Case Report

Functional paraganglioma of the bladder: Both radiographic-negative and laboratory-negative case

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Abbreviations & Acronyms
CT = computed tomography
MIBG = meta-iodobenzylguanidine
MRI = magnetic resonance imaging
T1WI = T1-weighted imaging

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Introduction: Paraganglioma has been determined to be an extra-adrenal pheochromocytoma. Paraganglioma of the bladder is a rare entity, accounting for 0.06% of all bladder tumors.

Case presentation: A 58-year-old woman had been annually followed up since being diagnosed with rectal cancer 5 years ago. In January 2018, follow-up computed tomography detected a bladder tumor, and she was referred to our department for a further examination. Cystoscopy revealed a submucosal tumor on her right bladder wall. We performed transurethral resection of the bladder tumor. When we first marked the tumor margin, the systolic blood pressure increased, so we abandoned resection. We performed meta-iodobenzylguanidine scintigraphy and acid urinary collection, neither of which revealed any abnormal findings. We therefore performed open partial cystectomy based on a clinical diagnosis of paraganglioma of the bladder. The pathological findings revealed paraganglioma of the bladder.

Conclusion: We herein report a case of paraganglioma of the bladder.

Key words: extra-adrenal pheochromocytoma, paraganglioma.

Keynote message

1 Functional paraganglioma of the bladder is seen in both radiographic-negative and laboratory-negative cases.
2 Partial cystectomy is a standard option for managing paraganglioma of the bladder.

Introduction

Paraganglioma has been determined to be an extra-adrenal pheochromocytoma. Paraganglioma accounts for 18% of all pheochromocytoma cases. Paraganglioma of the bladder is a particularly rare entity, accounting for 0.06% of all bladder tumors. We encountered a case of intraoperative high blood pressure at the time of tumor resection. We therefore re-tried tumor resection by surgical partial cystectomy.[1]

We herein report the first case of paraganglioma of the bladder with negative findings on both radiography and laboratory testing.

Case presentation

A 56-year-old woman underwent laparoscopic rectal tumor resection with annual follow-up using CT. In January 2018, CT revealed a bladder tumor on her right bladder wall. Cystoscopy confirmed a bladder tumor in the submucosa (Fig. 1). MRI revealed low intensity on T1WI and high intensity on T2WI (Fig. 2). The possibility of paraganglioma was considered after cystoscopy revealed a submucosal tumor. We then checked the adrenal hormone levels preoperatively, but no abnormalities were seen. We therefore planned transurethral resection of the bladder tumor.

In April 2018, she underwent transurethral resection of the bladder tumor, but when we marked the resection margin, her blood pressure dramatically increased to 230 mmHg. We therefore abandoned transurethral resection. We performed

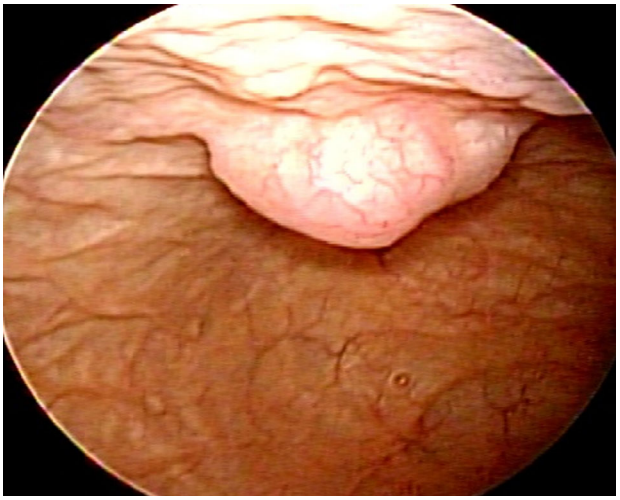

Fig. 1 Cystoscopic findings.

MIBG scintigraphy and acid urinary collection, neither of which revealed any abnormal findings (Fig. 2e). At this point, we clinically suspected paraganglioma and administrated a doxazosin mesilate (1.0 mg/day).

