

Unsuspected paraganglioma of the urinary bladder with intraoperative hypertensive peak: A case report

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ABSTRACT

Background. Bladder paraganglioma (BPG) is a very rare tumor.

Case report: We report the case of a 48-year-old woman with a history of isolated hematuria. Cystoscopy showed a solid mass on the bottom of the bladder. During the intervention the patient experienced a severe hypertensive episode. BPG was then suspected. Pathology findings confirmed the diagnosis. ¹²³I-metaiodobenzylguanidine scan showed a pathological tracer accumulation in the left bladder wall consistent with BPG. The patient underwent a transurethral resection of the bladder after drug preparation. The postoperative course was uneventful and our patient was normotensive.

Conclusion. Diagnosis of BPG is often made on histological examination of the tumor

Keywords: bladder tumor, paraganglioma,
¹²³I-metaiodobenzylguanidine scan, hypertensive peak

INTRODUCTION

Paragangliomas are extra-adrenal catecholamine-secreting neuroendocrine tumors derived from embryonic neural crest cells [1]. The bladder is an uncommon location for a paraganglioma. Bladder paraganglioma (BPG) are often misdiagnosed and may cause severe hypertension preoperatively when mobilizing the tumor. Herein we report a case in which a patient with unsuspected BPG experienced a severe hypertensive episode during cystoscopic tumor resection.

CASE PRESENTATION

A 48-year-old woman presented with isolated and intermittent total hematuria. She had a history of hypothyroidism and depression. Physical examination was normal, and there was no evidence of hypertension. Ultrasound did not show any abnormalities.

Subsequently, the patient was referred for cysto-ureteroscopy. Cystoscopy showed a 4-cm, pedicled well-limited solid mass on the bottom of the bladder.

When the resection began, the patient suddenly presented a hypertensive peak of 220/80 mm Hg and her pulse rate dropped to 37/min. The procedure was immediately stopped.

BPG was suspected and histologic examination of the resected specimen confirmed the diagnosis. It showed tumorous large cells, with a positive immunostaining for synaptophysin, a strong positivity for chromogranin, patchy for S-100 and negative for cytokeratin (Figure 1).

Twenty-four-hour urinary metanephrine and norepinephrine levels were normal.

The patient had no family history and there was no evidence of multiple endocrine neoplasia syndrome or Von Hippel Lindau (VHL) syndrome.

Further imaging with Iodine-123-metaiodobenzylguanidine (¹²³I-MIBG) scan was performed as part

