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PLASMACYTOID VARIANT OF UROTHELIAL CARCINOMA OF THE URINARY BLADDER: HISTOPATHOLOGIC RECOGNITION OF A RARE, AGGRESSIVE VARIANT

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ABSTRACT:
Background: Plasmacytoid variant of urothelial carcinoma(PUC) is a rare and aggressive subtype of urothelial carcinoma characterized by discohesive tumor cells having plasmacytoid morphology. It is frequently associated with advanced -stage disease and poor prognosis due to its infiltrative growth pattern. This entity may pose diagnostic challenges, particularly in limited biopsy specimens where it can mimic plamsa cell neoplasms and other poorly differentiated malignancies.
Case Report: We report a case of a 71-year-old woman who presented with hematuria. Imaging revealed bilateral mild hydroureteronephrosis with suspected vesicoureteric junction obstruction. Transurethral resection of bladder tumor (TURBT) was performed. Histopathological examination revealed a high grade malignant neoplasm composed of discohesive malignant cells with eosinophilic cytoplasm and eccentric nuclei showing plasmacytoid morphology with invasion into the muscularis propria. Immunohistochemistry showed strong membranous CD138 positivity with co-expression of GATA3 and CK7 in tumor cells, supporting urothelial differentiation. Based on the morphologic and IHC findings, a diagnosis of Plasmacytoid variant of urothelial carcinoma was established.
Conclusion: PUC is an uncommon but highly aggressive variant of urothelial carcinoma that often presents at an advanced stage. Recognition of the characteristic histopathologic features and appropriate use of IHC are essential to establish accurate diagnosis and facilitate timely clinical management.

KEYWORDS: Plasmacytoid urothelial carcinoma, bladder tumor, hematuria, TURBT, CD138.

INTRODUCTION

Urothelial carcinoma is the most common malignant neoplasm of the urinary bladder, accounts for the vast majority of bladder cancers. In addition to conventional urothelial carcinoma, several histologic variants have been recognized, including micropapillary, sarcomatoid, nested, plasmacytoid and divergent morphologic subtypes. Accurate diagnosis of these variants is clinically important because many are associated with distinct clinical behavior, therapeutic implications, and adverse prognosis. Among these, plasmacytoid variant of urothelial carcinoma (PUC) is rare, aggressive subtype comprising less than 3% of urothelial carcinoma variants. PUC is characterized by discohesive tumor cells with eccentrically placed nuclei and abundant eosinophilic cytoplasm, closely resembling plasma cells. Loss of cellular cohesion, often associated with altered E-cadherin expression, contributes to its infiltrative growth pattern and tendency for local extension. Clinically, PUC frequently presents at an advanced stage and has been associated with muscle invasion, perivesical spread, peritoneal dissemination, and poor clinical outcomes compared with conventional urothelial carcinoma. Because of its subtle infiltrative architecture and unusual cytomorphology, the diagnosis may be challenging, particularly in transurethral resection specimens. In such settings, important differential diagnoses include plasma cell neoplasms, poorly differentiated carcinoma, lymphoma, signet ring cell carcinoma, and metastatic malignancies. Recognition of this uncommon entity is essential for timely diagnosis and appropriate clinical management. We report a case of plasmacytoid variant of urothelial carcinoma involving the urinary bladder in a 71-year-old woman, highlighting its characteristic histopathologic features, diagnostic pitfalls, and the role of immunohistochemistry in establishing the diagnosis.

Case Presentation

A 71-years-old woman presented with complaints of painless hematuria. Routine urine examination showed turbid urine with proteinuria and the presence of red blood cells. Urine cytology revealed scant cellularity with inflammatory cells and no evidence of atypical or malignant cells and was reported as negative for high-grade urothelial carcinoma according to the Paris System for reporting urinary cytology (2022). Ultrasonographic evaluation revealed bilateral mild hydroureteronephrosis with Grade I pelvicalyceal system dilatation. Subsequent cystoscopic examination identified a bullous growth at the base of the urinary bladder involving both ureteric orifices, which were not clearly visualized.

Contrast-enhanced computed tomography further revealed narrowing at the vesicoureteric junction, suggestive of obstructive involvement by the lesion. The patient underwent transurethral resection of the bladder tumor (TURBT) for definitive diagnosis and management. Gross examination of the resected specimen revealed multiple grey-white soft tissue fragments from both superficial and deep portions. Microscopic examination demonstrated a high-grade malignant neoplasm composed of predominantly of discohesive infiltrating cells arranged singly and in sheets. The tumor cells exhibited moderate eosinophilic cytoplasm, eccentrically placed hyperchromatic nuclei with plasmacytoid morphology. Few cells showed prominent nucleoli. Adequate muscularis propria was identified and infiltrated by tumor, consistent with muscle-invasive disease. Based on the histomorphological features, a differential diagnosis of plasmacytoid variant of urothelial carcinoma, plasma cell neoplasm, lymphoma and poorly differentiated urothelial carcinoma was considered.

