Case Report

Nonfunctioning paraganglioma of the urinary bladder: A rare entity

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ABSTRACT

Paraganglioma of the urinary bladder is a rare tumor accounting for <0.06% of all bladder tumors and <1% of all pheochromocytomas. The distinction of paragangliomas from urothelial carcinoma is likely to be critical because of differences in therapeutic management. We report a case of 24-year-old female who presented with a complaint of intermittent hematuria and no other characteristic symptoms of paraganglioma. Ultrasonography revealed a lobulated mass arising from the anterior wall of the urinary bladder. Imaging studies and other relevant investigations were inconclusive. Transurethral resection was done and sent for histopathology. On histopathology, final diagnosis of paraganglioma was made. Patient is symptom-free postoperatively and is on regular follow-up 6 monthly.

Key words: Paraganglioma, urinary bladder, urothelial carcinoma

INTRODUCTION

Paraganglioma of the urinary bladder is rare, comprising <0.06% of all vesical tumors.[1] The tumor usually develops in young adult women.[2] The most common clinical presentation is painless hematuria, headache, palpitation, anxiety, and hypertension due to excess catecholamine secretion.[1] Most of the paragangliomas (~90%) are benign and can be cured by surgical resection alone.[3] Surgical removal either through partial cystectomy or transurethral resection, is still the gold standard of treatment. Herein, we report a case of nonfunctioning paraganglioma of the urinary bladder, which is a rare entity.

CASE REPORT

A 24-year-old-female without a history of hypertension presented with intermittent painless gross hematuria since 7 months. Physical and systemic examination were unremarkable. Urine examination showed a large number of red blood cells. Ultrasonography revealed a solid lobulated mass measuring 3.3 cm × 3 cm × 2 cm projecting from the anterior wall of the urinary bladder. Further, I^{131} metaiodobenzylguanidine (MIBG) scan was performed which showed normal study. Urine catecholamine levels were within normal limits that is 45 μg/24 h (normal range 13–57 μg/24 h). Clinically, possibility of urothelial carcinoma or paraganglioma was kept. Transurethral resection was performed. During transurethral resection (transurethral resection of bladder tumor), patient had sudden onset hypertension and tachycardia along with arrhythmia. Grossly, specimen was yellow tan and measured 3 cm × 3 cm × 2 cm, cut surface was homogenous and brown orange. On microscopic examination, tumor cells were arranged in nests surrounded by delicate fibrovascular stroma and showed infiltration in the muscle layer. These cells had round or ovoid nuclei having one or multiple nucleoli and having abundant, granular, eosinophilic cytoplasm with well-defined borders [Figure 1]. There was no evidence of infiltration in tumor margins. Immunohistochemical staining was positive for neuron specific enolase (NSE), synaptophysin, chromogranin in tumor cells and S100 was positive in the surrounding fibrovascular stroma, however tumor cells were negative for cytokeratin, which ruled out possibility of urothelial carcinoma [Figure 2]. Final diagnosis of nonfunctionaing paraganglioma of the urinary bladder was made. At present, the patient is symptom-free and is on regular follow-up every 6 months with no evidence of recurrence.

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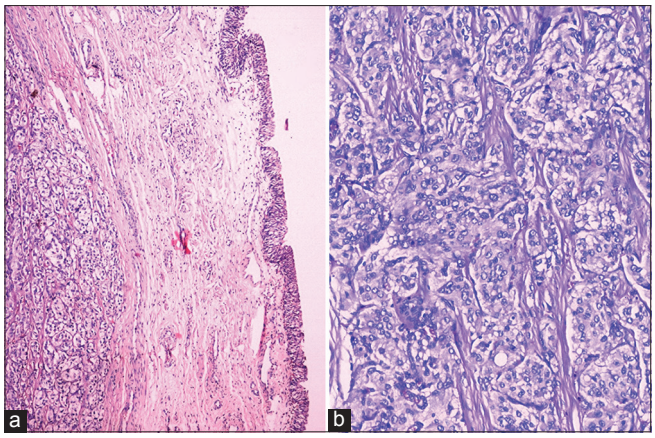

Figure 1: (a) H and E, (×10) section showing urothelial lining on right side and tumor cells on left side. (b) H and E, (×20) section showing tumor cells arranged in zellbellen pattern

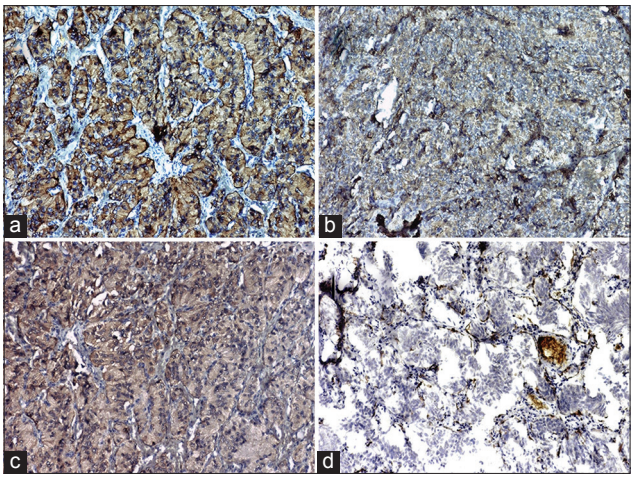

Figure 2: (a) Tumor cells showing positivity for synaptophysin. (b) Tumor cells showing positivity for chromogranin. (c) Tumor cells showing positivity for nonspecific enolase neuron specific enolase. (d) S100 positivity in fibrovascular stroma