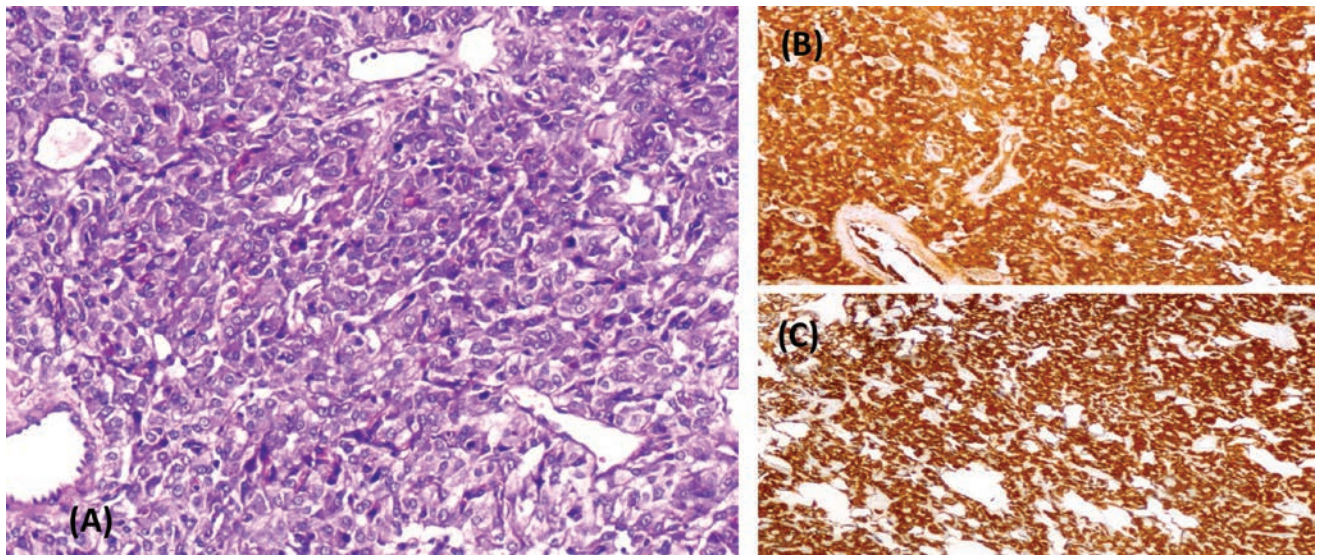


FIGURE 1. HE x10. The chromaffin cells of paraganglioma demonstrate immunore-activity for the neuroendocrine markers chromo-granin and synaptophysin (A). The tumor cells in this case were strongly positive for chromogranin (B) and synaptophysin (C) at immuno-histochemical analysis

of a staging protocol. It showed an intense focal uptake arising from the left bladder wall corresponding to the residual tumor. There was no other sign of any metastatic disease (Figure 2).

Computed tomography (CT) of the abdomen and pelvis revealed a 21 × 25mm heterogeneously enhanced mass at the posterior bladder wall consistent with BPG (Figure 3).

