

Multicentric Paraganglioma Of The Bladder - A Rare Case Report

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Citation

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Abstract

Paragangliomas arising from the urinary bladder are rare. We report a case of multicentric paraganglioma arising in a 27-year-old female with its characteristic zell ballen pattern and immunohistochemical studies, who was clinically misdiagnosed as papilloma. Failure to diagnose pre-operatively can have serious intraoperative consequences. We present this case because of its rare multicentric presentation, and to consider this as a differential diagnosis in bladder lesions to avoid complications during surgery.

INTRODUCTION

Pheochromocytomas are rare tumours, which arise from chromaffin cells derived from embryonic neural crest.^[1] Extra- adrenal pheochromocytomas are called as paragangliomas. It represents less than 1% of bladder tumours and 6% of paragangliomas. [2] The tumours usually develop in young adult women.^[3] The common symptoms and signs are dysuria, hematuria , hypertension and micturition syncope caused by local irritation of the tumour and increased catecholamine levels .^[4] In this report, we describe the classical histologic features that could help us to differentiate it from urothelial malignancy.

CASE REPORT

A 27-year-old married female presented with a history of hesitancy and occasional feelings of incomplete bladder emptying for a duration of 1 month. Physical examination was unremarkable. No constitutional symptoms due to endocrine activity like hypertension, palpitation, headache, sweating and micturition syncope were detected. A C T scan showed a mass lesion in the dome of the bladder (fig – 1). A cystoscopy was done, which showed two polypoidal masses arising from the dome of bladder. The larger mass was 1.5 cm and smaller mass was 0.8 cm. A clinical diagnosis of papilloma was made and transurethral resection was attempted to obtain tissue for histological diagnosis. During this procedure, there was a sudden surge in blood pressure (210/160), which was managed emergently with IV antihypertensives.^[5] This led to a clinical suspicion of paraganglioma and the procedure was aborted. The tissue

obtained showed only fibrocollagenous tissue.

Figure 1

Fig 1 contrast CT showing filling defect in dome of bladder as shown by arrow



Partial cystectomy was done after 3 week preparation of patient. We received two smooth polypoidal lesions. The larger lesion measured at 2.7x2 cm and the smaller lesion measured at 1.5x1 cm. C/S yellowish orange (fig – 2). Histologic section showed a cellular tumour with overlying intact epithelium. The tumour cells are arranged in nested or zell ballen pattern, extending into the muscularis propria. The neoplastic cells have large amounts of amphophilic cytoplasm with a round vesicular nucleus and prominent nucleoli. The foci showed an arrangement of tumour cells in

trabeculae, sheets and cord-like patterns were also seen .(fig 3) Immunohistochemical studies showed strong positivity for chromogranin , synaptophysin and negativity for cytokeratin (fig- 4,5,6).

