Case Report

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A Rare Cause of Macroscopic Hematuria: Primary Bladder Paraganglioma: A Case Report on Clinical, Imaging, and Treatment Approaches

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Abstract

Pheochromocytomas are tumors originating from the chromaffin cells of the adrenal medulla that can cause the release of catecholamines. Pheochromocytomas located outside the adrenal glands are referred to as paragangliomas and account for 10-15% of all pheochromocytoma cases. This case report presents a 30-year-old female patient diagnosed with primary bladder paraganglioma who presented to our clinic with the sole complaint of hematuria. After the detection of a mass in the bladder via abdominopelvic ultrasound to investigate the etiology of hematuria, further advanced investigations and histopathological examinations led to the diagnosis of the exceedingly rare primary bladder paraganglioma. By examining this disease clinically, radiologically, and histopathologically, we aim to expand our knowledge of this condition.

Keywords: Bladder, hematuria, paraganglioma

Introduction

Pheochromocytomas are frequently benign, non-epithelial tumors originating from the chromaffin cells of the adrenal medulla, causing catecholamine discharge. Pheochromocytomas located extra-adrenally are also referred to as paraganglioma, accounting for 10-15% of all cases (1). Primary bladder paraganglioma are exceedingly rare, accounting for only 0.06% of cases. They do not exhibit sex predilection, and the most common symptoms in these patients are hypertension, headache, palpitations, and hematuria (2). In addition to these symptoms, radiological imaging, such as ultrasound (US) and computed tomography (CT), may reveal a mass in the bladder, raising suspicion of a diagnosis of bladder cancer. However, a definitive diagnosis requires cystoscopic imaging and histopathological examination of a biopsy taken from the mass.

Currently, the treatment of primary bladder paraganglioma often involves transurethral resection of the bladder tumor (TURBT) or partial cystectomy, both of which typically result in curative outcomes (3). Nevertheless, because of the potential for local recurrence or metastasis even during long-term follow-up, especially in cases of malignant transformation, lifelong clinical monitoring is crucial.

Herein, we present the case of a 30-year-old female patient diagnosed with primary bladder paraganglioma following presentation to the urology outpatient clinic with macroscopic hematuria. Through clinical, radiological, and histopathological evaluation of this exceptionally rare condition, we aim to contribute to the existing literature.

Case Report

A 30-year-old female patient presented to our urology clinic with the sole complaint of macroscopic hematuria. Laboratory investigations revealed 2358 erythrocytes and 1 leukocyte in a complete urinalysis, while other biochemical parameters, such as complete blood count, renal function tests, and liver function tests, were within normal limits. Abdominopelvic US showing a hypoechoic mass measuring 25x35 mm with intraluminal extension in the right posterolateral wall of the bladder. Under

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local anesthesia, the patient underwent a diagnostic cystoscopy, revealing a solid mass approximately 2.5 cm in size with a polypoid extension on the right lateral wall of the bladder (Figure 1). Due to the patient's allergy to contrast medium, contrast-enhanced abdominopelvic CT could not be performed. Instead, 18-FDG-PET [2-deoxy-2-(fluorine-18) fluoro-D-glucose positron emission tomography] was performed, and the patient was preoperatively hospitalized for TURBT. The 18-FDG-PET scan revealed increased FDG uptake (SUV_{max}: 14) in a 28x36 mm soft tissue mass in the right posterolateral bladder wall, with physiological FDG uptake and distribution observed in other areas (Figure 2). Following preoperative verbal and written informed consent, TURBT was performed, achieving complete tumor resection along with its base (Figure 3).

Histopathological examination of the resected material revealed a tumor composed of nest structures (zellballen pattern) separated by fine fibrovascular septa, infiltrating the muscle layer beneath the urothelium-covered tissue samples. Tumor cells typically exhibit vesicular nuclei, occasionally large hyperchromatic nuclei, and extensive granular or clear cytoplasm. Necrosis and nuclear debris were observed in the center of the nests, leading to a definitive histopathological diagnosis of paraganglioma (Figure 4). The patient was discharged on postoperative day 2 without any complications after removal of the urethral foley catheter. Written and verbal informed consent was obtained from the patient prior to study participation.