DISCUSSION

Paragangliomas are extraadrenal neoplasms of the neural crest derivation.[2] These tumors are found most commonly in the retropritoneum arising from the sympathetic chain or from the organ of Zuckerland.[1] As many as 50% of the paragangliomas are hereditary and may be associated with familial paraganglioma, neurofibromatosis type 1, von Hippel-Lindau disease, and the Carney triad.[2] Approximately, 10% of all extra-adrenal pheochromocytoma are malignant. In the genitourinary tract, the urinary bladder is the most common site for paragangliomas (79.2%), followed by the urethra (12.7%), pelvis (4.9%) and ureter (3.2%).[4] Urinary bladder paraganglioma is a rare disease entity that occurs in <1% of all paragangliomas.[1] And accounting for <0.5% of all bladder neoplasms.[5] The first case of urinary bladder paraganglioma was published in 1953 by Zimmerman *et al*.[9] It originates from chromaffin tissue of the sympathetic nervous system in the urinary bladder wall and is most frequently seen in women than in men and mostly occurs at the age of 20–40 years.[6] The trigone and posterior walls have been stated as most common sites for paraganglioma.[2] Paragangliomas can be categorized into functional and nonfunctional disease.[6] Functional paraganglioma is characterized by paroxysmal hypertension, palpitation, micturition syncope and hematuria with elevated catecholamine levels and positive for MIBG or octreotide scintigraphy.[6] Assessments of plasma and/or urine catecholamine levels are very important in these patients even if they are asymptomatic.[7] Lenders *et al*. reported that plasma metanephrines are more sensitive and specific than urinary metanephrines for these lesions.[8] Magnetic resonance imaging and computed tomography (CT) have low specificity in diagnosis (as low as 50%), however MIBG scintigraphy offers a superior specificity (95–100%) but its sensitivity is not high enough to diagnose paraganglioma of nonfunctional nature.[1] Cystoscopic appearance of a yellow, submucosal tumor should raise the suspicion of bladder paraganglioma.[7] Surgical interventions include partial or total cystectomy and transurethral resection.[1] Biopsy should be avoided.[2] Histologically, paragangliomas show a "Zellballen" pattern of cells with abundant eosinophilic or amphophilic cytoplasm partitioned by delicate vascular stroma.[1] Generally, these tumors possess the capacity to invade and thus are deemed malignant, yet lack mitosis and the cellular dissociation that are usually associated with malignant tumors.[4] The prediction of biological behavior of a bladder paraganglioma cannot be based solely on the histopathological findings. Some criteria have evolved to suggest malignancy behavior that includes necrosis, angiolymphatic invasion, high mitotic index, absence of hyaline bodies, p53 alteration, and DNA ploidy analysis. However, the diagnosis of a malignant tumor is difficult and is often proved clinically through presence of metastasis.[7] Although it has characteristic histologic and immunohistochemical features, it is often misdiagnosed as urothelial cancer due to its frequent muscle invasion, morphology that sometimes overlaps with urothelial cancer and failing to keep paraganglioma as a differential diagnosis.[5] The differential diagnosis of the paraganglioma of the urinary bladder is broad, which includes urothelial carcinoma, metastatic renal cell carcinoma, prostate cancer, malignant melanoma, carcinoid or other neuroendocrine tumors, and granular cell tumor.[5] Out of these most crucial is to rule out urothelial carcinoma.[5] Immunostains provide a definitive answer; paraganglioma is positive for neuroendocrine markers like NSE. Synaptophysin, chromogranin and negative for cytokeratin, whereas converse is for urothelial carcinoma.[5] Most of the paraganglioma of the urinary bladder grows slowly and has a good prognosis.[6] Partial cystectomy with complete tumor removal usually for paraganglioma, even

when it invades the muscularis propria,[5] as was done in our case. The incidence of malignancy is 10–15%. and the rate of local recurrence ranges from 5% to 15%.[1] Therefore, long term follow-up is necessary.[1] Follow-up should be regular and include cystoscopic examination, plasma or urinary catecholamine levels and imaging study (CT, MIBG).[7] Adjuvant radiotherapy and chemotherapy with cyclophosphamide, vincristine and dacarbazine can improve survival and prevent recurrence.[1]

CONCLUSION

Though paraganglioma of the urinary bladder is a rare entity, but it should be considered in the differential diagnosis of urinary bladder tumors in the patients without the specific symptoms.

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