

Paraganglioma of the Urinary Bladder

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Abstract

Paraganglioma of urinary bladder is a rare tumour with characteristic histologic, Zellballen pattern and immunohistochemical features. In this case report, we describe classic histopathological features of paraganglioma of the urinary bladder which will help general consultant pathologists to recognize this rare tumour of the bladder along with a review of literature on histological features.

Introduction

Paraganglioma of the urinary bladder is a rare tumour with characteristic histologic and immunohistochemical features. Paragangliomas, also called extra-adrenal pheochromocytomas, arise from chromaffin tissue in the sympathetic ganglia. Paragangliomas of urinary bladder represent less than 1% of bladder tumours and 6% of all paragangliomas.¹ In this report, we describe histopathology of paragangliomas of the urinary bladder with emphasis on the histologic features that could lead to their being misdiagnosed as conventional urothelial cancer and, most importantly, those that will help pathologists recognize this rare tumour of the bladder.

Case Report

A 42-year-old male presented with a history of an episode of haematuria 2 years back. Since last 2 months, he had dysuria with increased frequency of micturition. Cystoscopy revealed polypoidal mass near the trigone and he underwent transurethral resection of bladder tumour (TURBT) and the tissue was sent for the histopathological examination.

Histopathologically sections showed a "cellular

neoplasm"; with overlying flattened intact urothelium (Fig. 1). Tumour showed characteristic nested or "Zellballen" pattern prominently seen in special stain i.e reticulin stain. These nests is associated delicate fibrovascular core. The tumour was found infiltrating muscularis propria. The neoplastic cells had abundant eosinophilic cytoplasm, sometimes with a slightly granular appearance (Fig. 2). The nuclei typically are round with smooth contours, even chromatin, small nucleoli, and occasional nuclear inclusions. There was no surrounding stromal reaction present. With areas showing "Zellballen" appearance in addition to chromogranin positivity, paraganglioma was diagnosed. The 24-hours urinary Vanillylmandelic acid was within normal limits. Periodic blood pressure measurements revealed the non-functioning status of the tumour.

Discussion

Paragangliomas of the urinary bladder constitute 6% of paragangliomas and 0.06% of all bladder tumours.¹ Most of the patients present with irritative voiding symptoms. Only a few present with the classic triad of episodic hypertension, haematuria and post-filling or post-voiding syncope. This typical presentation may be found in functional tumours. These tumours secrete catecholamines, ACTH etc.²

There is no morphologic criterion to distinguish benign from malignant tumours.³ Histologically, tumours demonstrate nests of spindle to polygonal cells with granular eosinophilic cytoplasm and hyperchromatic

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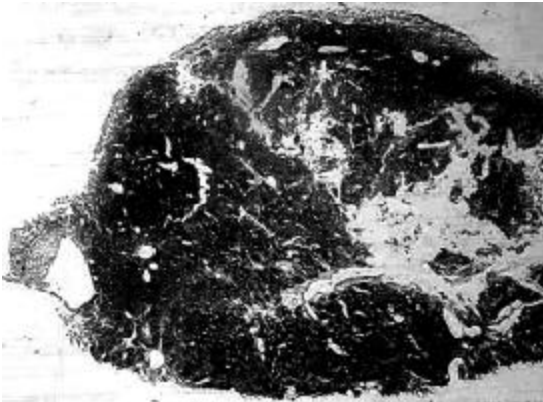


Fig. 1: H and E stained section of the bladder mass shows an expansile tumour with attenuated intact urothelium (white arrow) over the mass. The mass is involving the muscularis propria. (H and E X 40).

nuclei. Pleomorphism, mitoses and necrosis may be present in varying proportions in benign and malignant tumours. A minority of cases show a diffuse sheet-like growth pattern, but a nested pattern can usually be identified focally. Scattered pleomorphic cells with smudged, hyperchromatic nuclei are occasionally found as seen in other endocrine tumours (“Endocrine anaplasia”). Paragangliomas may be present anywhere within the bladder wall (including the muscularis propria), but no surrounding stromal reaction is present. The classical “Zellballen” (German for “balls of cells”) appearance will be present in most tumours.⁴ However, in some cases, it may be misdiagnosed as urothelial cancer because of its – a) frequent involvement of the muscularis propria; b) morphology that may suggest urothelial cancer in transurethral resection specimens, particularly if there are artifactual changes induced by that procedure; c) failure of pathologists to include it in their differential diagnosis when evaluating a bladder tumour which is uncommon and rare.

