



# Imaging manifestations of bladder paraganglioma

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**Background:** To investigate the imaging findings of bladder paraganglioma (BPG) and improve the imaging recognition and diagnostic accuracy of the disease.

**Methods:** The clinical and imaging data of 10 cases of BPG confirmed by operation and pathology were retrospectively analyzed from the aspects of tumor location, size and morphology, presence or absence of necrosis, cystic change and calcification, and enhancement methods.

**Results:** Of the 10 cases, 7 cases underwent basal and contrast enhanced computed tomography (CT) scan examination, 1 case underwent basal and contrast enhanced MRI scan examination, and 9 cases underwent ultrasonography examination; 5 cases were located in the right wall of bladder, 3 cases were located in the left wall, and 2 cases were located in the bottom wall; 2 cases showed necrosis, 1 case had cystic degeneration, and 2 cases had arcuate and semicircular calcification; both contrast enhanced CT and MRI examinations showed significant post-contrast enhancement; in 9 cases of ultrasonography examination, 5 cases had hypoechoic mass, 3 cases had moderate echoic mass, and 1 case had hyperechoic mass.

**Conclusions:** The imaging findings of BPG have certain characteristics, and combining with clinical history is helpful for accurate preoperative diagnosis.

**Keywords:** Bladder paraganglioma (BPG); tomography, X-ray computer; nuclear magnetic resonance; ultrasonography

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## Introduction

Bladder paraganglioma (BPG), also referred to as extra-adrenal pheochromocytoma, is a neuroendocrine neoplasm that originates from the chromaffin tissue of the sympathetic nervous system embedded in the muscle layer of the bladder wall, accounting for 0.06% of all bladder tumors and 1% of overall paragangliomas (1-3). It is an extremely rare but severe condition that may cause severe hypertensive crisis during handling and mobilization of the tumor (4). 35% of BPGs are malignant (5). However, almost one third of BPG patients do not present with tumor

specific symptomatology. Tumors are mostly located in the submucosa and myometrium and are potentially malignant and easily misdiagnosed as bladder cancer (6). The previous literature is mostly based on case reports. In this study, we studied 10 cases in order to provide support the diagnosis and treatment of BPGs.

## Methods

### General information

The clinical and imaging data of 10 cases of BPGs confirmed

by histopathological examination from June 2009 to May 2019 at Zhongshan Hospital of Fudan University were collected. Institutional review board approval with consent waiver was obtained for this retrospective study. 7 males and 3 females were enrolled, with an average age of 52.4 years (range, 16–79 years). Clinical manifestations: 4 cases of hematuria (3 cases of painless hematuria, 1 case with dysuria), 3 cases of hypertension (1 case with palpitations and palpitations after urination), 3 cases found by physical examination. All 10 cases were surgically resected. Postoperative pathology and immunohistochemistry confirmed the presence of BPG. Among them, 1 case had obvious abnormal cells, infiltrating the mucosal layer, and tumor thrombi were seen in the vessel. 4 cases were not followed up, and 6 cases had no recurrence and metastasis after 5 months to 3 years' follow-up.

### *Imaging examination methods*

#### **Computed tomography (CT) examination**

Siemens Somatom 64-row dual-source CT and TOSHIBA Aquilion One 320-row spiral CT were used, and 500–800 mL of water was consumed half an hour before the examination. Scanning parameters: 120 Kv, 250 mA, layer thickness 5 mm, 1 mm reconstruction. Flat scan was used, in intravenous phase (scan at 80 s after contrast injection) and renal pelvis phase (scan at 15–30 min after contrast injection), nonionic contrast agent Onipak was used, dose 1.5–2.0 mL/kg, injection rate 3 mL/s.

