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Case report

Extra-adrenal paraganglioma of a urinary bladder in an adolescent male: A rare case report

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ABSTRACT

Introduction and importance: Paraganglioma of the urinary bladder is unusual and reported rarely. The patient usually presents with the complaint of hematuria and fluctuating blood pressure.
Case presentation: We discuss the case of a 21-year old male, who had been experiencing gross hematuria, was found to have a mass on ultrasonography. Further evaluation with contrast-enhanced computerized tomography (CECT) revealed an irregular soft tissue density of endophytic mass arising from the left posterior wall of the urinary bladder. The histopathological examination of the excised mass was suggestive of a tumor of neural origin, which was further confirmed as paraganglioma by immunohistochemistry.
Clinical discussion: Imaging prior to the surgery must be done for a provisional diagnosis of paraganglioma to avoid fluctuating blood pressure during elective surgery. On histopathological examination tumor cells are arranged in the nest like fashion forming a specific 'Zellballen' pattern. Positive staining for synaptophysin and chromogranin in immunohistochemistry confirms the diagnosis.
Conclusion: It is difficult to diagnose paraganglioma of the urinary bladder with the aid of imaging only, particularly if the patient presents without specific symptoms of fluctuating blood pressure. So, a multidisciplinary approach is essential for the diagnosis and proper therapy of this entity. However, prompt surgical resection is the mainstay of treatment.

1. Introduction

Paraganglioma of the urinary bladder arises from the chromaffin cells of the sympathetic chain located in the muscle layer of the bladder wall [1]. It is a rare type of tumor that affects the urinary bladder, accounting for only 0.06 percent of all bladder cancers [2].

Syncope, hematuria, hypertension, headache, and palpitation are the common symptoms caused by an increase in endogenous catecholamines produced by the tumor cells [3].

Here we report a case of a 21 years old adolescent male who presented with hematuria for 4 days. Paraganglioma was suspected due to fluctuating blood pressure during the TURBT procedure. The histological examination followed by immunohistochemical studies confirmed it as paraganglioma of the urinary bladder.

This work has been reported in line with the SCARE criteria [4].

2. Case

A 21 years old Nepalese man presented in the outpatient department (OPD) with the chief complaint of gross hematuria for 4 days. Hematuria was evident throughout the micturition with the amorphous blood clot in the urine. He had no fever or retention of urine during that period of presentation. He denied having any recent trauma and similar problems with his parents and siblings. He recalled a trauma two years back which resulted in hematuria that went away without any medical intervention. He is a social drinker but does not use tobacco.

On examination, he was afebrile, was tachycardic at the presentation with a pulse rate of 110 beats/min, and had fluctuating blood pressures which ranged from 110 to 120/70 to 110 mm Hg. The abdomen was soft with mild tenderness in the suprapubic region. There was no tenderness at the renal angle. Other systems were grossly intact.

Laboratory tests show hemoglobin 10.4 g/dl, platelet count of

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444,000/μl, normal PT/INR and aPTT, and renal function test (urea: 6.3 mmol/l, and creatinine 74 μmol/l). A routine urine examination showed plenty of RBCs (red blood cells) per high power field.

He underwent ultrasonography (USG) of the abdomen and pelvis for additional evaluation, which revealed a heteroechoic lesion in the left posterolateral wall of the urinary bladder measuring around 4.1 cm × 4.0 cm. Computerized tomography (CT) urography performed to further characterize the mass revealed an irregular soft tissue density of endophytic mass arising from the left posterior wall of the urinary bladder with a size of 5.3 cm × 4.7 cm. The mass was extending the posterolateral wall with mild perivesical soft tissue strandings. It was abutting the left seminal vesicle with a loss of the fat plane. Post-contrast pictures revealed heterogeneous enhancement with non-enhancing patches within the mass indicating necrotic or cystic areas (Fig. 1). Hyperdense non-enhancing blood attenuating content, suggestive of clots, was noted within the bladder. MRI of abdomen and pelvis showed well-defined avidly enhancing lobulated heterogeneous endophytic mass in the left posterior wall of urinary bladder extending the underlying urinary bladder wall and inferiorly into the seminal vesicle (Fig. 2). All these imaging modalities direct the diagnosis as carcinoma of the urinary bladder (UB).

