CASE REPORT

Carcinosarcoma of the bladder following local schistosomiasis infection

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SUMMARY

A young patient from central Africa presented acute renal insufficiency due to extrinsic compression of the distal ureters by a pelvic mass. After initial medical management, a biopsy revealed poorly differentiated bladder cancer and *Schistosoma haematobium* eggs embedded in the bladder wall. The initial workup showed evidence of locoregional disease. Radical cystectomy with an incontinent urinary diversion was performed with no complications. Carcinosarcoma of the bladder was diagnosed by pathological analysis of the surgical specimen. After a short follow-up, the patient was readmitted presenting with lung and bone metastases. At 60 days after diagnosis, he died of respiratory insufficiency caused by pulmonary metastatic disease.

BACKGROUND

Genitourinary schistosomiasis is endemic in North and Central African countries and is associated with a higher risk of bladder malignancy. In Egypt, 53% of bladder cancer (BC) has a documented presence of *Schistosoma haematobium* eggs in pathological analysis of the surgical specimen.¹ Different histological types of BC have been described in association with such parasite affection; however, the association of *S. haematobium* and carcinosarcoma (CS) of the bladder has not been reported previously. CS is a rare but lethal disease known for short progression time, high metastatic potential and resistance to chemotherapy, making treatment difficult.

CASE PRESENTATION

A patient, in his 30s who was originally from Central Africa, presented with weight loss, dysuria, gross haematuria and increased urinary frequency that started 4 months earlier. He had no medical history. During this period, he developed hypogastric pain with progressively increasing intensity. Most recently, the patient had lost his appetite and presented vomiting. Physical examination revealed a profound and painful, palpable mass in the median inferior abdomen, with a maximum diameter of ~20 cm.

INVESTIGATIONS

Blood work showed a creatinine level of 10.87 mg/dL (range 0.7–1.2 mg/dL), urea at 133 mg/dL (range 10–50 mg/dL), potassium at 5.9 mEq/L (range 3.5–5.0 mEq/L) and haemoglobin at 10.3 g/dL (range 12–16 g/dL). Non-contrast CT revealed an intravesical mass measuring 16 cm, with diffuse

calcification of the bladder wall, severe bilateral hydronephrosis and moderate parenchymal loss of the left kidney (figure 1).

TREATMENT

The patient initially underwent haemodialysis and blood transfusion. At 2 days after admission, a nephrostomy was surgically placed at the right kidney, which had the thickest parenchyma. During the same procedure, a transurethral biopsy of the bladder tumour was performed. The cystoscopy identified a solid mass occupying the bladder lumen. At 2 weeks after nephrostomy placement, levels of creatinine, urea and potassium dropped to 1.32 mg/dL, 43 mg/dL and 5.1 mEq/L, respectively. The patient had good clinical recovery, but gross haematuria and hypogastric pain remained.

Pathological analysis revealed a malignant neoplasia with spindle cells and dysplastic urothelium. Interestingly, the presence of parasite eggs was noted, and they were later identified as *S. haematobium* eggs. Staging was completed with thoracic, abdominal and pelvic contrast CT, which showed locoregional disease and the absence of metastasis. Radical cystectomy with pelvic lymph node dissection and an incontinent urinary diversion with an ileal conduit were performed (Bricker reconstruction).

OUTCOME AND FOLLOW-UP

There were no intraoperative complications. The patient remained hospitalised for 14 days after the procedure, bringing his length of stay to 29 days since his arrival at our institution. By the time of discharge, he reported of mild gluteal pain that was attributed to postural causes. He was readmitted 15 days later with intense pain in the right leg and dyspnoea. Contrast CT and bone MRI showed multiple pulmonary, liver, muscular and bone metastases (figure 2), including a large tumour at the sacroiliac articulation with compression of the sciatic nerve. The patient died within 20 days from respiratory insufficiency caused by extensive pulmonary metastatic disease.

Assessment of the cystectomy specimen showed a malignant neoplasm consisting of spindle and epithelioid cells infiltrating the detrusor muscle, with transition to dysplastic urothelium. A large number of parasite eggs were found at the centre and periphery of the tumour. Lymph node metastasis was absent (42 dissected lymph nodes). Final staging was pT2N0. The immunohistochemistry examination was diffusely positive for vimentin, focal cytokeratin 5 and CD138. Muscle differentiation markers were negative. The cell proliferation

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Figure 1 Non-contrast CT revealing (A) a solid mass in the bladder lumen and calcification in the bladder wall corresponding to *Schistosoma haematobium* eggs (yellow arrow) and (B) bilateral hydronephrosis associated with loss of parenchyma of the left kidney.

index (Ki-67) was >50% (figure 3). The final diagnosis was CS of the bladder.