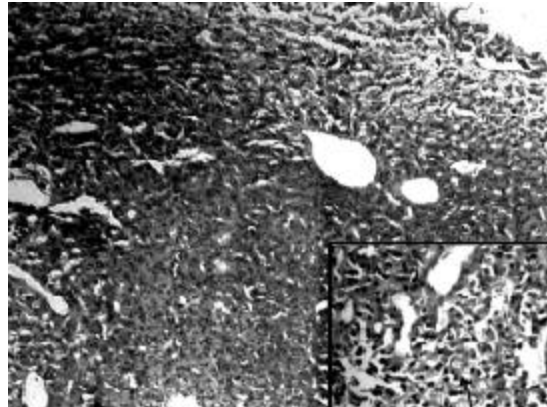


Fig. 2: The tumour shows nests of tumour cells with vascular septae. There is homogeneity to the mass with abundant eosinophilic cytoplasm (highlighted in the inset). (H and E X 400).

Zhou M *et. al*⁶ in his study of 15 cases of paraganglioma observed the following features- histologically, that “Zellballen” and diffuse patterns were present in 12 (80%) and 3 (20%) of the cases. Other patterns included irregular nests and pseudorosette formation. Tumour necrosis, significant cautery artifact, and muscularis propria invasion were present in 1 (7%), 3 (20%) cases, and 10 (67%) cases, respectively. All 15 tumours were composed of large polygonal cells with abundant granular cytoplasm. Focal clear cells were present in 3 (20%). The nuclei were mostly uniform, although occasional pleomorphic nuclei were seen in 6 (40%) cases, and 2 (13%) had frequent pleomorphic nuclei. Mitoses were rare overall, and no abnormal mitotic figures were found.

The major histologic features that usually lead to misdiagnosis include a diffuse growth pattern, focal clear cells, necrosis, and muscularis propria invasion, with significant cautery artifact compounding the diagnostic problems.⁵

Immunohistochemical markers like chromogranin, neuron-specific enolase and S-

100 are positive in paragangliomas⁶ MIB1 and p53 have been studied to assess the malignant potential.⁵ Most of the tumours are aneuploid but the same cannot be related to malignant potential.

Paraganglioma of the urinary bladder may be misdiagnosed as urothelial cancer. However, the characteristic nested pattern with fibrovascular septa, the usually bland cytology, the absence of a stromal reaction, and the absence of appreciable mitotic activity should suggest the diagnosis of paraganglioma. Immunohistochemistry is usually confirmatory, as paragangliomas are reactive for neuroendocrine markers (chromogranin and synaptophysin) and non-reactive for cytokeratin, while the opposite is true of carcinomas, Therefore, a careful search for the characteristic histologic features and, if necessary, supportive immunohistochemical studies, should lead to a correct diagnosis of this uncommon bladder tumour even by the general consultant pathologists.

References

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SMOKING DOUBLES RISK OF MAJOR DEPRESSION

Retrospective evidence from a study of osteoporosis in Australian women suggests that smokers are twice as likely to develop major depression.

This study suggests that we should encourage our depressed patients to stop smoking once they have achieved remission. However, we need to be aware that, by emphasising the role of lifestyle factors in depression, we may unwittingly make patients feel responsible for their illness, adding to their sense of guilt.

Phillip Bland, The Practitioner 2008; 252 (1712) : 7-15.