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Surgery

UNSUSPECTED PARAGANGLIOMA OF THE URINARY BLADDER WITH INTRAOPERATIVE HYPERTENSIVE CRISES: A CASE REPORT.

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ABSTRACT Paraganglioma of the urinary bladder are tumors of chromaffin tissue originating from the sympathetic innervations of the urinary bladder wall and are extremely rare. Being functional, in most of the cases they are recognized by their characteristic presentation of hypertensive crisis and post-micturition syncope. A silent presentation of a bladder paraganglioma is very unusual but quite dangerous as they are easily misdiagnosed and adequate peri-operative attention is not provided. Here, we are presenting one such silent paraganglioma in adult women who had no preoperative symptoms, but had intraoperative crises during surgery.

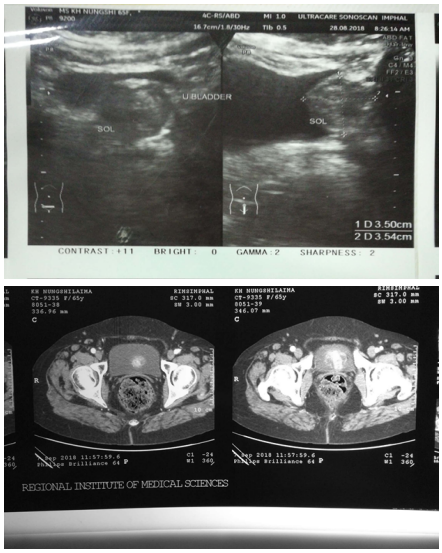
KEYWORDS :

INTRODUCTION

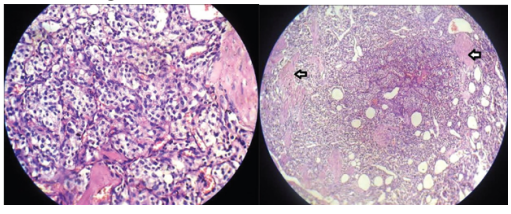
Tumors of chromaffin cells, derived from the embryonic neural crest, usually originate from the adrenal medulla and are designated as pheochromocytomas. However, 10% of these tumors occur at extra-adrenal sites and are known as paragangliomas.[1] Paraganglioma of the urinary bladder are extremely rare and are usually functional and symptomatic.[2] We are reporting here an almost silent paraganglioma of the urinary bladder with intraoperative hypertensive crises.

CASE REPORT

A 65-year-old woman with symptoms of red color urine on and off presented to urology OPD one year back. Physical examination was unremarkable. Urine analysis suggested few red blood cells and few pus cells whereas the culture was negative for any growth. Ultrasound scan demonstrated a mass on the anterior wall of the bladder with mixed echogenicity, measuring 3.5 × 3.5 cm. Metastatic workup was negative. Urine cytology for malignant cells was negative while cystoscopy revealed a smooth, well-vascularized mass on the anterior wall of the bladder. With presumed diagnosis of an urothelial bladder tumor, patient was subjected to trans-urethral resection of bladder tumor (TURBT). During trans-urethral resection, the blood pressure suddenly shoots up and raised up to 230/118 mmHg and pulse rate dropped to 48/min. This episode was controlled with intraoperative intravenous antihypertensives and atropine, procedure was abandoned and only biopsy was taken. Later while performing the definitive procedure (partial cystectomy) the blood pressure again raised which was managed adequately. Postoperative recovery was uneventful.



Histological examination of the TURBT specimen showed presence of round to polygonal cells arranged in small nests or zellballen, separated by highly vascularized fibrous septa. Individual cells had centrally located nuclei with clumped chromatin and moderately abundant fine granular cytoplasm and the occasional invasion into detrusor layer. These features were consistent with paraganglioma. Immunohistochemistry was strongly positive for IHC synaptophysis and chromogranin, while negative for cytokeratin that further confirmed the diagnosis.



Postoperatively, plasma and 24 hour urinary metanephrines with urinary vanillylmandelic acid (VMA) were checked, which were normal and contrast enhanced computed tomography kidney ureter bladder suggested no residual tumor local or distal metastasis. Patient is still on regular 3 monthly follow-up with history, physical examination, plasma and urinary metanephrines and cystoscopy. Till 1 year of follow–up, there is no recurrence of tumor.