DISCUSSION

Acute renal insufficiency is an unusual initial presentation of BC, such as that seen in the present case. Macroscopic haematuria manifests with small lesions and usually makes the patient seek medical care before a large tumour burden is present. Irritative urinary symptoms and localised pelvic pain are also common. Although urachal and ovarian cysts (in women) are differential diagnoses of large pelvic masses; most aetiologies are malignant. Transitional cell carcinoma is the most frequent tumour of the urinary bladder, corresponding to 95% of cases. Other primary neoplasms of the bladder are adenocarcinoma, squamous cell carcinoma and mesenchymal and neuroendocrine tumours. CS and sarcomatoid carcinoma correspond to <1% of BC and are considered a variant of transitional cell carcinoma.² Nonetheless, locally advanced secondary tumours also may affect the bladder and cause urinary symptoms, including rectal and uterine corpus carcinomas. The initial evaluation for a large pelvic mass comprises abdominal, digital rectal and vaginal examination. Urine analysis and contrast CT or MRI are mandatory; however, aetiological confirmation is performed with pathology assessment of a tumour biopsy acquired by cystoscopy. Surprisingly, in the present case, *S. haematobium* eggs were found embedded in the bladder wall.

The presence of *S. haematobium* in the urinary tract has been documented historically. Reports from the 18th century relate that Napoleon had such an affliction that was contracted during his campaigns in North Africa.³ More recently, the association of schistosomiasis and different variants of BC was noted. The International Agency for Research on Cancer has recognised *S. haematobium* to be a human carcinogenic agent since 1994.⁴ Later it was reported that the parasite egg led to a granulomatous inflammatory process creating a pro-oncogenic environment, generating hyperplasia, dysplasia, squamous metaplasia

and ultimately neoplasia.^{5–7} Mutations at gene p53 and chromosomal breakage have been observed; nevertheless, the exact molecular mechanism of carcinogenesis is not known.^{5 6} Clinical presentation of bladder schistosomiasis infection is urinary irritative symptoms; however, many patients remain asymptomatic and will have the parasite presence diagnosed during BC manifestation. In regions endemic for *S. haematobium*, squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma and mixed histology correspond to 60%, 20%, 10% and 10%, respectively, of the cases.⁸ To the best of our knowledge, there are no reported cases of bladder *S. haematobium* associated with CS. Nonetheless, it seems reasonable that the inflammation/carcinogenic sequence induced by the parasite could generate such an aggressive neoplastic variant.

The WHO has adopted a classification for BC that generalises all variants comprising mixed epithelial and mesenchymal cellularity, including CS, as sarcomatoid carcinoma.⁹ In contrast, other reports have demonstrated that the prognoses of this BC subtypes are distinct and propose that they should be categorised separately. The 5-year overall survival rates for CS, sarcomatoid carcinoma and high-grade transitional cell carcinoma are 17%, 37% and 45%, respectively.¹⁰ Despite this, the paradigm is that all mixed epithelial/mesenchymal BCs have high-grade histology and that most patients have advanced disease at initial presentation. It is known that 85% of patients with CS already have muscle-invasive and metastatic disease at diagnosis, and the mortality rate is 50% within 1 year.¹⁰ Haematuria is present in 70–100% of the cases; irritative urinary symptoms and localised pelvic pain are also common at presentation.² After histological diagnosis, staging should be performed with contrast CT of the thorax, abdomen and pelvis. Bone scintigraphy and head CT should be performed when specific lesions are clinically suspected.

Currently, there are no standards for CS treatment, which is mostly performed based on multimodal therapy comprising surgery, radiotherapy and chemotherapy. The 2-year cancer-

Figure 2 (A) Multiple pulmonary metastases (yellow arrow) are noted in thorax CT. (B) Paravertebral muscular metastases (yellow arrow) are shown in MRI.

Figure 3 Pathological assessment of the cystectomy specimen (×200): (A) transition spindle cell tumour and dysplastic epithelium (H&E stain), (B) *Schistosoma haematobium* eggs between neoplastic cells (yellow arrow; H&E stain), (C) immunohistochemistry for cytokeratin 5 revealing diffuse positivity and (D) immunohistochemistry for Ki-67 demonstrating a high index of cell proliferation.

specific survival rates for muscle-invasive disease after partial and radical cystectomy are 14% and 52%, respectively, making radical surgery reasonable and advised at all stages.¹¹ Neoadjuvant chemotherapy may be performed in patients with large tumour burden; however, it should not postpone surgery.

In the present case, we chose to perform the surgery as soon as the patient had proper medical conditions, aiming to provide the best chance of cure for such a young person. The short progression time demonstrated the aggressiveness of bladder CS; however, even though this tumour had a high mortality rate, this patient's outcome was surprisingly unfavourable. Unfortunately, the patient sought medical assistance too late to change the course of his disease.

Learning points

- Bladder schistosomiasis is a risk factor for bladder cancer of different histological types, including sarcomatoid carcinoma variants.
- Carcinosarcoma (CS) of the bladder is an aggressive tumour associated with poor prognosis and high lethality.
- No therapy protocols exist for CS of the bladder; however, treatment should be prompt and should use a multimodal approach.

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