Plasmacytoid variant of urothelial carcinoma of the bladder manifesting as bilateral ureteral and small bowel obstruction

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1. Introduction

Plasmacytoid urothelial carcinoma (PUC) is a rare variant of bladder cancer characterized by distinct histopathology and advanced stage at diagnosis. Multimodal treatment is usually indicated. We present a case of PUC causing bilateral ureteral obstruction with subsequent renal failure followed shortly by malignant small bowel obstruction, demonstrating the need for a high degree of clinical suspicion in diagnosis of this aggressive subtype. Moreover, the local invasiveness of the disease cannot be understated, given that it can rapidly spread with little radiologic evidence of progression until it is at an advanced stage.

2. Case report

Our patient is a 71-year-old Caucasian male who was initially found to have a 5.7 cm infra-renal abdominal aortic aneurysm on non-contrast CT abdomen/pelvis after presenting with vague abdominal pain, for which he underwent endovascular repair. He was found to have incidental asymmetric bladder wall thickening on imaging, for which urologic consultation was obtained. Patient underwent office cystoscopy 2 weeks later revealing sessile lesions on the dome and lateral walls with urine cytology suggesting high-grade urothelial carcinoma. He was scheduled for transurethral resection, however two days later the patient presented with acute renal failure requiring emergent hemodialysis. A non-contrast CT revealed new mild bilateral hydrourereteronephrosis. He underwent bilateral nephrostomy tube placement with normalization of renal function, and etiology of this was initially thought to be related to endograft-induced aortitis causing bilateral ureteral obstruction. After a subsequent admission for Klebsiella septicemia 1.5 months following initial cystoscopy, patient ultimately underwent transurethral resection revealing multifocal sessile tumors and notably a contracted and fixed bladder. Bilateral antegrade nephrostograms revealed bilateral distal ureteral strictures approximately 4–6 cm in length. Bilateral ureteral wash cytology was obtained.

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Patient was discharged the following day, however he presented again two days following discharge with abdominal distension and pain. He was diagnosed with a distal small bowel obstruction on CT scan despite no previous abdominal surgery (Fig. 1). After failure of non-operative management, patient was taken to the operating room for exploratory laparotomy. Diffuse inflammation involving a strictured segment of terminal ileum and appendix was noted requiring resection of 10 cm of ileum with appendectomy. Intra-operative frozen sections revealed urothelial carcinoma. These correlated with findings on transurethral resection. In addition, urine cytology from the upper tracts was positive for high-grade urothelial carcinoma. The patient continued to deteriorate despite surgical intervention and was ultimately seen by oncology, but not considered a candidate for systemic therapy due to poor functional status. The decision was ultimately made to transfer the patient to hospice care, less than 3 months from initial evaluation. Final pathology of exploratory laparotomy revealed the presence of carcinoma in the muscularis propria of the ileum, the mesoappendix and serosal surface of the appendix, and mesenteric fat. Transurethral resection specimen revealed diffuse high-grade invasive urothelial carcinoma with plasmacytoid morphology and eccentrically-placed nuclei in discohesive clusters (Fig. 2a). Invasive cells with irregular nuclear profiles were observed clustering in the muscle of the terminal ileum (Fig. 2b). Immunohistochemistry (IHC) showed that specimens were positive for CK20, CK7, GATA 3, CD138 with loss of e-cadherin expression. Prognostic stage IVB: pT2,cN0, pM1b with no evidence of enlarged pelvic or retroperitoneal lymphadenopathy.

3. Discussion

PUC is a rare variant of bladder cancer that is particularly aggressive in nature and locally invasive, and has distinct behavior separating it from most other urothelial carcinoma. Oftentimes, lower urinary tract symptoms and circumferential bladder wall thickening with indurated mucosa are the only initial findings with hematuria only presenting in advanced stages. In addition, the way in which this variant locally invades and behaves much like limitis plastica in certain GI malignancies provides some insight into its unique biology. The classical loss of e-cadherin expression exhibited in PUC contributes to its aggressive cellular invasiveness. In addition to the presence of CD138, the defect in e-cadherin expression is associated with a discohesive pattern of plasmacytoid differentiation. There have been a few cases of bowel obstruction and hydronephrosis as a results of locally invasive PUC, however the timing and severity of clinical sequelae in this patient presents a unique case illustrating the need for timely diagnosis and high clinical suspicion in a patient with seemingly localized disease.

Management of PUC is poorly defined. A multimodal approach including surgery and perioperative chemoradiation is suggested. There may be little prognostic difference with respect to muscle invasion and any plasmacytoid histology should be treated aggressively. There was no difference in overall survival in patients treated with neo-adjuvant chemotherapy compared to upfront surgery with PUC. Dayani et al. described treatment in fifteen patients with metastatic PUC; 60% were treated with cisplatin-based chemotherapy with an overall response rate of 53%. However, survival for those with metastatic disease was just over a year from the initiation of chemotherapy. Additionally, PUC has a strong predilection for recurrence in the peritoneum and poorer local recurrence-free survival than conventional urothelial carcinoma. Because of this tendency for peritoneal metastasis, epithelial tumor markers such as carcinoembryonic antigen, cancer antigen (CA) 125, and CA19-9 are suggested to assess for early disease progression prior asymptomatic or radiographic findings.

4. Conclusion

Plasmacytoid urothelial carcinoma can present with locally advanced and metastatic disease resulting in acute renal failure and small bowel obstruction. Early diagnosis of PUC is challenging and arguably the most important prognostic factor in influencing survival. The invasive nature and dismal prognosis of PUC demands increased...
multidisciplinary awareness in recognizing the characteristic markers and rapidly evolving clinical symptoms that are consistent with this rare malignancy.

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Alex Carsel: original drafting, review and editing, methodology, data curation.
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Declaration of competing interest

None.

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References

1. Sood S, Paner GP. Plasmacytoid urothelial carcinoma: an unusual variant that warrants aggressive management and critical distinction on transurethral resections. *Arch Pathol Lab Med*. 2019;143(12):1562–1567.
2. Fox MD, Xiao L, Zhang M, et al. Plasmacytoid urothelial cell carcinoma of the urinary bladder: a clinicopathologic and immunohistochemical analysis of 49 cases. *Am J Clin Pathol*. 2017;147(5):500–506.
3. Jibril A, Stevens AC. Plasmacytoid urothelial carcinoma of ureter with retroperitoneal metastatic: a case report. *American Journal of Case Reports*. 2018;19:158–162.
4. Wang Z, Lu T, Du L, et al. Plasmacytoid urothelial carcinoma of the urinary bladder: a clinical pathological study and literature review. *Int J Clin Exp Pathol*. 2012;5(6):601–608.
5. Dayyani F, Czeniak BA, Siccar K, et al. Plasmacytoid urothelial carcinoma, a chemo-sensitive cancer with poor prognosis, and peritoneal carcinomatosis. *J Urol*. 2013;189(5):1656–1661.