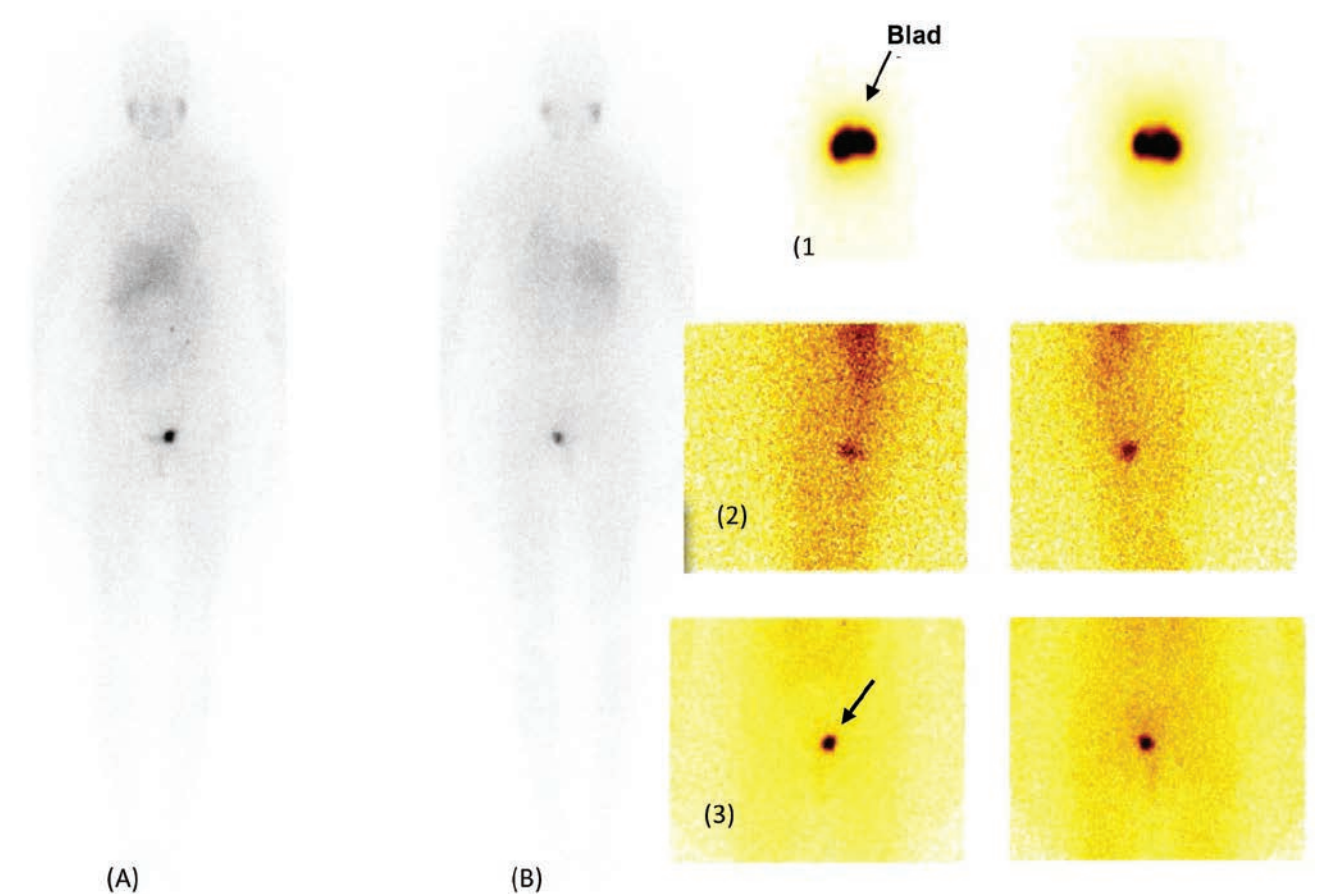


FIGURE 2. The whole-body planar ¹²³I-MIBG images (A: anterior, B: posterior) were obtained 24 hours post injection of 260Mbq of ¹²³I-MIBG. Because of the physiological urinary activity in the bladder, it is difficult to determine any abnormal uptake in the bladder. Therefor we placed a catheter to empty the bladder and injected 37Mbq of ^{99m}Tc-DTPA (1). BPG was confirmed by showing intense focal uptake (arrow) in the left bladder wall (2; 3)

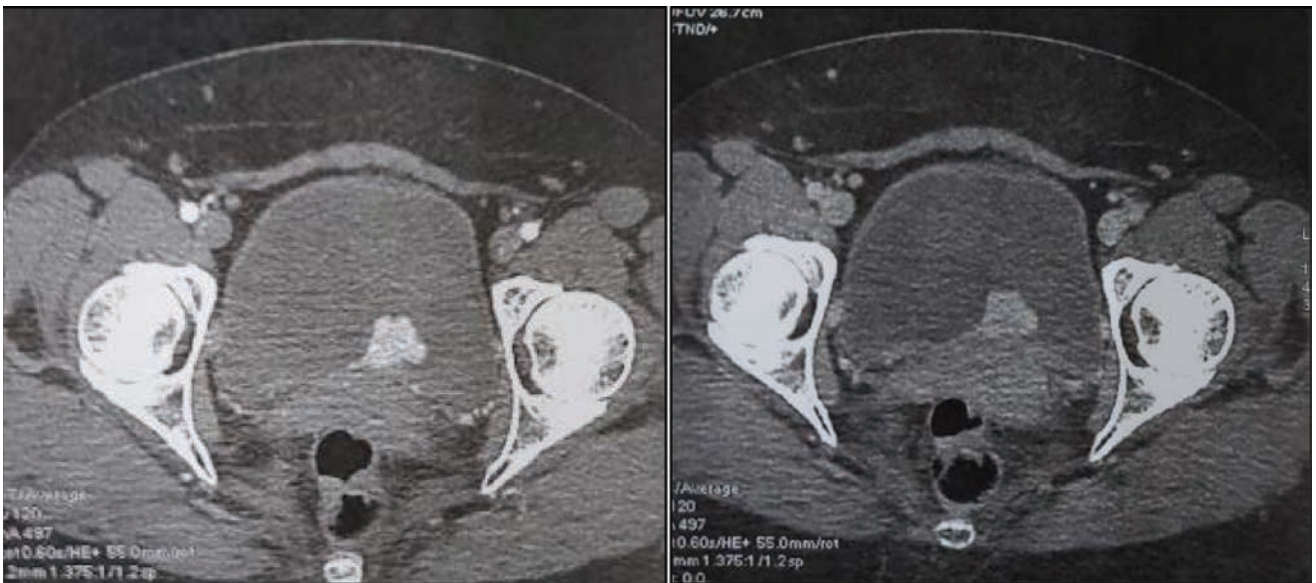


FIGURE 3. Axial CT images acquired after administration of intravenous contrast. A heterogeneously enhancing soft tissue mass (21 x 25mm) is seen arising from the posterior wall of the urinary bladder

