

Case Report

Nonfunctional urinary bladder paraganglioma: a rare case report and review of the literatures

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Abstract: Urinary bladder paraganglioma is a rare neuroendocrine tumor and nonfunctional bladder paraganglioma is extremely rare and difficult to diagnose due to their non-secreting nature. We report a rare female case of nonfunctional bladder paraganglioma with detailed clinicopathological data and follow-up information. The patient presented with supra-pubic pain. Computed tomography (CT) revealed a 11 mm×9 mm nodular lesion on the left posterior wall of the urinary bladder, and the lesion exhibited intense enhancement in the arterial phase. The patient underwent transurethral resection of bladder tumor (TURBT). By immunohistochemistry investigations, the cells were strongly positive for neuroendocrine markers such as Syn, and sustentacular cells stained positive for S-100. Staining for cytokeratin AE1/AE3 and CK20 was negative. Taken together with radiological features and immunohistochemical results of the tumor, a diagnosis of urinary bladder paraganglioma was made. However, it is difficult to identify malignancy on histopathology, regular follow-up is necessary for urinary bladder paraganglioma with malignant potential.

Keywords: Bladder, nonfunctional paraganglioma, diagnosis, therapy, prognosis

Introduction

Urinary bladder paraganglioma is a rare neuroendocrine tumor that arises from chromaffin tissue of the sympathetic nervous system. In general, urinary bladder paragangliomas defined as either functional (catecholamine secreting) or nonfunctional tumors [1], accounting for less than 0.05% of all bladder tumors [2]. The first case of urinary bladder paraganglioma was reported by Zimmerman et al in 1953 [3]. Several cases of urinary bladder paraganglioma have been reported [4-7], but case reports of nonfunctional bladder paraganglioma are quite rare [8]. In addition, there are no definite guidelines regarding diagnosis and therapy of such cases. The present study reports the rare case of the clinical features of nonfunctional bladder paraganglioma, and presents the related literature.

Case report

Clinical history

A 71-year-old female patient presented to our urology department within intermittent supra-pubic pain for the past five months. The patient had a 1-year history of hypertensive disease, and the highest blood pressure increased to 145/95 mmHg that had been well controlled to 120/80 mmHg with irbesartan (150 mg, every 24 h). The patient denied a history of headaches, vertigo, palpitations, sweating, blurry vision, nausea and paroxysms of hypertension associated with micturition. No abnormalities were revealed on physical examination of the patient. Routine blood investigations and results of the urinalysis were within the normal ranges. The abdominal ultrasonography revealed an 11 mm×9 mm lesion on the left poste-