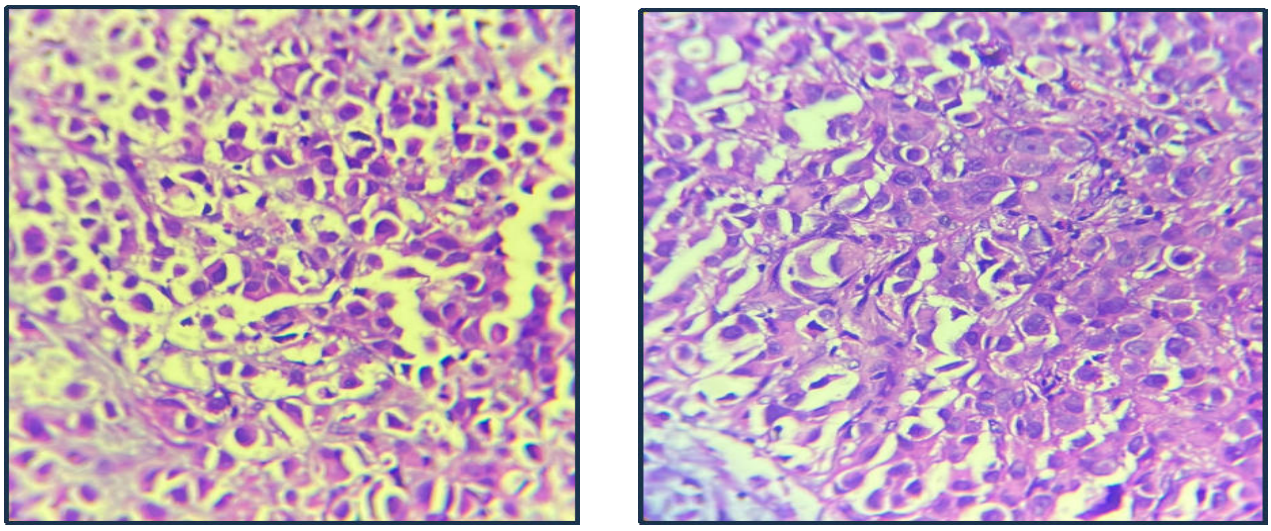

Fig (a,b) H&E showing characteristic discohesive plasmacytoid tumor cells with eccentric nuclei and abundant eosinophilic cytoplasm

To further characterize the tumor, immunohistochemical analysis was performed, which showed strong membranous positivity for CD138 with co expression of GATA3 and CK7 in tumor cells, supporting urothelial differentiation. In conjunction with the morphological features, these findings supported a diagnosis of plasmacytoid variant of urothelial carcinoma. The final diagnosis rendered was high-grade plasmacytoid urothelial carcinoma with invasion into the muscularis propria.

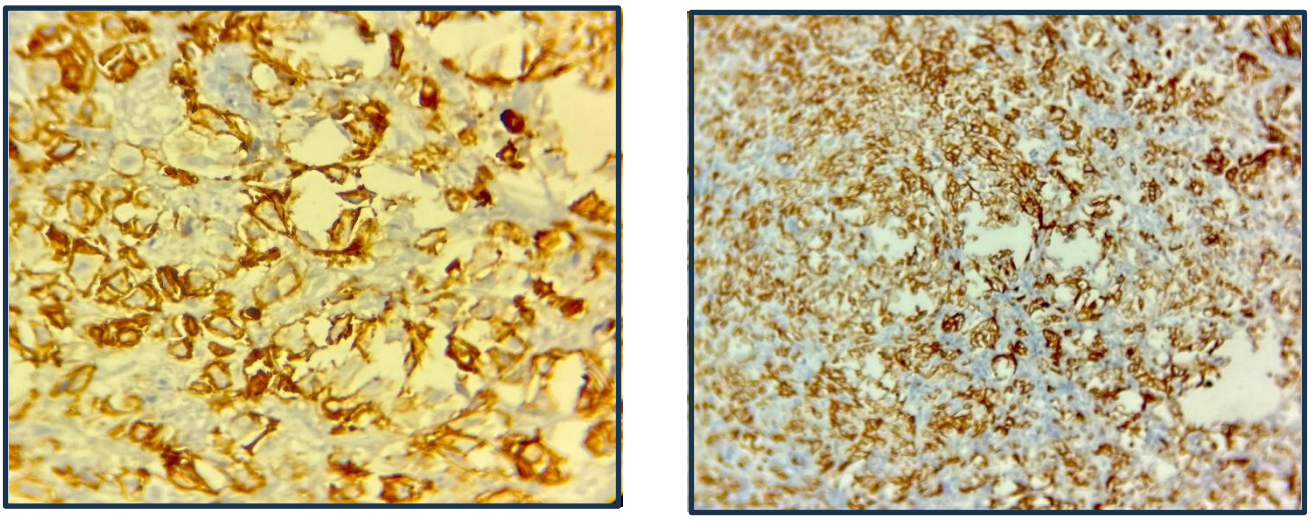

Fig (C)- Tumor cells showing diffuse CD138 immunoreactivity. (D)-Tumor cells demonstrating diffuse CK7 positivity.