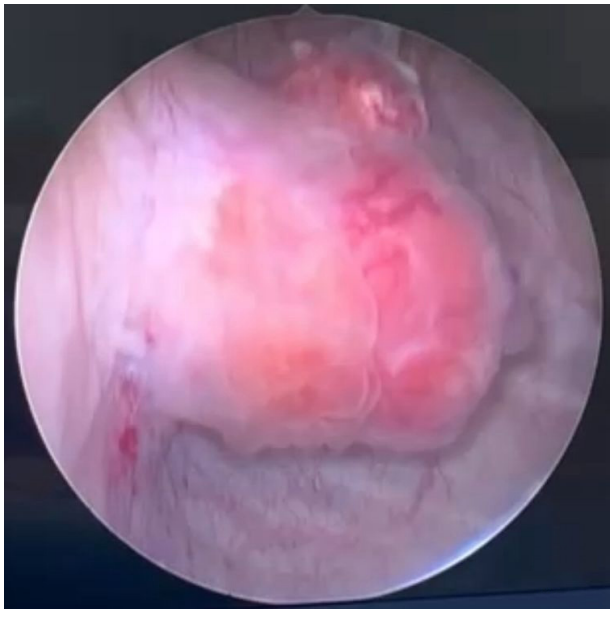

Figure 1. Cystoscopic view of the tumor on the right lateral wall of the bladder

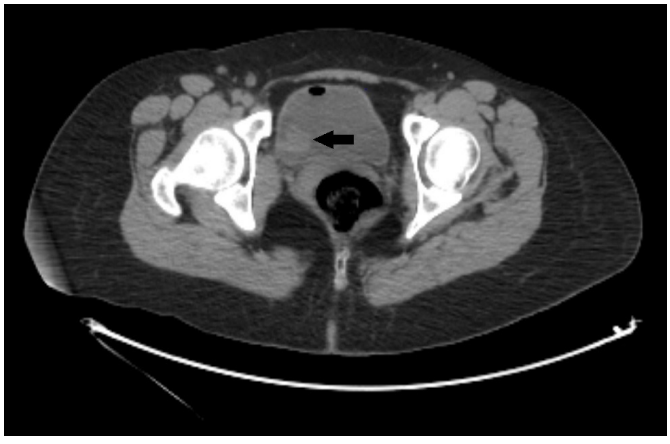

Figure 2. The mass showing increased FDG uptake in the soft tissue, measuring 28 x 36 mm in size, located in the right posterolateral aspect of the bladder, is indicated by the arrow (SUV_{max}: 14)

Discussion

Bladder paraganglioma are rare, non-epithelial neuroendocrine tumors originating from chromaffin cells (4). They constitute 0.05-0.06% of all bladder tumors and typically present between the ages of 43 and 50, with no gender predilection (2). The most common site of paraganglioma in the genitourinary system is the bladder (79.2%), followed by the urethra (12.7%), pelvis (4.9%), and ureter (3.2%) (5). The most frequent locations within the bladder are the dome and trigone. Bladder paraganglioma are submucosal in 45% and intramural in 42% of cases, with an average size of 2.5 cm (6). These tumors can present a wide range of clinical symptoms due to catecholamine release, including flushing, hypertension, palpitations, tremors, and hematuria (5,7).

Diagnostic imaging techniques for bladder paraganglioma include US, CT, and magnetic resonance imaging (MRI). On US, they appear as hypoechoic lesions with intraluminal extension (60%) and hypervascularity on Doppler (1,7). CT has a sensitivity of 91%, with the tumor appearing as a hyperdense, round, homogeneous lesion with prominent peritumoral vessels during the arterial phase; calcifications are seen in 10% of cases (2). MRI is more sensitive than CT and provides excellent soft-tissue resolution for detecting the tumor's location within the bladder