#### **Magnetic resonance imaging (MRI) examination**

Siemens Aera MR Scanner was used for T1-weighted images (T1WI) axial position, T2-weighted images (T2WI) sagittal and axial plain scanning and diffusion weighted imaging (DWI) sequence axial scanning. T1WI and T2WI used SE sequence. DWI used single-shot SE-EPI sequence plus fat suppression technology, and dynamic enhancement uses VIBE sequence. Scan parameters: TR 5500 ms, TE 82 ms, layer thickness 5 mm, field of view 400×400 mm, matrix 128×128, and diffusion coefficient b value selected 0, 1,000 s/mm<sup>2</sup>.

#### **Ultrasound examination**

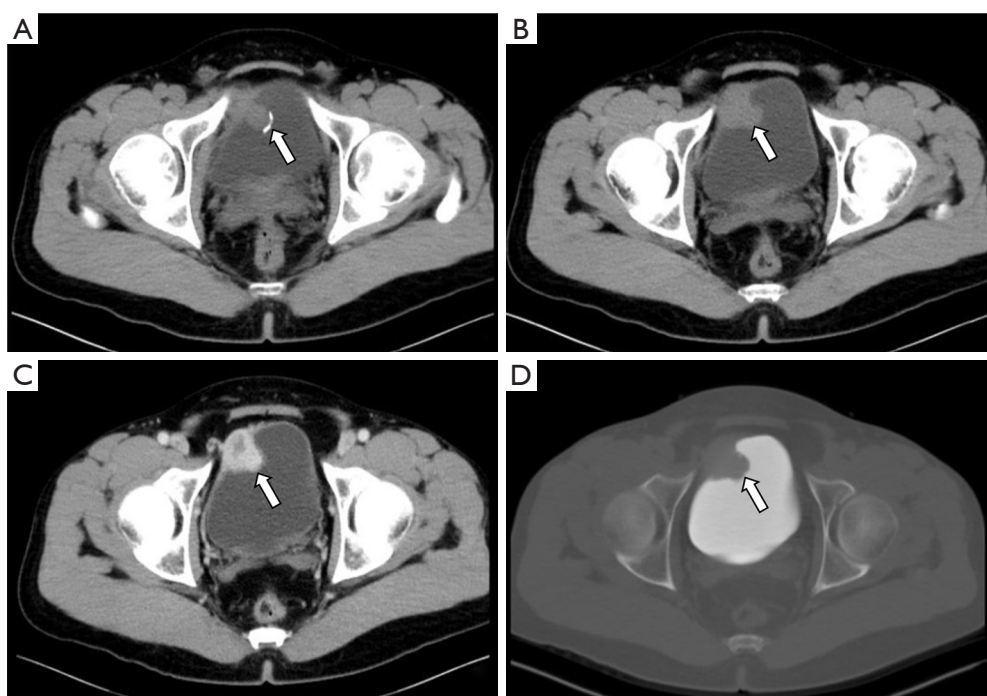
Philips EPIQ7-III and HITACHI EUB-8500 ultrasound diagnostic instrument were used. Probe frequency was set at 2.0–5.0 MHz. Patients were instructed to moderately fill the bladder, fully expose the lower abdomen to the pubic symphysis, and the longitudinally, laterally, and in multiple directions in the bladder area were scanned by the probes.