Consequently, the patient was referred for a transurethral resection of the bladder (TUR-Bt), a week after adequate preoperative drug preparation with low doses of α and β -blocking agents. Intra-operatively the patient remained hemodynamically stable without complications.

Histological findings were consistent with the diagnosis of BPG invading muscularis propria.

The postoperative course was uneventful. The patient remained normotensive without any drug. Also, there were no sign of recurrence in the cystoscopy, the CT-Scan and the ^{123}I -MIBG control scan with a follow-up of 12 months (Figure 4).

DISCUSSION

Paragangliomas, referred to as extra-adrenal pheochromocytomas, may occur in retro peritoneum, mediastinum, skull and more rarely in the bladder [2]. BPG originates from the chromaffin tissue of the sympathetic nervous system embedded in the muscle layer of the bladder wall. It accounts for less than 0.05% of all bladder malignancy.

BPGs occur over a wide age range, more commonly in females. They are mostly seen at trigone and

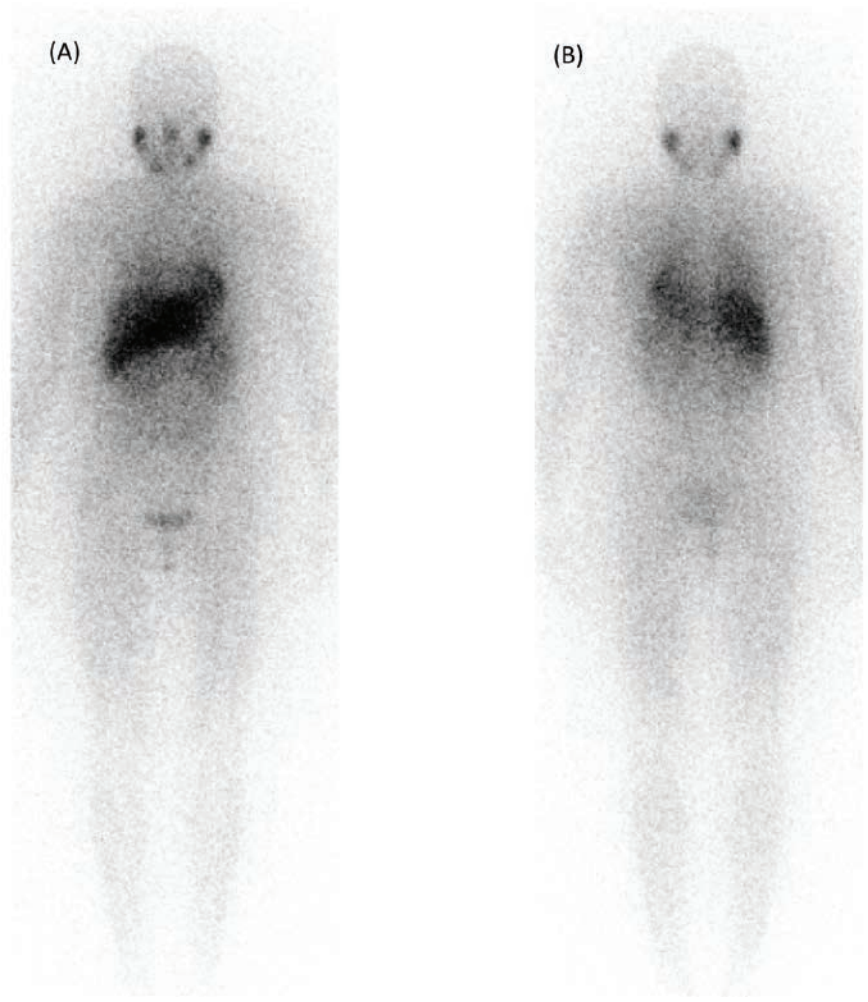


FIGURE 4. Whole-body planar ^{123}I -MIBG images (A: anterior, B: posterior), 12 months after the transurethral resection of the bladder (TUR-Bt), showing complete remission

posterior wall of the urinary bladder, like our patient.

