

Extraadrenal pheochromocytoma presenting with severe hematuria and postmicturition cephalgia, a case report of a rare bladder tumor entity

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ABSTRACT

Paraganglioma (PGL) of the urinary bladder are a very rare tumor entity. Treatment of a PGL requires a multidisciplinary approach. We report on a case of a malignant pheochromocytoma (PHEO) of the bladder in a male adult due to a succinate dehydrogenase B (SDHB) subunit gene mutation where a partial cystectomy was performed after preoperative alpha blocking.

1. Background

Pheochromocytomas are tumors of the adrenal medulla that derive from tissue of the neuroectoderm. If they are located outside the adrenal medulla, they are called paraganglioma (PGL) or extraadrenal pheochromocytoma.¹

These cells are highly stained with chromium salts and are therefore called chromaffin cells.

The incidence of pheochromocytoma (PHEO) and PGL is approximately 0.8 cases per 100'000 person-years.² Patients usually present with symptoms caused by the overproduction of catecholamines, such as headache, hypertension, profuse sweating, palpitations, tremors, panic and anxiety attacks.

Approximately 40% of PHEO/PGL are associated with a germline mutation with autosomal dominant transmission and variable penetrance and potential for malignancy.³ Here we present a patient with malignant PGL of the bladder attributable to a mutation of the succinate dehydrogenase B (SDHB) subunit of the gene.

2. Case presentation

A 55-year-old patient was admitted to our institution with painless severe hematuria. The patient described recurrent brownish discoloration of the urine and episodes of post-micturition headache over the past two years. The medical history included evidence of arterial hypertension, thalassemia minor and sporadic panic attacks. In addition,

the patient reported persistent nicotine use of 30 pack years. Sonographic and cystoscopic examination revealed an approximately 4 cm large bladder tumor of the bladder dome. The patient was admitted to in-patient care and a transurethral resection of the bladder (TURB) was performed the following day.

Intraoperatively, at the onset of resection, there was severe bleeding and the patient's blood pressure values exceeding 250 mmHg. Resection of the tumor had to be stopped, and adequate coagulation was performed at the resection site. The further postoperative course was unremarkable and discharge occurred on the second postoperative day.

Histological analysis revealed a PGL of the bladder. Immunohistochemical staining was positive for Chromogranin A, synaptophysin and GATA3 but negative for MNF-116. The KI-67 proliferation rate was 30%.

Blood samples showed excess of norepinephrine and dopamine.

Tumor staging by ⁶⁸GaDOTATATE-PET-CT (Fig. 1) revealed a PGL of the bladder-dome with 3cm thickness, encompassing ¼ of the bladder circumferential. Furthermore, two small metastases were detected, one in the fourth thoracic vertebrae and one in the dorsal right acetabulum column. After discussion in our multidisciplinary tumor board and consultation of our endocrinological colleague, local resection of the PGL of the bladder was recommended for preventing further local complications and to control future catecholamine excesses. Under close inpatient monitoring, preoperative alpha blockade with phenoxybenzamine was performed.

Due to the size and localization of the PGL and the sufficient bladder capacity, bladder-preserving surgery with a partial cystectomy of the

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bladder dome (Fig. 2) and limited pelvic lymphadenectomy was performed.

The intraoperative and postoperative course was unremarkable. Final pathological staging was: pT3a, pN (0/10), pM1a (bone), R0.

Biochemical constellation of norepinephrine and dopamine excess and metastatic abdominal PGL was highly suspicious for an underlying SDHB gene mutation, which was confirmed by genetic testing.

Immediately after surgery plasma metanephrines normalized, nine months after surgery normal bladder function was obtained.

Further treatment was initiated using peptide radionuclide therapy with Lutetium-DOTATOC.

However further bone metastasis were detected and a palliative chemotherapy with Cyclophosphamide, Vincristine and Dacarbazine and later a second line therapy with Sunitinib was established. The patient succumbed to the disease 2 years and 3 months after surgery.

3. Discussion and conclusions

Paraganglioma of the urinary bladder was first described in 1953 by Zimmerman et al.⁴ Since then, numerous cases have been reported, nevertheless this tumor entity is very rare and makes up for less than 0.05% of all bladder tumors.⁵

Less than 1% of all PHEO are found in the genitourinary tract and approximately 10% of all pheochromocytomas are considered as malignant.⁵

The majority of PGL in the bladder are functional. Most mentioned symptoms of PGL in the bladder are severe hematuria, headache, intermittent hypertension, palpitations and syncope; less commonly dysuria. If bladder PGL is suspected, further laboratory tests e.g. serum metanephrine levels are recommended and imaging studies e.g. MRI, PET/CT should be performed.