DISCUSSION

Paraganglioma of the urinary bladder is very rare and account for 0.06% of all bladder tumors and 6% of extra-adrenal pheochromocytomas.[1] However, in the genitourinary tract, the urinary bladder is the most common site (79.2%), followed by the urethra (12.7%), pelvis (4.9%), and ureter (3.2%).[3,4] These tumors originate from chromaffin tissue of the sympathetic nervous system associated with the urinary bladder wall and are most commonly situated at the dome or the trigone of the bladder and may be nonfunctional or functional.[2,5] They remain usually benign, but 15–20% tumors may show malignant behavior.[2,6] Bladder paraganglioma occur more frequently in women than in men, and clinical presentation occur mainly during the third decade of life.[2]

In functional tumors, presenting symptoms are usually resulting from excessive catecholamine secretion. The patient typically suffers from hypertensive crises that may be accompanied by headache, palpitations, hot flushes, and sweating. Postmicturition hypotension and syncope is another common presentation. These crises are mainly provoked by micturition, overdistention of the bladder, defecation, sexual activity, ejaculation, or bladder instrumentation.[2,3,6] About 17% of bladder paragangliomas are hormonally nonfunctional and can be asymptomatic.[2] Painless hematuria is a common presenting complaint in about 60% of reported cases, though it is nonspecific for paraganglioma and can be a presenting feature of any bladder tumor.[2,5,6] Both computed tomography (CT) scanning and magnetic resonance imaging are useful in the localization of both the primary tumor and any metastases however scanning with ^{131}Iodine metaiodinebenzylguinidine (MIBG) has been shown to have a very high sensitivity and specificity for pheochromocytoma detection.[4] Functional imaging that specifically targets the catecholamine

synthesis, storage, and secretion pathway is helpful in patients with paraganglioma, especially after surgical removal or in the detection of metastasis.[2,4] In symptomatic patients, functional assessments of plasma and/or urine catecholamine levels are crucial in the initial workup and in the follow-up afterward. Plasma metanephrines are more sensitive and specific than urinary metanephrines for these lesions.[2,3,5]

On cystoscopy appearance of a yellow, submucosal tumor should raise the suspicion of a bladder paraganglioma.[2] Tumor manipulation may release of catecholamines that leads to potentially lethal transient hypertension and should be biopsied or resected under appropriate alpha-adrenergic blockade (phenoxybenzamine or prazosin) and preoperative volume expansion that have been shown to significantly reduce peri-operative mortality and morbidity.[2,3,6] Fortunately, in our patient intraoperative severe hypertensive crisis was managed with intravenous antihypertensive drugs and procedure was completed.

On histopathology, tumor cells are seen as large polygonal cells with abundant granular cytoplasm arranged in a Zellballen pattern and are surrounded by a fibrous network rich in blood vessels.[1,6,7] Bladder paraganglioma can be confused histologically with urothelial carcinomas, especially the nested variant of urothelial carcinoma, and other tumors including bladder granular cell tumors, metastatic large cell neuroendocrine carcinoma and malignant melanoma.[6] Presence of diffuse growth pattern, focal clear cells, necrosis, and muscularis propria invasion, with significant cautery artefact, and failure of pathologists to include it in their differential diagnosis may lead to their misdiagnosis as urothelial cancer.[7] In these circumstances, immunohistochemical analysis helps in their differentiation where these tumors are positive for neuroendocrine markers, such as neuron-specific enolase, chromogranin and synaptophysin but negative for urothelial marker cytokeratin.[6,7] In our case also tumor was strongly positive for synaptophysis and chromogranin, while negative for cytokeratin.The diagnosis of a malignant tumor is difficult and is often proved clinically through presence of metastases.[2,4,6]

Surgery is the mainstay of the treatment that requires total excision. If diagnosed preoperatively, a partial cystectomy is preferred over trans-urethral resection as majority of these tumors extend in the deep layers of the detrusor muscle.[2,3,5] Chance of recurrence is high following resection and should not be considered as evidence of malignancy.[2] Total cystectomy is reserved for large lesions when bladder preservation is impossible or in the presence of lymph node metastasis.[2,3,5] Bladder paraganglioma is a chemo-resistant and radioresistant tumor, though radiation and chemotherapy, either in the neoadjuvant or adjuvant setting, has been used in a few cases.[8,9]

Because bladder paragangliomas are likely to recur and to metastasize, lifelong follow-up with appropriate history, annual measurement of plasma and urinary catecholamine levels and cystoscopy is essential. Imaging study (CT scan and 123 I-MIBG scintiscan) should be done to locate recurrence and metastasis sites if reappearance of symptoms or resurgence of catecholamines occurs.

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