In July 2018, partial cystectomy was performed after observing the bladder tumor cystoscopically. During tumor resection, we used Message Tseng Baum scissors instead of an acusector. She was discharged home 3 days postoperatively and was free from recurrence for 6 months after surgery. A hormonal examination showed almost normal findings (adrenaline 25 pg/mL, noradrenaline 122 pg/mL, dopamine <5 pg/mL, urine metanephrine 0.09 mg/day, urine normetanephrine 0.22 mg/day).

The pathological findings revealed rich endoplasmic reticulum cells growing with an alveolar form. Immunohistochemical staining showed positive findings for chromogranin A, synaptophysin, and CD56 (Fig. 3). Based on these findings, paraganglioma of the bladder was diagnosed.

Discussion

Paraganglioma has been defined as an extra-adrenal pheochromocytoma and consists of paraganglion cells, accounting for 15–22% of all pheochromocytomas.[2]

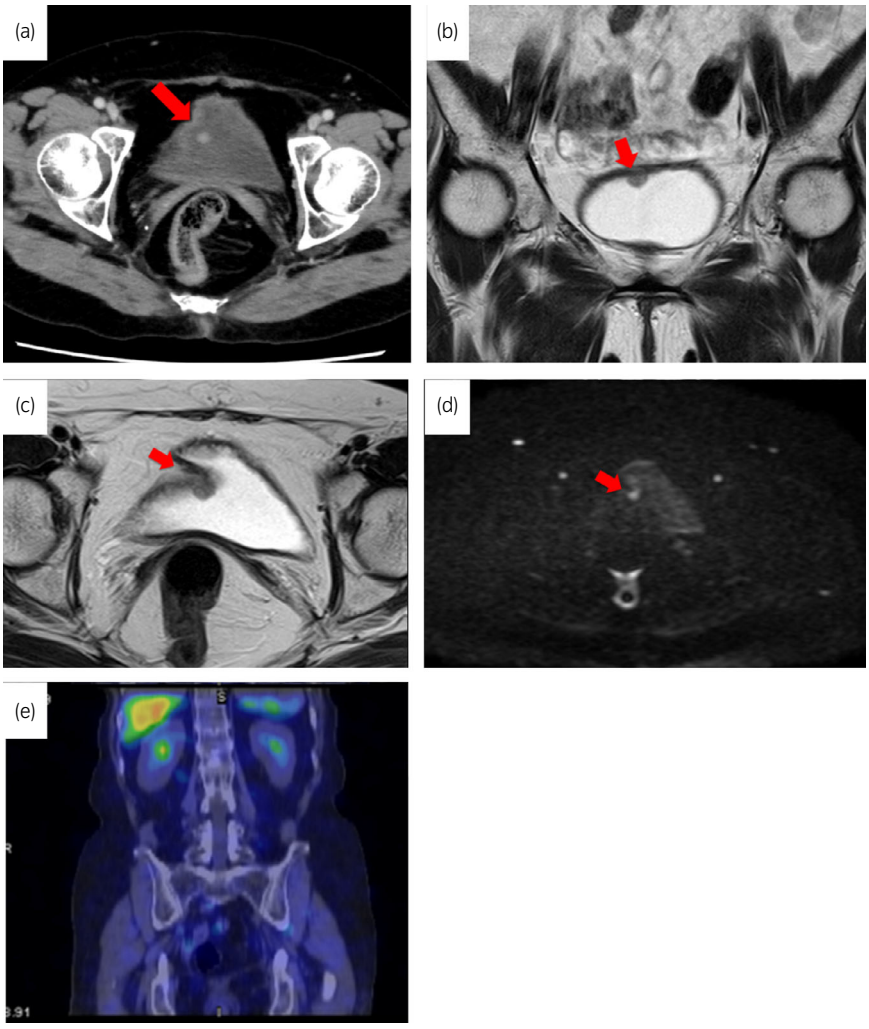

Fig. 2 (a) Contrast-enhanced CT. MRI: (b) T1WI, (c) T2WI, and (d) DWI. (e) MIBG scintigraphy.