## **Results**

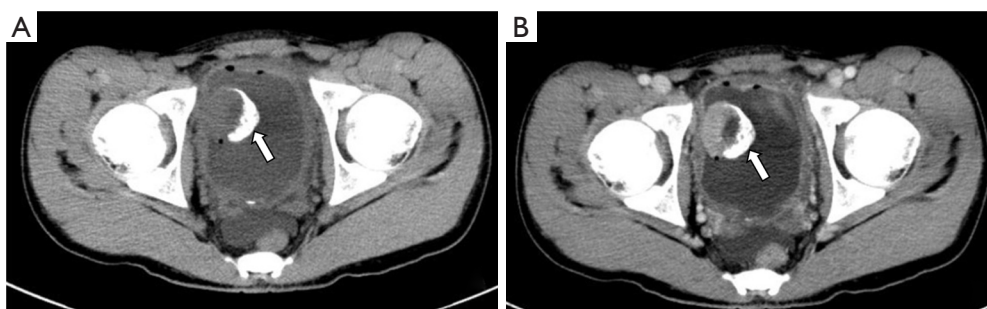
All ten neoplastic lesions were single. Among them, 5 tumor lesions were located in the right wall of the bladder (1 in the right wall, 1 in the right anterior wall, 3 in the right posterior wall), and 3 were in the left wall (1 in the left wall and 2 in the left Back wall), and 2 cases were located on the bottom wall. Nine lesions were round in shape (of which 7 cases grew inside the cavity and 2 cases grew inside and outside the cavity), and one case had irregular shapes and grew inside and outside the cavity (*Figure 1*). The borders of 10 cases were clear, with a length of 1–3.5 cm. Two cases of necrosis were found within the lesion (*Figure 2*). One case showed cystic characteristics within the solid tissue (*Figure 3*). Two cases were accompanied with marginal arc and semicircular calcification (*Figures 1 and 2*). Post-contrast CT exam showed markedly enhancement of the pathological tissue. The CT value was increased by 30–85 Hu, with an average increase of 60.1 Hu. MRI showed tumor T1WI equivalent signal, T2WI slightly higher signal accompanied by small capsule-like high signal, and DWI high signal, and the enhancement was obviously sustained (*Figure 3*). These data were similar to previous study, which showed that all tumors exhibited slight hyperintensity on T1WI and hyperintensity with "salt and pepper" appearance on T2WI. DWI indicated strong hyperintensity, and all cases exhibited conspicuous enhancement after intravenous Gd-DTPA injection (7). Of the 9 cases subjected to ultrasound examinations, 5 showed hypoechoic masses, and 3 were moderately echogenic masses, and 1 was hyperechoic masses. Color doppler flow imaging (CDFI) demonstrated that 5 cases showed rich color blood flow or spot-shaped, line-shaped color blood flow, 2 cases had no clear blood flow in CDFI, and 2 cases did not describe blood flow.

## **Discussion**

BPG is a rare tumor derived from the medullary tissue of the bladder wall sympathetic nervous system, which mostly occurs in the submucosa and muscularis mucosa (8). The majority of BPGs are benign, and the only absolute criterion for malignancy is the presence of metastases at sites where chromaffin tissue is not usually found (9). BPGs could be divided into functional and non-functional according to catecholamine content and active degree of release (8). The clinical manifestations of non-functional paraganglioma are mainly painless hematuria or urinary tract obstruction. Functional paraganglioma can develop



