Plasmacytoid urothelial carcinoma of the bladder with extensive scrotal wall invasion

Yong Gang Wang, Marlon Perera, Jacob Gleeson
Department of Urology, Toowoomba Base Hospital, Queensland 4350, Australia

INTRODUCTION

Plasmacytoid urothelial carcinoma (PUC) is an extremely rare and aggressive variant of urothelial carcinoma. We describe here, a case of a patient with locally advanced PUC presenting with a rapid scrotal extension following initial surgery and palliative chemotherapy. We also performed a literature review regarding this tumor.

CASE REPORT

A 62-year-old male presented with the left flank pain and weight loss of 8 kg over 1 month. The patient denied any history of macroscopic hematuria, dysuria, or frequency. Medical history was unremarkable, and the patient was a life-long nonsmoker. Ultrasonography showed a severe left hydronephrosis, and computerized tomography (CT) showed an irregular filling defect measuring 2.5 cm × 2 cm on the left lateral wall of the bladder.

Subsequent cystoscopy revealed a large volume lesion involving the left wall and occluding the left ureteric orifice. Histology showed a high-grade muscle invasive PUC and complete staging did not identify any metastatic spread [Figure 1]. Following this, the patient proceeded to radical cystectomy. Intraoperatively, the bladder was unexpectedly found to be fixed with an extensive pelvic disease that was not amenable to surgical resection. The patient was staged as T4N0M0 and received palliative chemotherapy with cisplatin and gemcitabine.

Three-month postchemotherapy, the patient reported noticing a hard region at the base of his scrotum. This area spread...
rapidly over the following 2 months and became symptomatic with frequent pain. Clinically, the patient’s entire scrotum was uniformly hard with a woody consistency and nodular. The firm tissue extended to involve the root of the penis [Figure 2]. Pelvic magnetic resonance imaging (MRI) demonstrated nonspecific inflammatory changes involving the entire scrotal wall extending from the inguinal canals [Figure 3]. Radiologically guided fine-needle aspirate of the scrotum confirmed high-grade PUC [Figure 4]. The patient then underwent an urgent second course of chemotherapy and experienced a significant regression of the affected area and symptomatic improvement.

**DISCUSSION**

Since it was first reported in 1991 by Sahin et al., there have been less than 100 cases of PUC reported in the literature. To date, the two largest case series included only 32 and 31 patients, respectively. It is estimated to account for about 3% of all muscle invasive urothelial carcinoma.

Histologically, these tumors are characterized by discohesive cells with plasmacytoid morphology. Plasmacytoid cells are described as having eccentrically placed nucleus with abundant eosinophilic cytoplasm. PUC typically stains positively for CD-138, which is a plasma cell marker. However, they also stain positively for epithelial markers such as cytokeratin and epithelial membrane antigen but not for hemopoietic markers such as CD-79a. Loss of E-cadherin expression has also been found to be a prominent feature of PUC and may account for its highly aggressive nature. E-cadherin is important in cell-to-cell adhesion and its loss has been associated with the loss of cellular differentiation and increased invasiveness.

The mean age of initial diagnosis is in the 60s, and there is a male predominance. The most common presenting symptom is hematuria which can be associated with urgency, frequency or lower abdominal pain. However, diagnosis is often delayed due to the absence of hematuria until late stages of the disease. Clinically, PUC is characterized by advanced stage at diagnosis and poor prognosis. Dayani et al. reported 64% of patients had ≥ T3 disease at diagnosis and 48% had metastatic disease. Median overall survival was 17.7 months. The presence of
PUC on transurethral resection of bladder tumor (TURBT) is associated with a 4x increased risk of extravesical disease and 2x increased risk of death compared to non-PUC muscle invasive disease.[7] Initial understaging is common because even extensive disease may not be evident on imaging. This has been the experience in this patient where the initial staging CT severely underestimated the extent of the pelvic spread. Furthermore, despite clinically apparent extensive scrotal extension, MRI showed only nonspecific inflammatory changes.

PUC has been reported to demonstrate an interesting behavior of invasion along fascial planes.[7] The previous cases have noted the extensive involvement of pararectal, perirectal, and perivesical fascial planes with circumferential thickening in both bladder and rectum.[3] The spread of tumor cells along the subserosal surface and ureteral adventitia, instead of along the luminal aspect of the ureter has been described as a new mode of invasion associated with this variant.[7] The scrotal spread in this patient is thought to reflect this behavior.