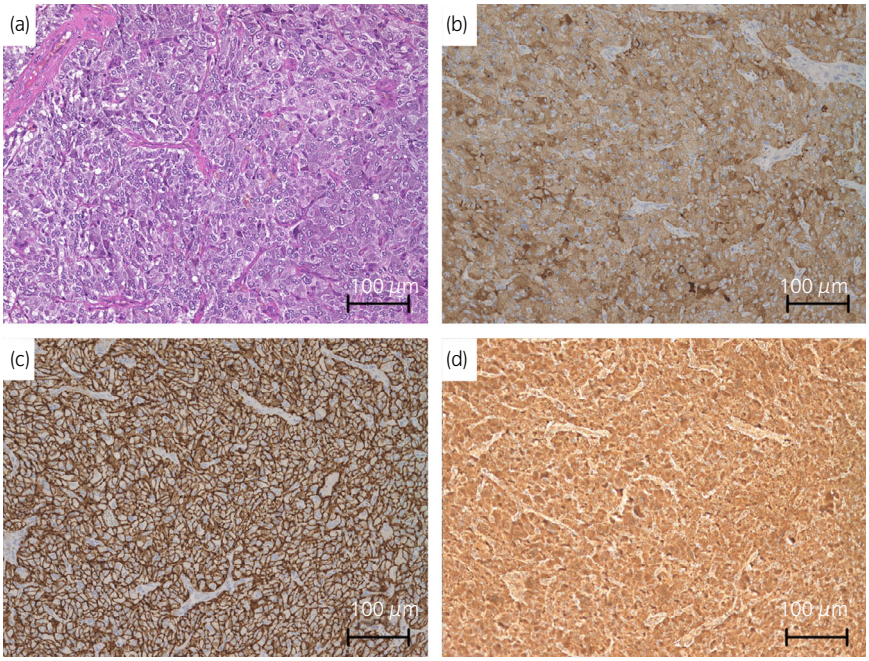

Fig. 3 (a) HE findings: The carcinomatous element consisted of urothelial carcinoma with squamous differentiation. Immunohistochemistry of (b) synaptophysin, (c) CD56, and (d) chromogranin A.

Paraganglioma of the bladder is a relatively rare disease, accounting for 0.06% of all bladder tumors. In the urinary system, the bladder shows most frequent in 79.2%, followed by the urethra (12.7%), renal pelvis (4.9%), and ureter (3.2%).[3,4] Although paraganglioma is most likely to be seen in the dome, trigone, and posterior wall, we examined a total of 39 reports including information on the tumor site, with no typical distribution observed (Fig. 4). A previous report showed that paraganglioma of the bladder tended to occur more frequently on the right side than on the left side; however, no mechanism for this finding has been suggested.

This case was suspected of being paraganglioma because when we started to resect this tumor, the patient's blood pressure increased to over 200 mmHg. Seventeen percent of paraganglioma cases are reported to be nonfunctional tumors. The functional groups are characterized by the presentation of various disease-associated symptoms, elevated levels of catecholamine and metabolites in plasma and/or urine, and positive reaction on MIBG or octreotide scintigraphy; however, no apparent cut-off point has been determined.[5]

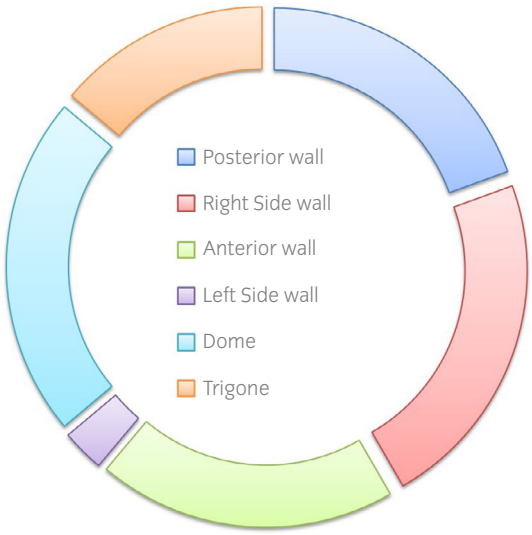

Fig. 4 Distribution of reported paraganglioma sites in the bladder.