As mentioned earlier, approximately 30–40% of all PHEO are associated with a germline mutation, so genetic testing is strongly recommended.³

Partial cystectomy is to be favored over radical cystectomy because the main goals of the procedure are local tumor control and control of catecholamine excess. Because the sympathetic plexus is scattered throughout all layers of the bladder, TURB is not an alternative.

Preinterventionally patients should be hospitalized to establish an

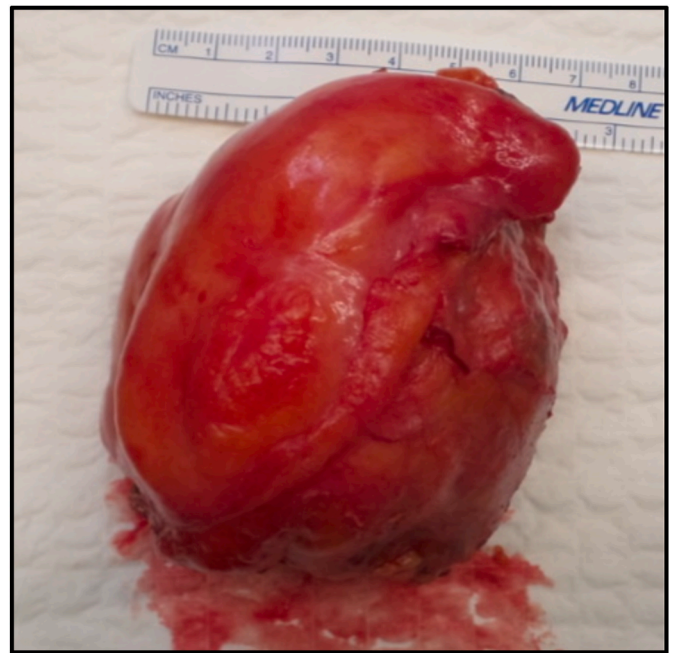


Fig. 2. Specimen after partial cystectomy.

alpha blockade under close monitoring. Overall, a multidisciplinary approach is of utmost importance.

Regular follow-up with catecholamine monitoring and imaging is recommended in the literature. Beilan et al.⁵ recommend catecholamine monitoring within the first postoperative months and then every 6 months for two years and computed tomography every 3 months in the first year, then every 6 months for two years, and then annually for another 3 years.⁵

Informed consent and patient details

Informed consent and patient details were obtained from the patient by the author.

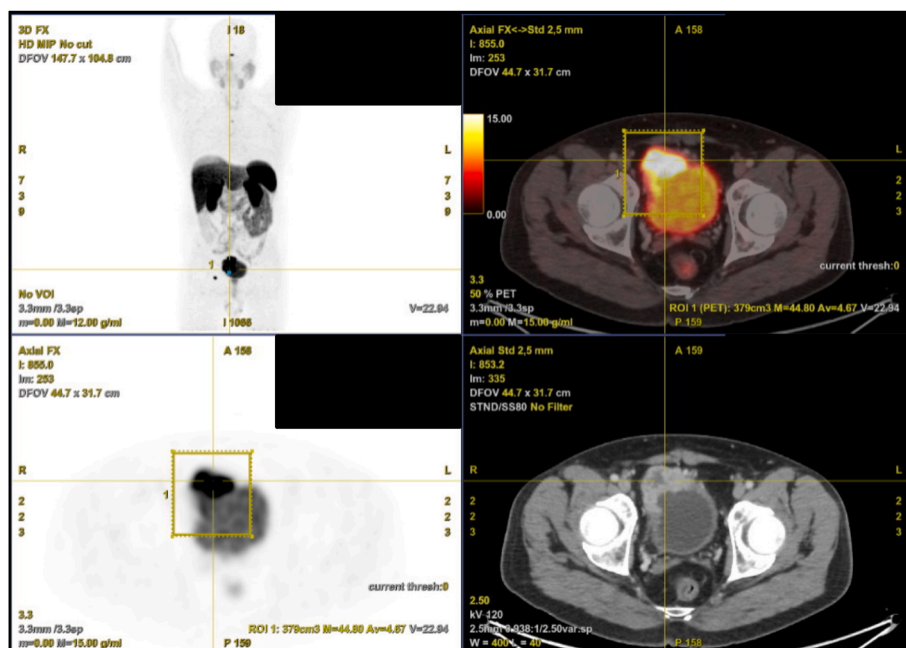


Fig. 1. Staging ⁶⁸GaDOTATATE-PET-CT showing the PGL of the bladder-dome with 3cm thickness, encompassing ¼ of the bladder circumferential.

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Declaration of competing interest

None.

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