Thus, with a preoperative diagnosis of UB carcinoma with clot retention and hematuria, the patient underwent cystoscopic-guided clot evacuation and transurethral resection of bladder tumor (TURBT) while considering the surgery's prognosis. Cystoscopic findings were noted before tumor resection began using a bipolar cutting loop. The operation took place in a lithotomy position under general anesthesia. Due to the patient's fluctuating blood pressure and significant hypertension during the procedure, tumor excision halted before complete resection of the tumor. Sodium nitroprusside was infused intravenously for bringing BP back to the normal range. After confirming hemostasis, a 22-french three-way Foley catheter was inserted to irrigate the resected site. Postoperative findings included a huge mass involving the left lateral wall, posterior wall, and trigone of UB. The left ureteric orifice was not invaginated by tumor mass. Finally, the excised specimen was sent for histopathological examination.

The gross specimen for histopathological analysis consisted of multiple pieces of grey-white tissue to dark brown tissue measuring 5.0 cm × 5.0 cm. Histological sections of the specimen demonstrated multiple fragments with focal urothelial lining. The subepithelial layer and muscularis propria showed infiltration by tumor cells arranged in the nest with a specific 'Zellballen' pattern (Fig. 3). Tumor cells exhibited mild nuclear pleomorphism with round to oval nuclei, salt and pepper chromatin, and moderate to abundant clear cytoplasm with infrequent mitosis. A large area of tumor necrosis was also seen. In immunohistochemistry, tumor cells revealed negative CD10, positive CD56, positive synaptophysin, and positive chromogranin (Fig. 4). These investigations (histopathological and immunohistochemistry) ultimately derived a diagnosis of paraganglioma.

The patient recovered well through an uneventful postoperative period. The patient was not ready for the surgery for the time being. Hence, he was planned for a discharge because his vitals were stable and all appropriate laboratory parameters had normalized. The patient was well counseled about his disease as being a benign tumor. However, the tumor still required surgical resection. He is symptomless and is satisfied with the current treatment modalities.

3. Discussion

A paraganglioma is a group of tumors arising in the paraganglial location (categorized as head and neck region paraganglia and sympathoadrenal paraganglia). A paraganglioma is a non-epithelial tumor of paraganglion cells at any site [5,6]. Pheochromocytoma is a specific term reserved for the paraganglioma of the adrenal medulla. 5% to 10% of paragangliomas are extra-adrenal in location and they can be found anywhere from the base of the skull to the pelvic floor [7]. Among all extra-adrenal paragangliomas, 71% are located were located in the superior or inferior para-aortic area followed by 12% in the intrathoracic region and 9.8% in the urinary bladder [8]. Multifocal paragangliomas can also occur at different sites as was reported in a patient with 21 paragangliomas [9].

Urinary bladder paragangliomas are thought to arise from embryonic nests of chromaffin cells in the sympathetic plexus of the detrusor muscle. However, they account for only less than 0.05% of the non-urothelial bladder. In an autopsy study performed on 409 patients, Honma identified paraganglia in 52% of examined bladders. Most of them were present in the anterior and posterior walls, trigone being is the least common site [11]. The SDHB gene mutation is thought to be associated with a high risk of malignancy [12]. Other familial syndromes associated with paragangliomas are NF1, MEN2, and VHL. It has a high female preponderance (3:1). It tends to occur in younger patients with a mean age of 45 years.

The functionally active tumor tends to be smaller than the non-functioning tumor [13]. The average size of bladder paraganglioma is 2 cm, with a range between 0.3 and 5.5 cm [14]. Our patient had a mass of 5.3 × 4.7 cm mass on the left lateral wall of the urinary bladder. More than 80% of patients are symptomatic, major symptoms being hematuria and hypertension exacerbated during voiding. Nonfunctional paraganglioma of the urinary bladder presents with lower abdominal pain or dysuria [15]. Cystoscopic examinations show small dome-shaped nodules covered by normal mucosa in the trigone, dome, or lateral wall. In contrast to other extra-adrenal paragangliomas (10%), urinary bladder paraganglioma bears a higher risk (20%) of malignancy [10].