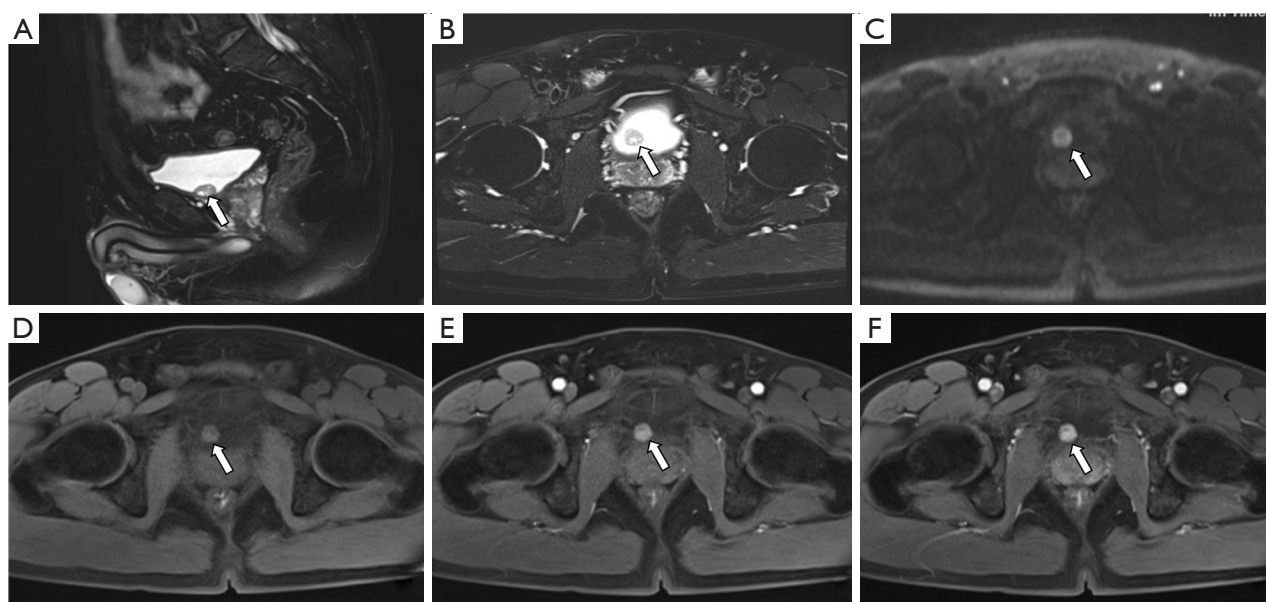
**Figure 1** Male, 35 years old. Irregular soft tissue mass in the right anterior wall of the bladder, growing inside and outside the cavity, arc calcification at the edge (A), plain CT value 42 Hu, enhanced CT value 123 Hu. Arrow, lesion location. CT, computed tomography.



**Figure 2** Male, 16 years old. A soft tissue mass on the right wall of the bladder, which grows into the cavity, has a semicircular calcification on the edge, and has necrosis in the small piece. The CT value is 27 Hu and the CT value is 90 Hu. Arrow, lesion location. CT, computed tomography.

palpitations, dizziness, high blood pressure, and elevated urinary blood pressure (10). In addition, the majority of non-functional BPGs were positive for chromogranin A and Synaptophysin, but were negative for cytokeratins (11), which may be the most appropriate way to diagnose nonfunctional BPGs. Seven patients in this group were non-functional and 3 patients were functional BPG in this study. Paraganglioma of the bladder can occur anywhere in the bladder wall, mostly single. The 10 cases in this group

were all single, with no specific location. Foreign literature reported that the average age of BPG was 43.3 years (11–84 years), and the male to female ratio was 1.07:1 (12). The 22 cases of BPG reported by Zhai *et al.* in China had an average age of 49.8 years (16–76 years), and the ratio of male to female was 1:1 (1). The average age of this group was 52.4 years (16–79 years), and the male to female ratio was 2.33:1, which was not consistent with the previous literature reported, but the sample size of current study



**Figure 3** Male, 52 years old. Nodules on the bottom wall of the bladder, sagittal, axial T2WI slightly higher signal, the small cystic high signal (cystic change), DWI high signal (A,B,C), T1WI fat pressure equivalent signal, enhancement showing significant continuous enhancement (D,E,F). Arrow, lesion location. T2WI, T2-weighted image; DWI, diffusion weighted imaging; T1WI, T1-weighted image.

and previous study is small, so it is not clear whether there is a correlation between gender and age and tumor occurrence.