Figure 2

Fig 2 shows two polypoidal lesion with orange yellow areas on cut section

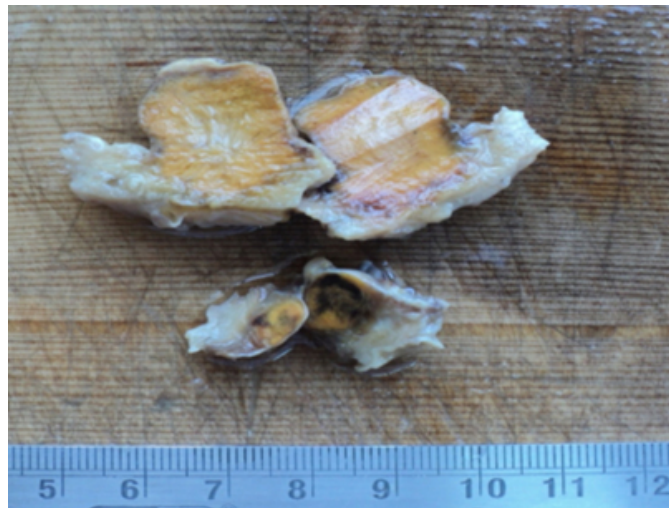


Figure 3

Fig 3 40x showing arrangement of tumour cells in zellballen pattern

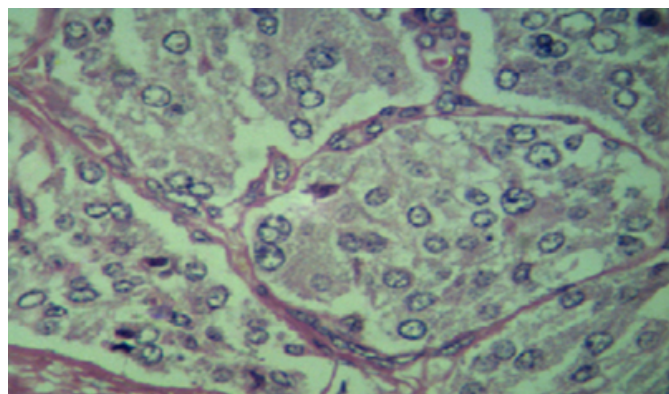


Figure 4

Fig 4 IHC showing strong cytoplasmic positivity of tumour cells to chromogranin

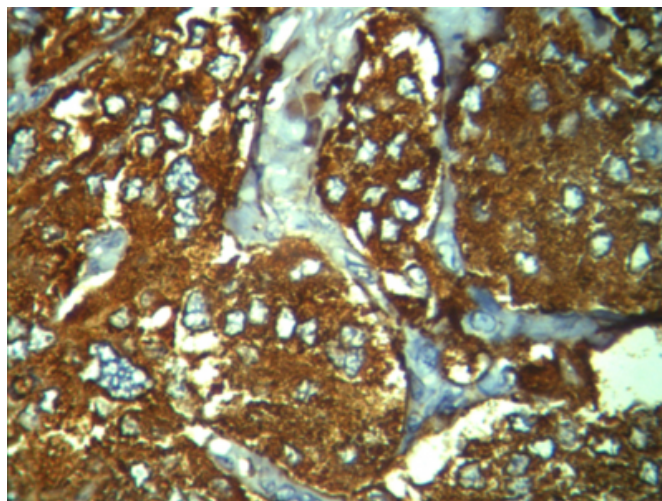


Figure 5

Fig 5 IHC shows strong cytoplasmic positivity of tumour cells to synaptophysin

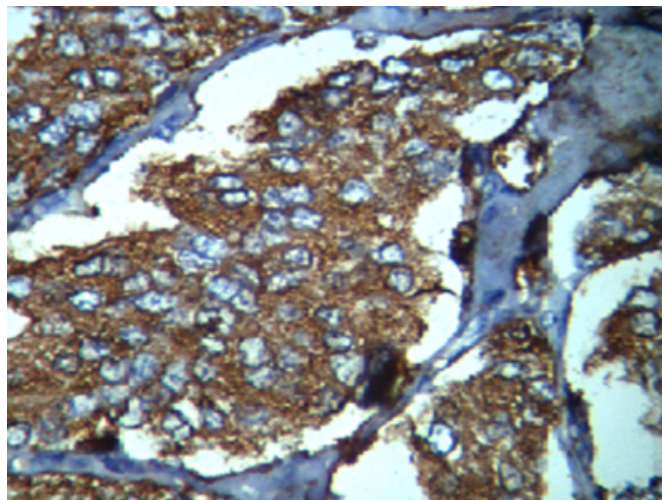
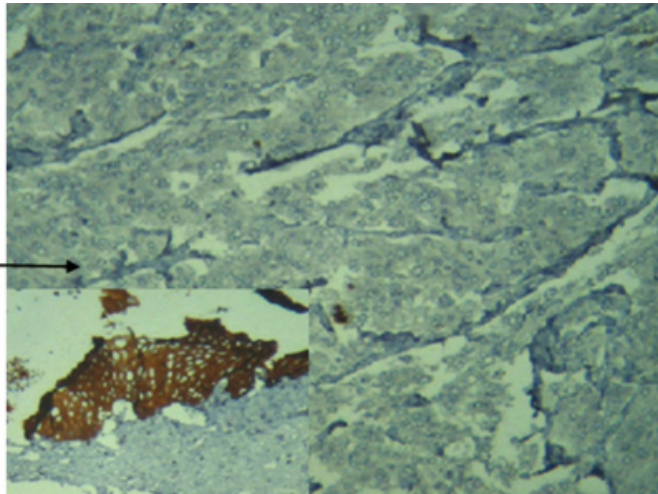