BPGs may be functional or nonfunctional. The most common symptoms of functional BPG are a hypertensive crisis with headache, palpitations, hot flushes and sweating. These crises are typically provoked by micturition or over distention of the bladder [3]. Our patient had only painless hematuria, which is common in bladder disease and therefore does not specifically indicate the presence of BPG.

Assessments of plasma and/or urine catecholamine levels are important for biochemical confirmation. Elevated urinary metanephrine levels are both sensitive and specific for active paragangliomas. However, the majority of paragangliomas are not hormonally active, thus preoperative catecholamine levels maybe normal, making non-functioning paragangliomas more difficult to diagnose.

On histological examination, BPGs are usually composed of solid nests known as “zellballen” of round to oval or elongated cells with abundant granular cytoplasm, within a vascular stroma. Paraganglioma is positive for neuroendocrine markers like neuron-specific enolase (NSE), synaptophysin, chromogranin and negative for cytokeratin.

Paragangliomas are characterized by a high frequency of hereditary forms (overall, 25%). The most common genetic cause of hereditary paragangliomas are mutations in the succinate dehydrogenase (SDH) subunit (genes: SDHB, SDHD, SDHA or SDHAF2). They are also associated with clinical syndromes such as VHL disease, Multiple Endocrine neoplasia type 2 (MEN2) and neurofibromatosis type 1.

Our patient had no family history, however, the genetic status was not available before surgery. In this case the possibility of multifocal or metastatic disease should be considered, and functional imaging is recommended.

Both CT-Scan and magnetic resonance imaging (MRI) are useful for the diagnosis of BPG to exactly delineate the extent of the disease. ¹²³I-MIBG scintigraphy is a well-established traditional imaging modality for catecholamine-secreting tumors and it has been shown to have a very high sensitivity and specificity for pheochromocytoma detection, with a reported specificity of 99% and a cumulative sensitivity of about 90% in paragangliomas [4].

Positron emission tomography (PET) imaging seems to be very promising with higher accuracy. The higher spatial resolution of PETscan enables the

detection of small lesions not visualized with ¹²³I-MIBG. It should be performed with specific ligands, such as [18F]-dihydroxyphenylalanine ([18F]-DOPA) and gallium-68 (68Ga) DOTANOC.

68Ga DOTANOC PET/CT is an excellent tool in the imaging of paragangliomas [5,6,7]. It shows tracer avidity in neural crest tumors, due to somatostatin receptor (SSTR) expression [8]. Unfortunately, it is not available in Tunisia, nor is 18F-DOPA.

The mainstay of treatment for urinary BPG is surgical resection, with common methods being transurethral resection, partial cystectomy, and radical cystectomy in case of malignancy [9]. For localized tumors, surgical resection is the only treatment required along with preoperative and intraoperative adrenergic blockade to avoid a hypertensive peak.

Intraoperative uncontrolled hypertension may be life-threatening and thus, it is important to consider a paraganglioma in the differential diagnosis for bladder tumors.

Long term follow-up is necessary. It should be regular and include cystoscopic examination, plasma or urinary catecholamine levels and imaging study (CT and MIBG).

Most often, BPGs are not locally invasive, nor likely to metastasize, with a favorable prognosis following proper treatment.

CONCLUSION

Owing to their rarity and symptomatic variability, BPGs are commonly misdiagnosed. Diagnosis is often made on histological examination of the tumor, which is risky due to the potential malignant properties and cardiovascular events.

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Conflict of Interest

Authors declare that they have no conflict of interest regarding the publication of this article.

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