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Case Report

Urothelial Carcinoma Medley with Diversity and Heterogeneity: A Rare Case Report

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Abstract

Urothelial carcinoma is well recognised to show morphological plasticity and differentiation to variant morphological types and heterologous components. Some morphological patterns are rare, but some of the subtypes have shown definite implications in prognosis with an aggressive course. The current WHO classification has not only reiterated its importance but has also provided clarification and definite factual points for better categorisation. The advent of recent diagnostic tools and tailored therapeutic implications has further validated the classification. The accurate recognition is vital and a poses real challenge to the pathologist in this scenario. We present to you a case of high-grade urothelial carcinoma with diverse and varied differentiation including small cell neuroendocrine carcinoma, adenocarcinoma and sarcomatoid carcinoma with rhabdomyosarcoma and chondrosarcoma as heterologous components.

Keywords: Urothelial Carcinoma; Plasticity; Heterogeneity

Introduction

Urothelial carcinoma can exhibit diverse morphological patterns and the commonly used term 'variant' now being actively replaced. In this case report, I outline some of the most common histological variants of urothelial carcinoma, all in a single case. The incidence of variant histology reported in published literature is increasing due to awareness and recognition. Nonetheless, accurate subtyping can be challenging due to sampling limitations and interobserver variability. The majority of muscle invasive tumours are associated with advanced stage at presentation, although; it is well documented in literature that the survival outcomes for most variants do not differ significantly compared with pure urothelial carcinoma of the same stage. Controversy persists on the standard of care for these patients and also as a result of few available evidence and data. For the majority of cases, a radical surgical option with bilateral lymph node dissection with or without neoadjuvant chemotherapy is offered.

Case Discussion

This is a 76-year old gentleman who presented with persistent hematuria with passage of clots, and was subsequently investigated for a suspected bladder tumour. He underwent laboratory investigations and imaging; which showed a distended bladder secondary to a soft tissue mass, and an early right hydronephrosis with no distant metastatic deposits identified. He subsequently underwent magnetic resonance imaging (MRI) of the bladder which revealed a 120mm, highly vascular bladder mass arising from the anterior wall. It contained solid and cystic areas, and foci suggestive of myxoid change. Radiologically the features were not characteristic of a pure squamous or urothelial carcinoma, however; there were no features to suggest tumour extension outside the confines of the bladder.

The bladder tumour was biopsied via a transurethral approach. Histopathology showed predominantly necrotic debris with ghost outlines of degenerate, tumour cells whose cytology could not be appreciated. Immunohistochemistry was attempted and the rare viable cells and the necrotic cells were focally positive with Chromogranin A, Synaptophysin and pancytokeratin, although a paranuclear accentuation was not appreciated. A working diagnosis predominantly necrotic tumour with possible, questionable neuroendocrine differentiation was suggested.

The patient subsequently underwent a radical cystoprostatectomy which included an ileal conduit formation. At cut-up the bladder specimen showed a large polypoid tumour attached to the anterior bladder wall with a relatively thin fleshy stalk and completely fill-

ing up the bladder and measuring up to 90mm in maximum dimension. The tumour showed a variegated appearance with visible necrosis. Representative sections were taken from viable looking foci with care to include regions of varied morphological appearances.

Histopathological examination of the tumour sections confirmed a partly necrotic tumour with heterogeneous and high grade morphological appearances. There were areas of atypical spindle cells with a fascicular and whorled arrangement, including scattered giant 'bizarre' nuclei and multinucleated forms. There was a focus of cartilaginous differentiation with atypical chondrocytes, and other areas of poorly-differentiated small round cells with high nuclear cytoplasmic ratio, moulded nuclei and high mitotic activity. Elsewhere there were entrapped banal glands of colonic type and atypical glands with pleomorphism within the tumour. The stroma showed an admixture of fibrous and chondromyxoid appearance.

The tumour was infiltrating into muscularis propria (pT2) and showed extensive lymphovascular invasion. There was no invasion into the surrounding structures such as prostate or seminal vesicles. Interestingly, no unequivocal conventional urothelial carcinoma was identified within the tumour, although we noted flat urothelial carcinoma in situ with focal glandular differentiation. Additionally, the prostate gland showed an incidental small focus of low volume, prostatic acinar adenocarcinoma, amounting to Gleason score 6.

Immunoprofile of the tumour showed about 55% by proportion of the tumour to be of neuroendocrine morphology with patchy positivity for CD99, CD56 and Synaptophysin. The sarcomatoid areas comprised of 30% by ratio and included both components, with majority being rhabdomyosarcoma. The remaining 5% and 10% were adenocarcinoma component and tumour necrosis respectively.

Conclusion

The 2016 WHO book on Tumours of the Urinary System and Male Genital Organs describes the sarcomatoid and the neuroendocrine morphological types to be poor prognostic entities and has emphasized the importance of providing percentage of each subtype which will dictate further management. The direct role of divergent morphology is still controversial in management decisions [1]. Although one paper particularly proposed early cystectomy in non-muscle invasive bladder cancer (T1) with sarcomatoid morphology [2], the group from MD Anderson [3] did not support this approach, however; the National Comprehensive Cancer Network (NCCN) advocates a more rigorous approach in T1 disease.

In another well recognized study by Veskimae E, *et al* [4], tumours with neuroendocrine differentiated were known to benefit from neoadjuvant chemotherapy. It is well established that urothelial carcinoma has a propensity for divergent morphologies with some associated with prognostic value and a knowledge of the same is prudent until further studies on elucidation of molecular classification and pathways gains precedence.

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Conflict of Interest

The author(s) do not have any conflict of interest.

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