Imaging studies are required for accurate identification of the paragangliomas before the surgery to avoid excessive hemorrhage and potentially fatal complications caused by the release of catecholamines from these tumors during anesthesia induction and surgical manipulation. When the cause of the catecholamine-induced metabolic event is known, it can be treated with volume expanders and prevented by using

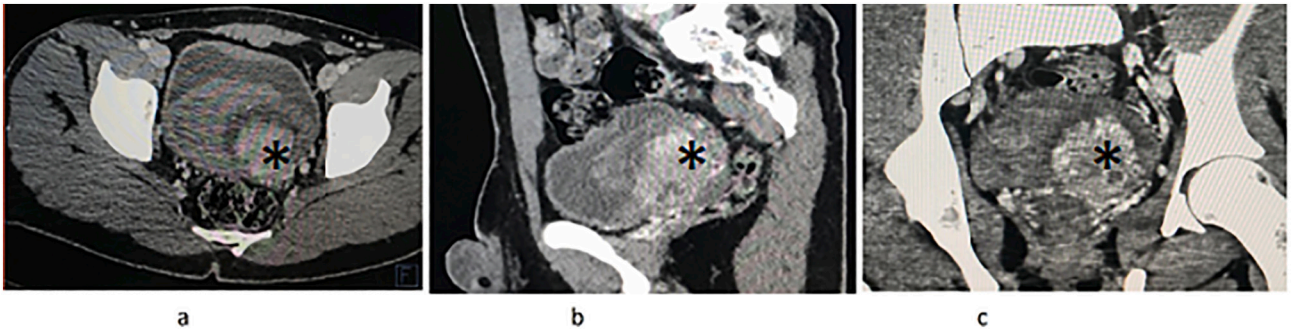

Fig. 1. Contrast enhanced CECT showed endophytic mass (shown with asterisk) from posterolateral wall of the urinary bladder extending to perivesical soft tissue and left seminal vesicle with areas of calcification and necrosis.

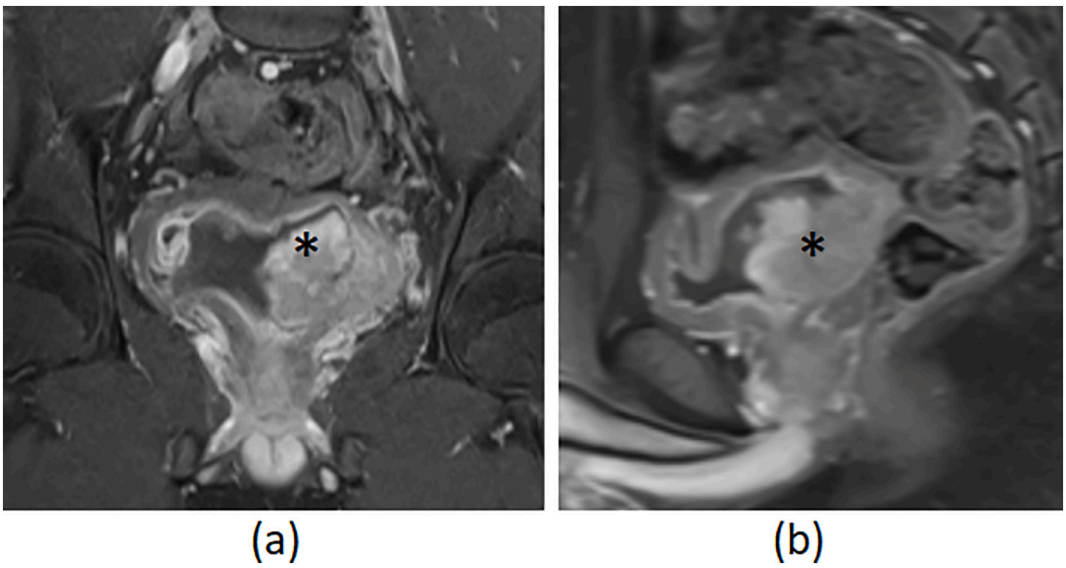

Fig. 2. MRI showed well defined avidly enhancing lobulated heterogeneous endophytic mass (shown in asterisk) in the left posterior wall of urinary bladder extending (a) the underlying urinary bladder wall and inferiorly into the seminal vesicle (b).

