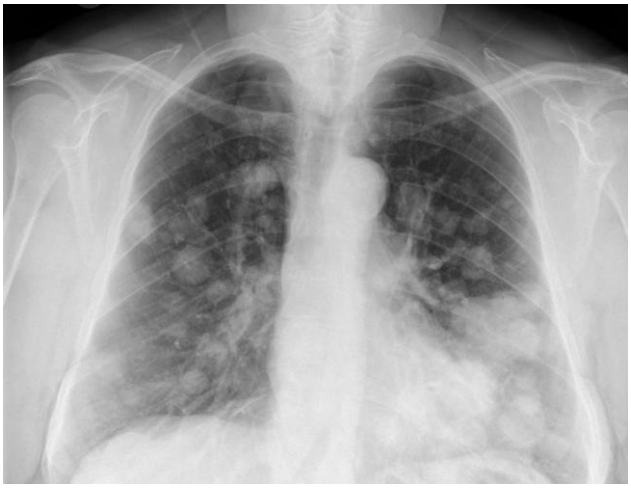

Fig. 4. Chest Xray showing multiple canon ball opacities (metastatic foci) in the chest of the patient

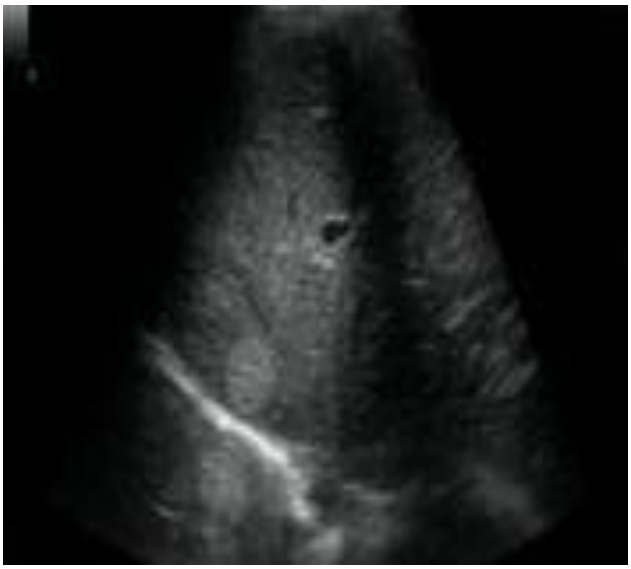

Fig. 5. Abdominal ultrasound scan with metastatic foci in the liver of the patient

3. Discussion

Cigarette smoking, exposure to naphthalene dye, arsenic, bladder stones, cytotoxic drugs such as cyclophosphamide, schistosomiasis, aromatic amines, and exposure to chemicals use in rubber industries have been identified as the major risk factors in the etiology of bladder cancer [11]. However, children before the second decades of life might not have gotten significant exposure for a relevant time to warrant the development of this cancer; thus, the exact cause of bladder cancer among the under-20 age group is still poorly understood. In addition, the clinical suspicion of bladder cancer among patients in this age group is understandably low [10]-[12], even though the incidence of bladder cancer in the young is increasing. Our patient has had no history of cigarette smoking or exposure to any of the well-known carcinogens for bladder cancer, and has no family history of bladder cancer or any other cancers among his first-degree relatives. However, he had a history of swimming in fresh water ponds and recurrent hematuria. The cystoscopy findings of sandy patches were consistent with a diagnosis of chronic vesical schistosomiasis. In addition, the cystoscopy observations of exophytic masses, one of which appeared to infiltrate the urethral orifice raise concern for possible malignant change. As it turned out, multiple biopsies taken from these sites confirmed the presence of an invasive urothelial carcinoma.

Chronic infection with *Schistosoma* haematobium in developing countries, especially Africa have been identified as the major cause of bladder cancer. [13], [14] A higher burden of bladder cancer is seen in regions endemic for *Schistosoma haematobium* such as Egypt and other countries around the Nile River with high incidence of *Schistosoma haematobium* infestation [15], [16]. An association has also been made between chronic urinary schistosomiasis and the development of bladder cancer in North-western Nigeria, where the predominant histological type seen in as much as 50% of the cases were squamous cell carcinomas, in keeping with the chronic irritation-metaplasia-neoplasia theory [17], [18]. However, urinary schistosomiasis had been associated with other histological subtypes of bladder cancer, including Urothelial carcinoma and Aden-carcinoma. Bladder cancers are generally seen mainly around the fifth and sixth decades of life and are less common among the younger age group [19], [20]. Therefore, the etiologic cause of bladder cancer in the young has remained vague. The knowledge of the causal factors for this cancer in the younger age group may help in the institution of preventive measures for this condition among patients of this age group and thereby prevent the deleterious outcome of its diagnosis. The clinical history, urine microscopy findings of *Schistosoma haematobium* and the cystoscopy findings of sandy patches in our index patient suggests the likelihood of Schistosoma infestation as the likely etiological factor in this index case.

The etiology and molecular characteristics of bladder cancer in young adult has not been fully elucidated, although, an immunohistochemical study carried out among 72 young patients with bladder cancer shows *p53* gene product over expression [20] which is also a significant marker of poor prognosis in bladder cancers, especially the poorly differentiated forms. Other studies have also indicated the presence of *p53* gene mutation in Schistosoma bladder cancer mainly seen around the fifth decade of life, suggesting that p53 over-expression in these tumors is not age-specific [21], [22]. Bladder cancer among younger patients has poor prognosis as they are associated with delayed diagnosis, and more aggressive tumors with early metastasis, and higher incidence of recurrence.

At the time of diagnosis of our index case, the cancer had already invaded the lower/distal ends of the ureter on both sides. There were no clinical or radiological evidence of distant spread at the time of diagnosis and the pelvic lymph node and fat cleared during the surgery were tumor free. Surgical margins were also tumor free. However, the inability to institute adjuvant chemotherapy post-surgery due to financial constraints eventually resulted in clinical and radiological evidence of pulmonary and liver metastasis, ultimately leading to his demise.

4. Conclusion

There is rising incidence of bladder cancer in the young. These cancers are aggressive with high potential for recurrence. Increased index of suspicion of bladder cancer among young adults with hematuria is necessary to aid early diagnosis and aggressive management in order to prevent the morbidity and mortality that will arise from late diagnosis and /or presentation. More studies are however required to further characterize the molecular events that underpin the development of bladder cancer in young patients with schistosomiasis.

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Compliance with Ethical Standard

A. Conflict of Interest

The authors declare that they have no conflict of interest.

B. Ethical Approval

Ethical approval was obtained from the ethical board of Abubakar Tafawa-Balewa University Teaching hospital, Bauchi to conduct the study.

5. Informed Consent N/A

A. Author Contribution

All authors have been directly involved with the various aspects of the study. We attest to the fact that all authors have participated in the research, read the manuscript, attest to the validity and legitimacy of the data.

B. Funding

No benefits in any form was received from any commercial party directly or indirectly related to this work.

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