### CT and MRI manifestations

Most single-shot round soft tissue density or slightly lower density were found in BPG by CT plain scan, with uniform or uneven density and clear boundaries. MRI showed low signals for T1WI in tumors, slightly higher signals for T2WI, lower ADC signals with high signals in DWI, and enhanced scan was uniformly or unevenly enhanced. Post-contrast CT exam showed markedly enhancement of the pathological tissue, and the obvious enhancement of the lesions was helpful for the diagnosis of BPG. It reflects the characteristics of rich blood supply of BPG, which is consistent with the pathological characteristics of tumors composed of main cells and support cells and rich blood sinuses to form a vascular network (13-15). The literature reported that BPG was mostly a single submucosal and muscular layer mass growing into the bladder cavity (1). Of the 10 cases in this group, 7 cases grew inside the cavity, and 3 cases grew inside and outside the cavity, which is basically consistent with previous study, indicating that most of the BPG is closer to the submucosa, which is easy to grow into

the cavity. Paraganglioma is susceptible to degeneration, so tumors show bleeding, necrosis, cystic changes, and calcification. Of the 10 patients in this group, 2 cases had lesions within the lesion and 1 case had lesions within the lesion. Asbury *et al.* believed that circular calcification of tumor margins was helpful for the diagnosis of BPG (14,16). Only 2 of the 10 cases in this group have marginal arcs and semi-annular calcifications. Therefore, whether ring calcification has diagnostic value needs larger sample analysis. Previous literature reported that if BPG appeared liquefied necrosis, unclear borders, and metastases, it may indicate malignancy (1). In this group, only one tumor with necrosis and calcification growing inside and outside the cavity was confirmed to be potentially malignant by pathology (no follow-up after 5 months of follow-up). The rest of the patients with necrosis, cystic changes, and calcification did not find malignancy after surgery. Therefore, the presence or absence of necrosis, cystic changes, and calcification cannot be used as a criterion for judging the benign and malignant nature, nor can the benign or malignant nature be judged solely by the abnormality of the tumor cells (1). Direct invasion of nearby organs and structures and the appearance of lymph nodes or distant organ metastases are the reliable criteria for judging the malignancy.



### Ultrasound manifestations

Ultrasound examination mainly manifested as round low-echo mass with clear boundaries, and some internal echoes were uneven. CDFI showed speckled and striped blood flow signals within the mass (9). Previous study showed that BPGs were solitary, and 40% were located on the dome. The longest diameters in 80% of the BPGs were in the range 1.1–3.0 cm, and 40% of the BPGs were highly vascular (17). Of the 9 cases of ultrasonography in this group, 8 cases showed low echo and medium echo mass, and 5 cases of CDFI showed rich colored blood flow or dot-shaped, linear colored blood flow, which basically accorded with previous literatures. No clear blood flow was found in 2 cases of CDFI, which may be caused by necrosis, cystic changes, or calcification.

### Differential diagnosis

BPG needs to be distinguished from other tumors of the bladder: (I) Leiomyoma is the most common non-epithelial benign tumor of the bladder, accounting for about 35% of benign tumors of the bladder and 0.5% of all tumors of the bladder (18,19). Leiomyoma is more common in young and middle-aged women. The tumoral lesions is with uniform density and signals, and the boundaries are clear. The enhancement scan displays mild to moderate strengthening. (II) bladder cancer (urinary epithelial cancer) is the most common malignant tumor of the bladder. It is more common in the elderly and is often located in the triangular area. The bladder wall is locally thickened irregularly, the size of the mass varies, and the shape is diverse (20). The boundary is less clear, and enhancement displaying uneven enhancement (21); (III) rhabdomyosarcoma, which is more common in children, has high malignancy, early metastasis, and poor prognosis. It is a grape-like lobulated mass (22,23), and enhancement displays significantly strengthened; (IV) lymphoma is more common in middle-aged and elderly women, with a wide range of lesions (24), uniform density, rare necrotic sacs, and enhancement displays mild to moderate enhancement.

In short, CT and MRI demonstrate the BPG has the characteristics of single shot, clear borders, and rich blood supply. Necrosis, cystic changes, and calcification (curved, annular) are often found in BPG. The ultrasound examination for BPG shows low or medium echo mass with blood flow signals. Combined with clinical manifestations, we can make a more accurate preoperative diagnosis.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by ethics board of Zhongshan Hospital, Fudan University (No. Y2018-193).

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