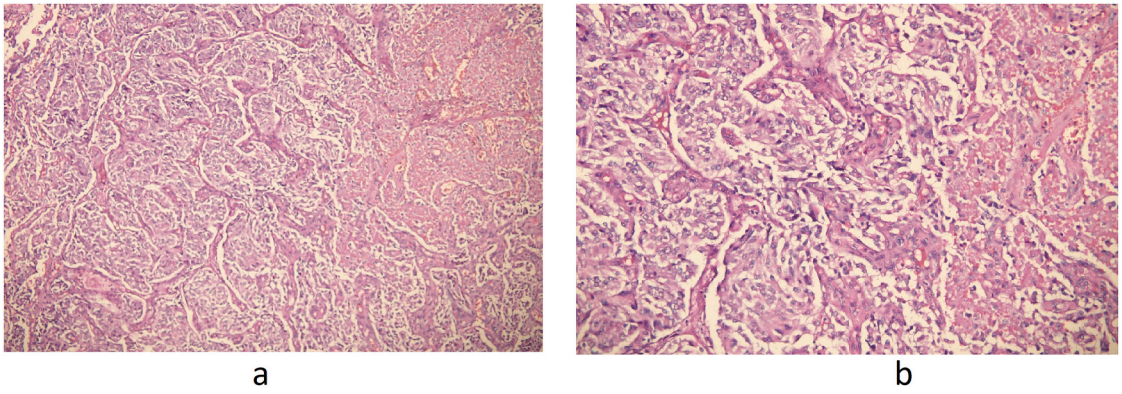

Fig. 3. Histopathological examination showed tumor cells arranged in nests with typical "Zellballen pattern" surrounded by sustentacular cells (a). Higher magnification shows tumor cells having moderate amount of cytoplasm with salt and pepper chromatin (b).

an appropriate pharmacologic receptor blocking agent [13].

Due to increased vascularity, these tumors are red-brown and show areas of hemorrhage on cross-sections with focal cystic degeneration. Microscopically, these tumor cells are arranged in anastomosing cell cords or trabeculae. Rarely organoid pattern, solid or diffuse growths as seen in head and neck paragangliomas are also seen. These cells tend to have relatively abundant, acidophilic, and finely granular cytoplasm. The normal overlying urothelium is present in most cases [10]. There are no reliable histological criteria to distinguish malignant from benign neoplasms. Nuclear pleomorphism, mitotic figures, and necrosis do not predict the clinical outcome of the patient [16,17]. In a study done by Cheng and associates, muscularis propria was involved in 94% of patients with 37% having extravesical extension or pelvic involvement [10].

These tumor cells show immunoreactivity for neuroendocrine markers like CD56, synaptophysin, and chromogranin but lack CK7, CK20, and AE1/AE3 [12]. The granular cell tumor shows strong immunoreactivity for S100 protein and lacks a Zellballen growth pattern [18]. Immunostain in our case showed positive CD56, synaptophysin, chromogranin, and negative AE1/AE3.

The recurrence or metastases does not occur in tumors confined within the bladder wall [10]. Malignancy can be confirmed only by the occurrence of regional or distant metastases.

Surgically paraganglioma of the urinary bladder is managed by partial cystectomy. Complete resection along with the removal of lymph nodes is done only in the case of a proven malignant tumor [19]. In our case partial resection of the tumor mass was done due to uncontrolled BP rise amid surgery. Surgical management was the most appropriate therapy for our patient.

4. Conclusion

Paragangliomas are rare tumors affecting the urinary bladder. So, appropriate clinical evaluation, imaging, histopathological and immunohistochemistry as a diagnostic approach after controlled surgical resection of the tumor mass are necessary for the confirmation of paraganglioma. Teamwork of multidisciplinary specialties is essential for the proper therapy of the patient.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