Figure 6

Fig 6 IHC shows tumour cells, which are negative for cytokeratin .Inset shows transitional cells positive for cytokeratin



DISCUSSION

Paragangliomas of urinary bladder are rare tumours and represent < 1% of all bladder tumours.^[2,5] The earliest case was reported by Zimmerman et al in 1953.^[6] They occur more frequently in women, during their 20s and 30s. Most paragangliomas of the bladder are solitary and are localized in the dome or trigone of the bladder. Histopathological examination shows polygonal cells with a round vesicular nucleus and amphophilic cytoplasm arranged in a zellballen pattern, and some places in solid sheets. Some cells show pleomorphic and hyperchromatic nuclei. These cells are positive for immunohistochemical markers like synaptophysin, chromogranin, s – 100 and NSE and Negative for cytokeratin .

Most of these tumours are benign. Histologically, there are no definite characteristic features by which we can distinguish benign from malignant lesions .^[7] A review of studies looking at other factors (including biochemical and genetic markers) for determination of malignancy by Pattarino et al (1996) came to the conclusion that metastatic dissemination is the only real proof of malignancy .^[8] The diagnosis of pheochromocytoma in general is established by measurement of catecholamine and catecholamine metabolites (metanephrine and nor-metanephrine) in plasma and 24 hrs urine sample . 83 % of paraganglioma of urinary bladder are hormonally active.^[9]

The interesting features of the case presented above is that this patient had no evidence of the micturition- induced symptoms of catecholamine release typical of primary

paraganglioma of the bladder or any other symptoms of hormonal excess. In the present case, it led to an unexpected intra-operative hypertensive crisis. If these tumours are suspected pre-operatively the patient can be appropriately prepared with adequate β -blockade and volume expansion to prevent hypertensive crisis.

A review of literature of available case reports regarding primary bladder paragangliomas tells us that 63-75% of patients present with at least one of the typical symptoms or signs.^[10] One third of the patients do not produce symptoms or signs characteristic of this tumour .^[10] The most useful investigations to localize primary and metastatic paraganglioma of urinary bladder are cystoscopy, CT, and MRI. A MIBG scan is essential to search for multiple or metastatic tumours . If the MIBG scan is negative, a PET scan should be performed with specific ligands, like 6(I8F)-fluorodopamine or (I8F) – dihydroxyphenylalanine .^[11]

Pheochromocytomas generally occur sporadically, but may also be inherited as part of several distinct syndromes such as MEN – Type IIA and type II B , von hippel Lindau syndrome and von – recklinghausen’s neurofibromatosis type I or paraganglioma syndromes associated with germ – line mutation of genes encoding SDH subunits B,C and D (SDHB,SDHC,SDHD).^[12,13,14] Carriers of the SDHB mutation are at an increased risk of extraadrenal or metastatic pheochromocytomas, as well as recurrence.^[17] It has been suggested that all patients <50 yrs of age with bilateral pheochromocytomas, multiple pheochromocytomas, extra-adrenal pheochromocytomas and a family history of pheochromocytomas should undergo genetic testing.^[12,13,15,16,17,18] In the case presented above, hypertensive crisis was only provoked by intraoperative tumour manipulation due to the lack of a preoperative diagnosis. This patient fit into the category of 36% of patients without typical symptoms in whom a preoperative diagnosis was not made.^[10]

Paraganglioma of the bladder may be misdiagnosed as urothelial cancer in the absence of classical symptoms. The characteristic histological and immunohistochemical findings should suggest the diagnosis of paraganglioma.

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