Treatment of PUC is difficult because of late presentation, and there are no clear guidelines. Patients with PUC treated with cystectomy and adjuvant cisplatin-based chemotherapy have half the median survival compared to similarly treated patient with conventional ulcerative colitis.[4] An aggressive approach is recommended given the high invasive potential and tendency for understaging. Radical cystectomy is considered the first line treatment when there is evidence of PUC on TURBT regardless of invasion.[5,9]

Both neoadjuvant and adjuvant treatment should be considered in the management. The previous case reports have shown a complete response in locally advanced but nonmetastatic PUC (T4N0M0) to chemotherapy.[10] However, in a larger case series, it was found that while neoadjuvant chemoradiation resulted in downstaging of 80% of patients and a complete response in 3, the response rate was short-lived, and the majority of cases recurred rapidly.[3] Our patient similarly had a good initial response that was followed by rapid progression postchemotherapy.

We believe this is the first reported case of PUC causing rapid and extensive involvement of the scrotal wall. This consistent with a pattern of spread along fascial planes previously reported in this variant. Our case also highlights the tendency of initial understaging and rapid progression after chemotherapy seen with PUC.

Acknowledgment
We thank Dr. Maneesha Saxena, Department of Pathology, Toowoomba Base Hospital, Queensland, Australia for providing the histology slides.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Sahin AA, Myhre M, Ro JY, Snejige N, Dekmezian RH, Ayala AG. Plasmacytoid transitional cell carcinoma. Report of a case with initial presentation mimicking multiple myeloma. Acta Cytol 1991;35:277-80.
2. Keck B, Stoehr R, Wach S, Rogler A, Hofstaedter F, Lehmann J, et al. The plasmacytoid carcinoma of the bladder – Rare variant of aggressive urothelial carcinoma. Int J Cancer 2011;129:346-54.
3. Dayyani F, Czemiak BA, Sirac K, Munßell MF, Millikan RE, Dinney CP, et al. Plasmacytoid urothelial carcinoma, a chemosensitive cancer with poor prognosis, and peritoneal carcinomatosis. J Urol 2013;189:1656-61.
4. Keck B, Wach S, Stoehr R, Kunath F, Bertz S, Lehmann J, et al. Plasmacytoid variant of bladder cancer defines patients with poor prognosis if treated with cystectomy and adjuvant cisplatin-based chemotherapy. BMC Cancer 2013;13:71.
5. Wang Z, Lu T, Du L, Hu Z, Zhuang Q, Li Y, et al. Plasmacytoid urothelial carcinoma of the urinary bladder: A clinical pathological study and literature review. Int J Clin Exp Pathol 2012;5:601-8.
6. Nigwekar P, Tamboli P, Amin MB, Osunkoya AO, Ben-Dor D, Amin MB. Plasmacytoid urothelial carcinoma: Detailed analysis of morphology with clinicopathologic correlation in 17 cases. Am J Surg Pathol 2009;33:417-24.
7. Kaimakliotis HZ, Monn MF, Cheng L, Masterson TA, Cary KC, Pedrosa JA, et al. Plasmacytoid bladder cancer: Variant histology with aggressive behavior and a new mode of invasion along fascial planes. Urology 2014;83:1112-6.
8. Erdemir F, Ozcan F, Kilicaslan I, Parlaktas BS, Ulucocak N, Gokce O. The relationship between the expression of E-cadherin and tumor recurrence and progression in high-grade stage T1 bladder urothelial carcinoma. Int Urol Nephrol 2007;39:1031-7.
9. Kaimakliotis HZ, Monn MF, Cary KC, Pedrosa JA, Rice K, Masterson TA, et al. Plasmacytoid variant urothelial bladder cancer: Is it time to update the treatment paradigm? Urol Oncol 2014;32:833-8.
10. Hayashi T, Tanigawa G, Fujita K, Imamura R, Nakazawa S, Yamamoto Y, et al. Two cases of plasmacytoid variant of urothelial carcinoma of urinary bladder: Systemic chemotherapy might be of benefit. Int J Clin Oncol 2011;16:759-62.