Two cases of plasmacytoid variant of bladder cancer

Stacy Fan

Faculty Reviewer: Dr Nicholas Power, MD, FRCSC (Department of Urology)

ABSTRACT

Introduction: Plasmacytoid urothelial carcinoma (PUC) is a rare and aggressive variant of bladder cancer. Since PUC is infrequently encountered, its management continues to be a formidable challenge.

Case 1: A 74-year-old gentleman was admitted with a 1-month history of gross hematuria and urinary overflow incontinence. Cystoscopy revealed an abnormal growth at the bladder base and biopsies were taken. This patient had high grade PUC sparing the muscularis propria (MP). He underwent nephrostomy tube insertion and subsequent conversion to internal stents 8 weeks later. Repeat resection showed muscle-invasive PUC. Repeat CT showed subcentimeter bilateral inguinal and external iliac lymphadenopathy. The surgeon discovered a dense infiltrative reaction within the retroperitoneum and colonic obstruction during radical cystoprostatectomy and palliative colostomy, confirming metastatic PUC.

Case 2: A 72-year-old gentleman presented with gross hematuria, bleeding from an established end ileostomy, and bowel obstruction symptoms. Cystoscopy identified an anterior bladder tumour and CT staging confirmed a small bowel obstruction (SBO). Transurethral resection showed PUC with invasion of the MP and lymphovascular space. Obvious positive margins were identified during radical cystoprostatectomy, as the tumour clearly invaded bone and the rectal stump. Ileostomy output ceased post-operatively on day 4, and bowel contents began leaking through his urethra the following day. Reassessment of goals of care resulted in cessation of significant interventions. Unfortunately, he passed away 2 weeks post-operatively due to sepsis.

Discussion: These cases illustrate the aggressiveness of PUC bladder tumours and how imaging frequently under-stages these patients. Neoadjuvant chemotherapy prior to attempting surgical control may be beneficial.

INTRODUCTION

Bladder cancer is the ninth most common cancer worldwide. Approximately 430 000 incident cases of bladder cancer, predominantly in men, were reported worldwide in 2012. Interestingly, the incidence and mortality rate of bladder cancer is higher in more developed countries, which is associated with the higher prevalence of tobacco use in these regions.

The risk of developing bladder cancer is associated with genetic variants, such as mutations in N-acetyltransferase 2, and environmental exposures, primarily tobacco smoke. Tobacco smoke contains aromatic amines and hydrocarbons, which are renally excreted and are carcinogenic to the urinary system. Tobacco smoking is the most important and modifiable risk factor and may contribute to half of all bladder cancers. Other environmental exposures include analgesic overuse, occupational exposures, and chronic Schistosoma haematobium cystitis.

Urothelial carcinoma (UC) accounts for 90% of all bladder cancer cases in the United States and Western Europe. Invasive UC often differentiates into specific cell types and variants. Immunohistochemical identification of these subtypes is critical due to their potentially aggressive nature. These UC subtypes may warrant novel approaches to management.

Plasmacytoid urothelial carcinoma (PUC) is a rare variant, accounting for 2.7% of UC. Histologically, it appears as discohesive cells with eccentric nuclei and abundant eosinophilic cytoplasm in a single cell growth pattern. It is generally diagnosed at advanced stages and is associated with poorer survival rates than conventional UC. Treatment of PUC with transurethral resection or open cystectomy +/- adjuvant chemotherapy has been described in the literature. More recently, clinicians have considered the role of neoadjuvant chemotherapy in PUC management due to its aggressive nature.

In this report, we describe the cases of two patients with PUC who presented with macroscopic hematuria and were diagnosed with PUC of the bladder. They offer important insights into how patients should be counseled and managed differently than those with common UC.

CASE REPORTS

Case 1: A 74-year-old gentleman with a history of non-insulin dependent type 2 diabetes mellitus, hypertension, atrial fibrillation, dyslipidemia, gout, and hypothyroidism was admitted to the medicine service after a fall and upper gastrointestinal bleed. He was a lifelong non-smoker and drinks minimal alcohol. Upper endoscopy revealed a mass, which was a presumed gastrointestinal stromal tumour. He developed an acute-on-chronic kidney injury with a creatinine of ~500 µmol/L. Renal ultrasound and computed tomography (CT) of the abdomen/pelvis revealed bilateral hydronephrosis and a stone in distal left ureter, which was later treated with laser lithotripsy.

The patient had a month-long history of gross hematuria and urinary overflow incontinence. Abnormal urothelium at the bladder base was biopsied during investigation of the hydronephrosis. Surprisingly, this biopsy showed invasive high-grade PUC, with involvement of the lamina propria, while the muscularis propria remained clear. Ureteral stents could not be inserted since the ureteric orifices were not visualized; consequently, the patient required nephrostomy tubes. The patient underwent repeat transurethral resection 8 weeks later with an attempt to convert the nephrostomy tubes to internal stents. Repeat resection identified muscle-invasive PUC, demonstrating further progression of his disease.

Two weeks later, he presented to the emergency department with malaise and fatigue. Basic bloodwork revealed a serum potas-
There are currently no prospective and 9 months, respectively. Importantly, they noted transurethral resection of PUC was associated with more disseminated disease, and cystectomy of PUC was associated with doubled mortality risk as compared to regular UC.

Treatment of PUC continues to be a challenge due to the advanced presentation and frequent metastases at initial work-up. PUC has a tendency for intraperitoneal spread, frequently discovered at cystectomy. There are currently no prospective randomized controlled trials that have investigated optimal treatment of PUC due to the rarity of this subtype. Consequently, management is largely guided by case reports and retrospective studies, with no standard treatment regimens.

These two cases demonstrate how rapidly and aggressively PUC can metastasize to potentially cause obstructive symptoms and how imaging may be imprecise. Since PUC spreads through single cells, it is rare for CT to accurately stage these patients. Therefore, it may be beneficial to consider neoadjuvant systemic therapy prior to surgical attempts. Early delivery of chemotherapy may destroy locally metastatic cells preventing any distant spread and may limit the inflammatory response associated with locally advanced disease to increase surgical success.

There are limited studies that have investigated the role of neoadjuvant chemotherapy in PUC. Kohno et al was the first to describe successful pathologic response after two cycles of neoadjuvant chemotherapy (cisplatin, etoposide, methotrexate and vinblastine) and radical cystectomy, with no evidence of recurrence at 3-year follow-up. In 2011, Hayashi et al treated a patient with metastatic PUC with neoadjuvant cisplatin and gemcitabine, then radical cystectomy. Although patients from both reports remained disease-free, death occurred at 3 years and 9 months, respectively. Dayani et al used cisplatin, doxorubicin, methotrexate, vinblastine regimens in 12 patients with PUC. Many patients demonstrated pathologic improvement, but the authors did not identify a survival difference between receiving neoadjuvant chemotherapy and initial radical cystectomy.

**CONCLUSION**

These case reports emphasize the importance of identifying PUC because of the unique therapeutic and prognostic implications this UC variant carries. Early diagnosis is critical but difficult in these patients due to its aggressive yet insidious nature. An additional obstacle is that PUC spreads via individual cells. Consequently, the need for more prospective studies to guide the management of this rare tumor is evident.
quently, CT drastically under-stages locally advanced disease. Radical cystectomy and lymph node dissection, the standard of care for simple UC, is extremely difficult in these patients and is often unsuccessful (with positive surgical margins when attempted) due to dense desmoplastic response and fibrosis. Therefore, consideration for neoadjuvant systemic therapy prior to attempts at surgical extirpation is highly warranted in this rare disease.

REFERENCES