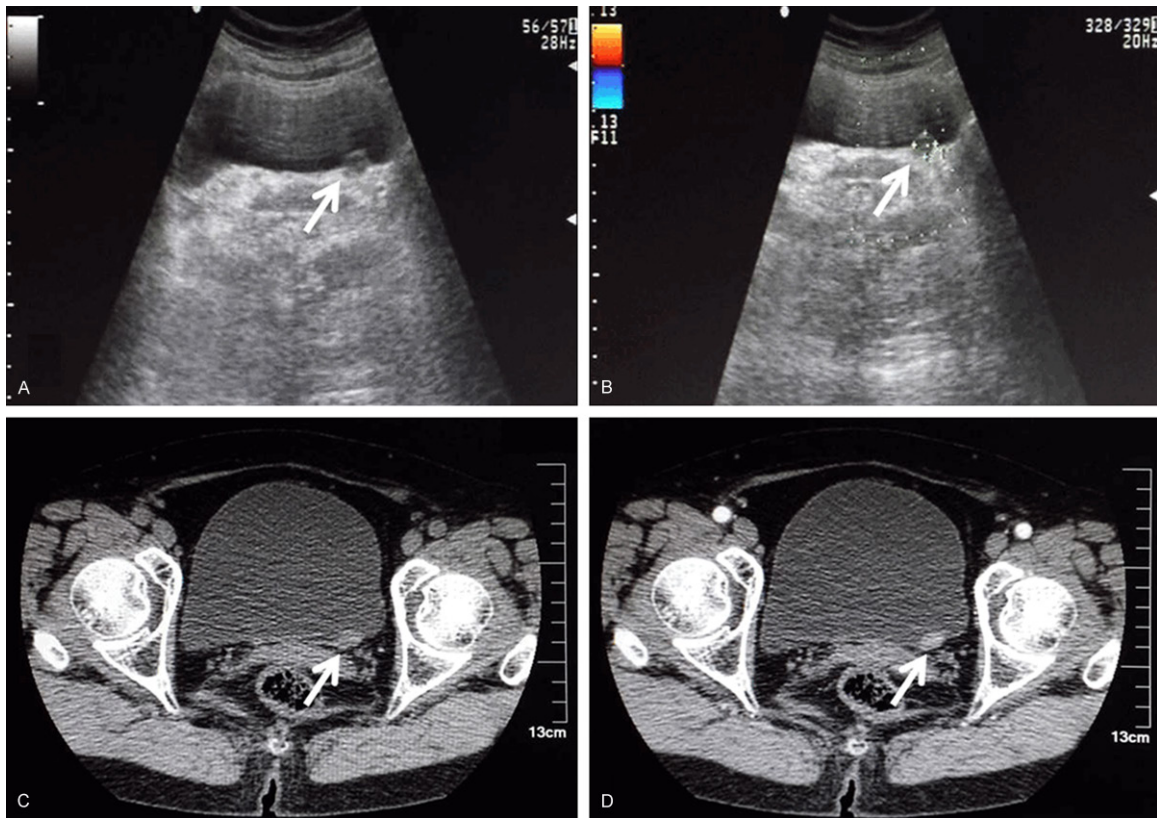


Figure 1. A: The abdominal ultrasonography revealed an 11 mm×9 mm lesion of the left posterior bladder wall. B: Color Doppler sonography demonstrated the hypervascular nature of this lesion. C: Plain CT image showed a mass protruding into the bladder cavity with homogeneous iso-density. D: Contrast-enhanced CT scan revealed the mass with contrast enhancement.

rior wall of the urinary bladder (**Figure 1A**), and color Doppler sonography demonstrated the hypervascular nature of this lesion (**Figure 1B**). A contrast-enhanced computerized tomographic (CT) scan of the abdomen and pelvis revealed a mass on the left posterior wall of the bladder with contrast enhancement (**Figure 1C** and **1D**). There was no evidence of lymph node or distant metastases on ultrasound examination or CT scans. On surgical exploration there was a small, smooth and protruding tumor on the left posterior wall of the bladder with normal mucosa. The patient underwent transurethral resection of bladder tumor (TURBT). During the operative procedure, blood pressure remained stable and no massive bleeding and attacks of hypertension occurred. In the clinical course, post-operative continuation of irbesartan treatment was required to control the hypertension. The patient was free of recurrence until the last follow-up (3 months).

Pathologic findings

Through the cystoscopy examination, the tumor measured around 10 mm×10 mm and was observed on the left posterior wall of the urinary bladder with normal mucosal covering. Histologically, the resected tumor was composed of polygonal cells that were arranged in a nested pattern (**Figure 2A**). Immunohistochemically, the tumor cells showed strong positivity for neuroendocrine markers such as Syn (**Figure 2B**), and sustentaculum cells are strongly positive for S-100 (**Figure 2C**). Staining for cytokeratin AE1/AE3 and CK20 was negative (**Figure 2D**). Staining was also negative for Ki67. Taken together with all the clinical features and pathological evaluation, the tumor was therefore confirmed as a nonfunctional urinary bladder paraganglioma.

Discussion

Urinary bladder paraganglioma is extremely rare tumor subtype [9]. In the 2004 World