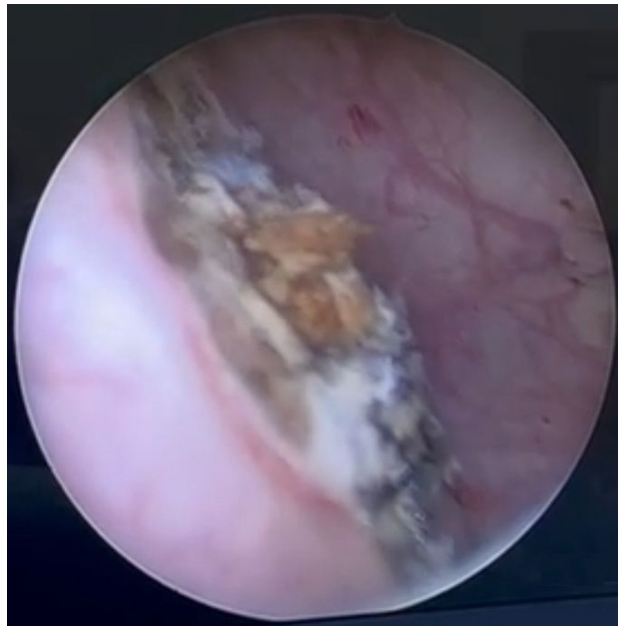

Figure 3. Cystoscopic appearance of the tumor bed after complete resection

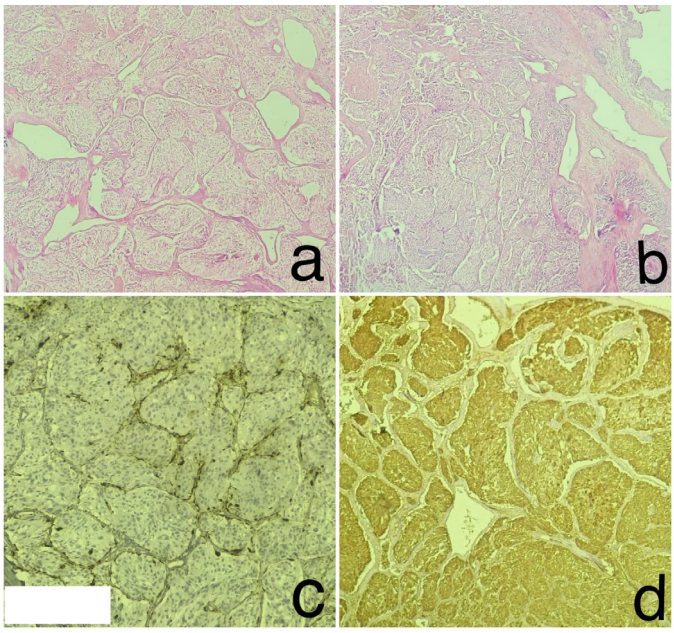

Figure 4. a) Tumor cells with large hyperchromatic nuclei, occasionally with a wide granular or clear cytoplasm, and visible in a vesicular appearance (H&E x100). **b)** Tumor cells with large hyperchromatic nuclei, occasionally with a wide granular or clear cytoplasm, and visible in a vesicular appearance (H&E x40). **c)** Nest structures, separated by fine fibrovascular septa, are believed to infiltrate the muscle layer from beneath the surface epithelium, as seen in tissue samples covered with urothelium, displaying the "Zellballen pattern" (S-100). **d.** Positive staining of sustentacular cells with synaptophysin and chromogranin

layers. Bladder paraganglioma typically appear hyperintense compared with the muscularis propria on T1- and T2-weighted images and often exhibit diffusion restriction (1,2,8).

Other imaging modalities, such as nuclear medicine studies, are particularly useful for identifying metastatic disease. These imaging techniques (Gallium-68 DOTATATE, 18F-FDG, and 18F-DOPA) have higher sensitivity and specificity for the imaging of abdominopelvic paraganglioma (2). However, in our case, due to the patient's contrast medium allergy, we used 18-FDG-PET along with US for imaging before obtaining a histopathological diagnosis. Additionally, screening with iodine-131 metaiodobenzylguanidine (MIBG) is highly sensitive and specific for detecting pheochromocytomas (2).