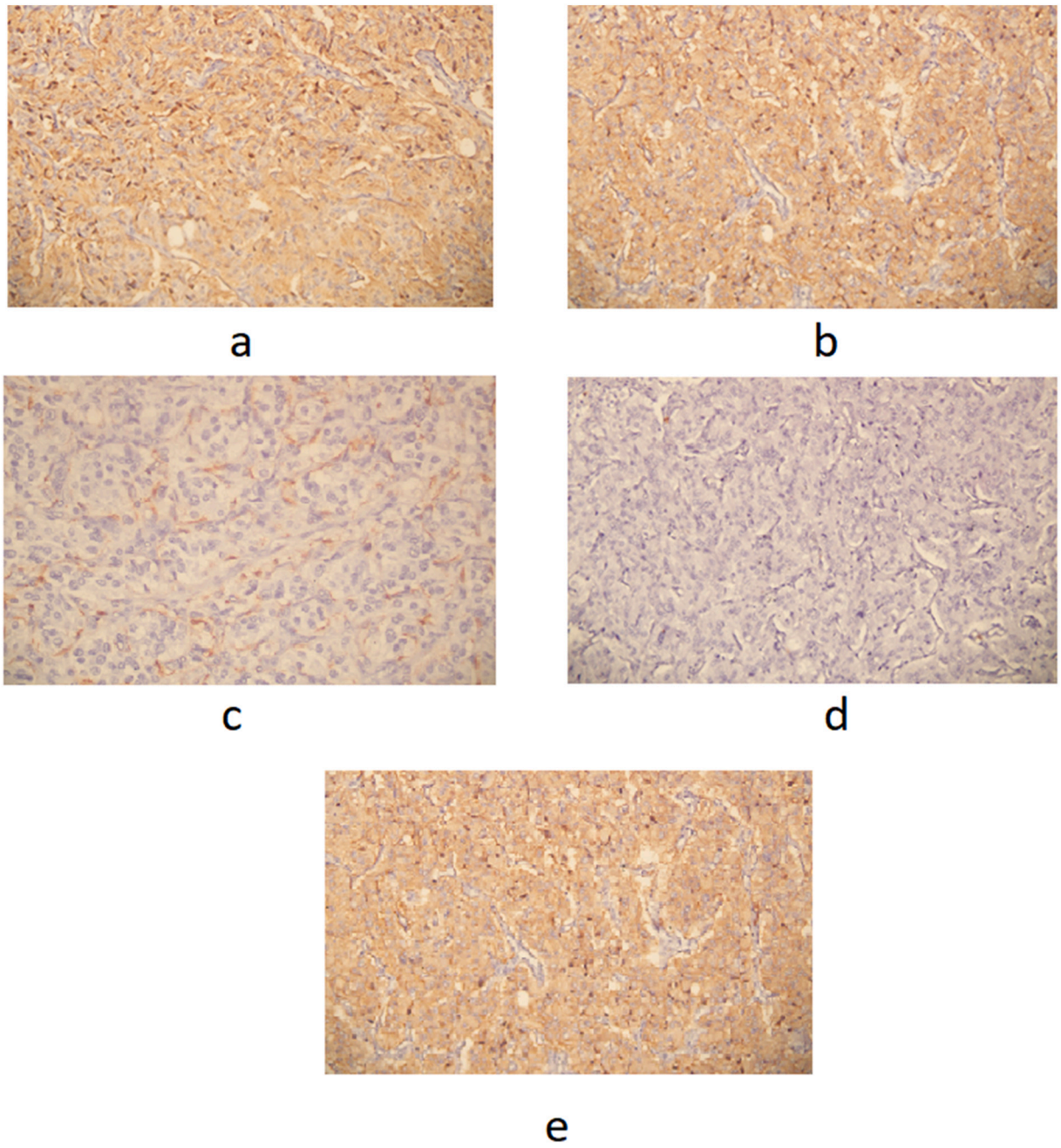

Fig. 4. Immunohistochemical studies showed tumor cells are strongly positive for CD56 (a), chromogranin (b) and synaptophysin (e). Sustentacular cells showed S-100 positivity (c). However, these cells are non-reactive with CD10 immunostain (d).

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Sansar Babu Tiwari (SBT) accepts full responsibility for the work and/or the conduct of the study, has access to the data, and controls the decision to publish.

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CRediT authorship contribution statement

Sansar Babu Tiwari (SBT), Brijesh Ghimire(BG), Kamal Gautam (KG), Shreya Shrivastav(SS) = Study concept, Data collection, and surgical therapy for the patient
Sansar Babu Tiwari (SBT), Kamal Guatam (KG) = Writing- original draft preparation
Brijesh Ghimire(BG), Ramesh Paudel (RP) = Editing and writing

Nisha Sharma (NS), Shreya Shrivastav(SS) = Senior author and manuscript reviewer.

All the authors read and approved the final manuscript.

Declaration of competing interest

None.

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