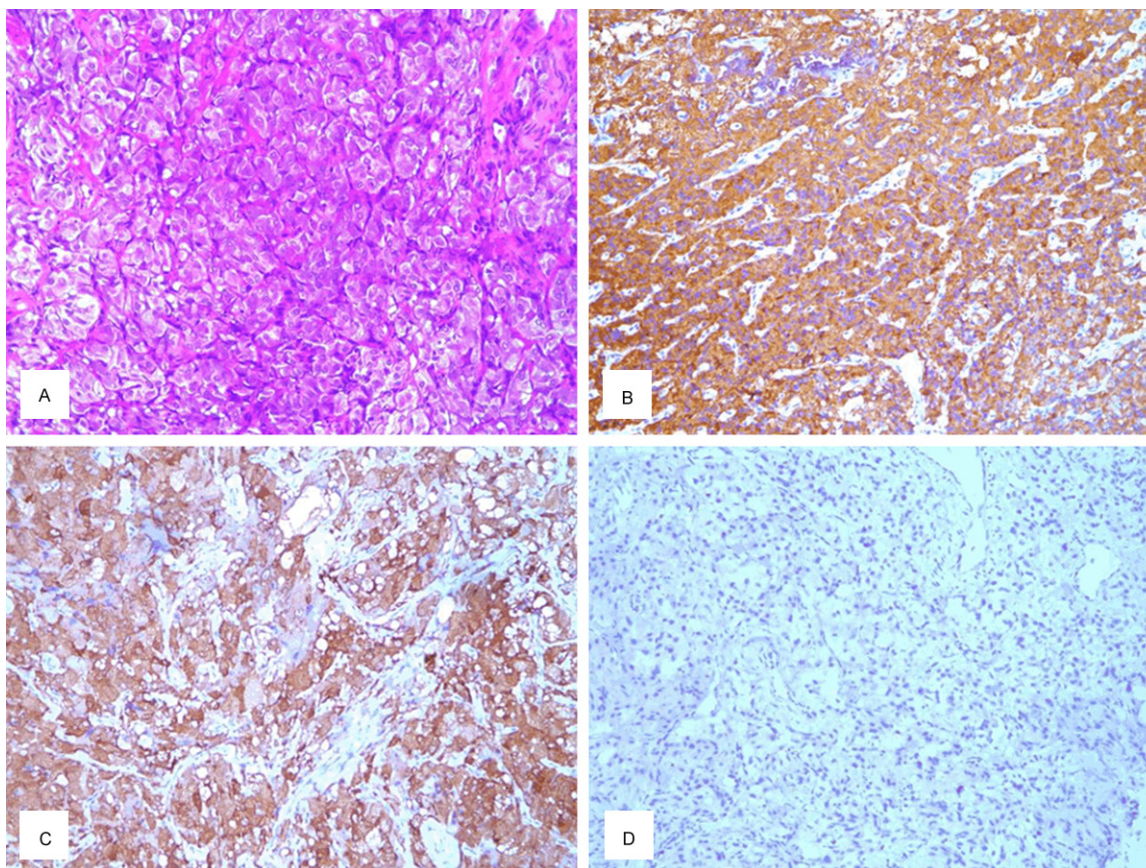


Figure 2. A: Hematoxylin and eosin image showed a characteristic nested growth pattern of the tumor cells ($\times 100$). B: Histological section showed the tumor was positive for Syn. C: The tumor cells demonstrated strongly expression for S-100. D: Staining was negative for cytokeratin AE1/AE3, and similar staining was seen for CK20 and Ki67.

Health Organization Classification of Tumors, pheochromocytoma are classified as endocrinetumors arising from chromaffin cells of adrenal medulla while extra-adrenal tumors are classified as paraganglioma. Bladder paraganglioma may occur in patients of any age, but have strong female predilection, with a 3:1 predominance of women over men in previous reports [10]. The most common clinical feature of urinary bladder paraganglioma was provoked by micturition due to an excess of catecholamines, including headaches, vertigo, palpitations, blurry vision and paroxysms of hypertension [11]. The characteristic clinical symptoms in patients with bladder paraganglioma are almost diagnostic, nonfunctional urinary bladder paraganglioma are extremely rare and difficult to diagnose due to their non-secreting nature [12].

In the current case, the patient did not present with any of the typical symptoms associated with bladder paraganglioma. An abdominal

ultrasonography is the first image modality of choice in the diagnostic algorithm to localize the tumor. A contrast-enhanced computerized tomographic scan of the abdomen and pelvis used next for the detection of primary tumor and metastatic disease. Radiologically, urinary bladder paraganglioma appeared as a mass on the wall of the bladder with contrast enhancement on computerized tomographic scan and thus could mimic other bladder tumors [13]. Recently, positron emission tomography (PET) has been described for detecting urinary bladder paraganglioma with a highly sensitive [14]. It was difficult to establish a precise diagnosis of bladder paraganglioma preoperatively due to lack of any typical radiological features, thus, histopathological examination study of the excised bladder tumor were necessary for post-operatively definitive diagnosis.

Treatment modalities of surgical resection include transurethral resection and partial cystectomy. However, the optimal treatment mode

Nonfunctional urinary bladder paraganglioma: a rare case report

remains uncertain [15]. In the present case, the tumor was on the left posterior wall of the bladder that was close to the trigone of the bladder. Due to its size and position, TURBT is considered to be feasible in this tumor. For patients with functional bladder paraganglioma, it is necessary to stabilize hypertension by using alpha-blocking agents preoperatively [16], whereas patients with nonfunctional bladder paraganglioma, do not consider any special medical treatment before the operation. In this case, alpha-blocking agents were not considered, and blood pressure remained stable during the operative procedure.

Histological studies revealed the bladder paraganglioma was characterized by cells arranged in discrete nests. A positive staining with Syn and S-100 and a negative staining with cytokeratin AE1/AE3, CK20 and Ki67 were observed in the present case, which was compatible with bladder paraganglioma. Definitive diagnosis is made by histological examination of the specimen and special staining, but histology cannot distinguish benign and malignant paraganglioma. Therefore, postoperatively regular follow-up is necessary to observe clinical behavior of bladder paraganglioma.

Conclusion

The current study presented the case with nonfunctional urinary bladder paraganglioma, and the case showed no recurrence or metastasis until the last follow-up at 3 months. TURBT may be a treatment of choice for nonfunctional bladder paraganglioma in small size, offering several benefits such as reduced invasion and rapid recovery. Because histological features cannot distinguish between benign and malignant tumors, life-long follow-up is recommended in the urinary bladder paraganglioma.

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Disclosure of conflict of interest

None.

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Nonfunctional urinary bladder paraganglioma: a rare case report

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