Paraganglioma is defined as a benign tumor, but 15–20% of cases show a malignant phenotype and develop metastasis or recurrence. The pathological determination of whether the tumor is benign or malignant is difficult and clinical follow-up is the only way to diagnose a paraganglioma as benign or malignant. Furthermore, malignant paraganglioma has shown resistance to systemic chemotherapy and radiation therapy.[6,7] The standard treatment of paraganglioma of the bladder is partial cystectomy because this tumor tends to extend into the muscle layer. Radical cystectomy is sometimes selected for difficult cases. Based on these previous findings, imaging examinations should be scheduled to check for metastasis or recurrence using MRI or cystoscopy.

In conclusion, we herein report a rare case of paraganglioma of the bladder with negative findings on both radiography and laboratory testing.

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Conflict of interest

The authors declare no conflict of interest.

Declarations

Written informed consent to participate in this study and for the publication of this report was obtained from the patient for ethics approval.

Consent for publication

Written informed consent was obtained from the patient. A copy of the written consent form is available for review from the Editor-in-Chief of this journal.

Availability of data and material

Due to ethical restrictions, the raw data underlying this paper are available upon request to the corresponding author.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1. Previous published reports in Japan containing information on tumor sites.

Editorial Comment

Editorial Comment to Functional paraganglioma of the bladder: Both radiographic-negative and laboratory-negative case

Cases of pheochromocytoma of the urinary bladder are quite rare, accounting for 0.05% of bladder tumors and less than 1% of all pheochromocytomas.[1] Pheochromocytomas are clinically important, and functional tumors have been reported by Zhai *et al.*[2] to account for over 63.6% of cases of paraganglioma in the bladder. Clinicians must be vigilant for signs of severe hypertension subsequent to the surgical procedure, which can result in fatal outcomes such as intracranial hemorrhage. Therefore, a preoperative diagnosis is essential to avoid such undesirable outcomes.

Low-intensity T1-weighted and high-intensity T2-weighted magnetic resonance imaging (MRI) are important diagnostic tools for pheochromocytomas. Additionally, iodine 131 metaiodobenzylguanidine (MIBG) scintigraphy can be used to definitively diagnose the tumor. Other than these imaging modalities, laboratory tests for measuring the concentration of catecholamine or its metabolic products in addition to blood tests or acid urinary collection are helpful diagnostic tools for determining whether the tumor is functional or nonfunctional.

Sugimura *et al.*[3] reported functional paraganglioma of the bladder, which was negative in both radiographic and laboratory examinations. They also noticed that the tumor they were about to incise had some hormonal activity because of the rapid elevation in blood pressure during the transurethral resection of bladder tumor (TURBT). Ceasing the endoscopic procedure was a wise decision. Even though the preoperative MRI scan indicated paraganglioma, the MRI findings were not specific.[4] In contrast to MRI, MIBG scintigraphy has high specificity.[5] If MIBG scintigraphy and laboratory tests were performed before TURBT and those examinations showed positive results, partial cystectomy could have been selected as the initial treatment. However, in this case, those examinations showed negative results.

Overall, in spite of negative findings of MIBG scintigraphy and laboratory tests, functional paraganglioma cannot be completely ruled out. Therefore, urologists must pay careful attention to perioperative vital signs during TURBT for atypical intravesical tumors, and the procedure must be stopped when a major change in the patients' condition is observed during the operation.

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Conflict of interest

The author declares no conflict of interest.