Approximately 10-26% of bladder paraganglioma undergo malignant transformation, potentially leading to lymph node involvement or distant metastasis (7,9). Staging is classified as T2 for muscle invasion, T3 for peripheral fat extension, and T4 for invasion into adjacent organs or muscles. Bladder paraganglioma do not have a T1 stage. N1 indicates pelvic lymph node involvement, and metastasis is considered when non-adrenal, non-parasympathetic ganglia are affected, with common sites being lymph nodes, bones, liver, and lungs (2).

Histologically, there are no definitive features that distinguish benign from malignant paraganglioma. The best-defined pathological indicators include positive immunohistochemical staining for synaptophysin and chromogranin, with the "Zellballen pattern" highlighted by S-100 in sustentacular cells.

The treatment options for paraganglioma vary depending on the tumor stage and include catecholamine blockade, surgery, chemotherapy, and radiotherapy. Surgical treatments, such as TURBT or partial cystectomy, are effective for localized or locally advanced bladder paraganglioma (2,10). Even after resections in which no tumor is observed at the surgical margins, approximately 15% of cases experience local recurrence, underscoring the importance of regular imaging follow-ups, ideally annually with MRI (2). Tsai et al. (11) recommended postoperative follow-up protocols including annual cystoscopy, plasma or urine catecholamine analyses, and MIBG scan, whereas Young et al. (12) considered urinary and serum vanillylmandelic acid levels as the best tools for detecting clinical recurrence or distant metastasis. In our case, we evaluated the postoperative follow-ups at 1 month using urine and serum catecholamine levels, supplemented with MIBG. Both urine and serum catecholamine levels were within the normal reference range, and no pathological findings were observed during the MIBG scan. During the 6th and 12th-month follow-ups, we only measured serum and urine catecholamine levels and, given their normality, recommended annual follow-up. The initial postoperative cystoscopy was performed after 3 months after the surgery. Because we did not observe any pathology in the bladder during the 3-month cystoscopy, we scheduled the subsequent cystoscopy for 6 months later.

There are significant differences and similarities between the various case reports in the literature and our case. In the case presented by Orsini et al. (13) the patient suffered from hypertension and post-micturition tachycardia attacks and was treated with robotic partial cystectomy. In the case reported by Pérez Barón et al., (14) the patient had complaints of hypertension, vertigo during micturition, and macroscopic hematuria; therefore, laparoscopic partial cystectomy and robot-assisted pelvic lymphadenectomy were chosen as treatment.

Hajji et al. (15) performed laparoscopic partial cystectomy in a patient with asymptomatic and incidentally detected paraganglioma. In the study by Üre et al. (16) a patient with post-micturition tachycardia and headache attacks underwent partial cystectomy.

Our case differs significantly from those of the literature. Our patient had only macroscopic hematuria as a symptom, and TURBT, a less-invasive method, was preferred for treatment. No recurrence was observed during follow-up. This approach is similar to the case presented by Doorn et al. (17) in which a paraganglioma incidentally detected during control cystoscopy in a patient who underwent nephroureterectomy for urothelial carcinoma was treated with TURBT.

The series of 10 cases by Qin et al. (8) focused on imaging methods and diagnostic stages, whereas our study comprehensively addressed all clinical, radiological, and histopathological stages from diagnosis to treatment. Although the ten-case study by Zhang et al. (18) showed similarities with our case in terms of patient selection and treatment methods, it differed in follow-up periods.

Conclusion

In conclusion, although bladder paraganglioma are rare, recognizing and clinically suspecting them is crucial. Accurate diagnosis, appropriate use of characteristic imaging techniques, and proper planning of interventions are vital to avoid unnecessary emergency surgeries or misdiagnoses inconsistent with the tumor's nature.

Ethics

Informed Consent: Verbal and written informed consent was obtained from the patients before surgery.

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Publication: The results of the study were not published in full or in part in form of abstracts.

Contribution: There is not any contributors who may not be listed as authors.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.N., Ö.I., Concept: B.S., Design: A.N., Data Collection or Processing: Ö.I., Analysis or Interpretation: B.S., Literature Search: A.N., Ö.I., Writing: A.N., Ö.I.

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