DISCUSSION

Plasmacytoid urothelial carcinoma (PUC) is a recognized rare and aggressive variant of urothelial carcinoma as described in the WHO Classification of Tumours of the Urinary System. It constitutes less than 3% of all urothelial malignancies and is characterized by distinctive morphological features, aggressive biological behavior, and poor clinical outcomes. Mircoscopically, PUC demonstrates discohesive tumor cells with plasmacytoid morphology, with abundant eosinophilic cytoplasm, eccentrically placed hyperchromatic nuclei and occasional prominent nucleoli. A key

pathological hallmark emphasized in WHO literature is the loss of cell adhesion, frequently associated with alterations in E-cadherin expression, contributing to the infiltrative growth pattern and early dissemination. In the present case , the tumor showed classic plasmacytoid morphology with discohesive cells infiltrating the muscularis propria, consistent with muscle-invasive disease. This aligns with existing literature that reports most PUC cases present at an advanced stage, often with muscle invasion at the time of diagnosis. The involvement of the bladder base with associated bilateral hydroureteronephrosis in this patient further reflects the locally aggressive nature of this variant, particularly its tendency to involve the trigone and ureteric orifices. One of the major diagnostic challenges in PUC, as emphasized in WHO descriptions, is the morphological overlap with plasma cell neoplasms, signet ring cell carcinoma, lymphoma, poorly differentiated carcinoma and metastatic carcinomas. This challenge is particularly significant in limited biopsy specimens or transurethral resections, where architectural patterns may be less evident. In the present case, an initial differential diagnosis of plasma cell neoplasm versus poorly differentiated carcinoma was appropriately considered based on morphology. In this case, plasma cell neoplasm was an important consideration because of the plasmacytoid cytomorphology and CD138 expression. However, the the tumor cells lacked classical features such as clock-face chromatin and well-defined perinuclear hof . In addition, co-expression of epithelial-associated markers GATA3 and CK7 supported urothelial differentiation. CD138 expression, while helpful, is not specific and should be interpreted in conjunction with morphology and a broader immunohistochemical panel. When required, additional markers such as pan-cytokeratin, p63, CD45, and light-chain studies may assist in excluding hematolymphoid neoplasms and confirming epithelial lineage. Signet ring cell carcinoma was ruled out due to the absence of true intracytoplasmic mucin vacuoles displacing the nucleus. The tumor cells instead showed eosinophilic cytoplasm without mucinous differentiation. Metastatic carcinoma was also considered; however, no primary tumor was identified on clinical and radiological evaluation. The tumor location and morphology and IHC supported a primary urothelial origin. Urine cytology was negative in the present case despite an invasive tumor. This finding may be explained by scant cellular yield, sampling limitations, degenerative change, or the subtle cytologic atypia that may occasionally occur in variant histologies. Therefore, a negative cytology result does not exclude clinically significant bladder malignancy when imaging or cystoscopic findings are suspicious. This limitation is also acknowledged in WHO-based discussions and underscores the importance of histopathological evaluation in suspicious cases. Prognostically, PUC is associated with an adverse outcome compared to conventional urothelial carcinoma. WHO and previous literature studies indicate that patients frequently present with advanced-stage disease, and the tumor exhibits a high rate of local invasion, peritoneal dissemination, and resistance to conventional therapies. Consequently, early recognition is critical, as management often requires aggressive multimodal treatment, including radical cystectomy and systemic chemotherapy. In summary, this case highlights the classical morphological and immunohistochemical features of plasmacytoid variant of urothelial carcinoma and underscores the diagnostic challenges posed by its resemblance of other discohesive malignancies. Recognition of this entity, in accordance with WHO classification criteria, is essential due to its aggressive clinical behavior, advanced stage at presentation, and significant implications for patient management and prognosis

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CONCLUSION

Plasmacytoid variant of urothelial carcinoma is a rare and highly aggressive variant of bladder cancer that often presents at an advanced stage with muscle invasion and poor prognosis. Its characteristic plasmacytoid morphology can morphologically mimic plasma cell neoplasms and other malignancies, posing a significant diagnostic challenge, particularly in limited biopsy specimens. This case highlights the importance of careful histomorphological evaluation supported by immunohistochemistry including interpretation of CD138 positivity in conjunction with urothelial markers, to accurately distinguish this entity from its mimickers. Early recognition is crucial, as plasmacytoid variant of urothelial carcinoma is associated with an infiltrative growth pattern, higher risk of local spread, and the need for aggressive clinical management. Accurate diagnosis, guided by WHO classification principles, plays a vital role in ensuring appropriate treatment planning and improving patient outcomes.

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