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SURGERY

Paraganglioma of the Bladder: a Case Report

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Abstract

A paraganglioma of the bladder is a rare condition. Paraganglioma may case general symptoms of illness like sweating or headache. When performing a transurethral resection of the bladder of the paraganglioma, an antiadrenergic intervention is advised since the resection can trigger a hypertensive crisis. A 65-year-old female was under surveillance after a radical nephroureterectomy because of pTaG2 urothelial carcinoma of the renal pelvis. A year later, she had a recurrence in the bladder (pathology: TaG1 urothelial carcinoma). During follow-up, another suspicious lesion at the bladder wall was seen and resected by transurethral resection of the bladder. The pathology showed a paraganglioma. No other paragangliomas elsewhere in the body were detected. In retrospect, the patient reported to suffer from intermittent palpations and headaches, which are related to a paraganglioma. Paragangliomas are neuro-endocrine tumours and can occur at any age. Paragangliomas of the bladder are accountable for 0.05% of the tumours of the bladder. Eighty-three percent of the paragangliomas of the bladder are symptomatic due to production of catecholamines. Clinical symptoms include sweating, palpitations and hypertension during micturition and haematuria. Cystoscopy and resection of a hormone-producing can be dangerous in patients with symptomatic paragangliomas because of possible provocation of hypertensive crisis. Differentiating between malignant and benign tumours is difficult due to lack of histological criteria. Therefore, life-long monitoring is warranted.

Keywords Paraganglioma · Oncology · Urology · Bladder

Introduction

Paraganglioma of the bladder is a rare but potentially dangerous condition. Symptoms include headaches, sweating, palpitations, hypertension and paleness. In case of suspecting a paraganglioma of the bladder, it is important to perform further diagnostics before treatment in order to prevent a possible hypertensive crisis. Studies on the long-term follow-up of bladder paragangliomas are lacking. Since the risk of recurrence is high and it is challenging to differentiate between benign and malignant paragangliomas, lifelong follow-up is recommended.

Case Presentation

A 65-year-old female was under surveillance after a radical nephroureterectomy because of pTaG2 urothelial carcinoma of the renal pelvis in 2006. A year later, diffuse redness of the bladder was observed during cystoscopy and a transurethral resection of the bladder (TUR-B) was performed (pathology: TaG1 urothelial carcinoma). During follow-up, another suspicious solid and alveolated lesion at the anterior bladder wall was seen during cystoscopy and resected by a TUR-B.

The (histo)pathological examination showed cells in strands and nests that showed a large amount of granular cytoplasm. Additional immunohistochemistry showed positive CD56 and synaptophysin staining. An intense reaction of most likely sustentacular cells was seen when a staining with S100 was performed. Multiple keratin stains remained negative (Fig. 1 and Fig. 2). The findings were highly suspect for a paraganglioma. The lesion was limited to the mucosa and the musculus detrusor was free of tumour.

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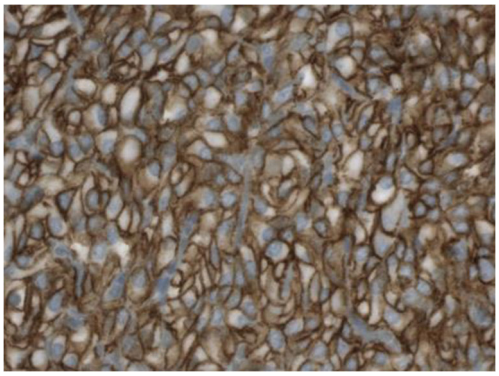

Fig. 1 Positive CD56 staining

In laboratory tests, increased counts of chromogranin A and plasma normetanephrine were found, which supported the diagnosis of paraganglioma. An iodine-131-m-iodobenzylguanidine scan was performed to rule out possible pheochromocytomas/paragangliomas elsewhere in the body. The scan showed no evidence of MIBG-uptaking lesions in the bladder or elsewhere in the body.

When asked afterwards, the patient stated to suffer from episodes of intermittent palpitations, becoming pale, headaches and sweating for years. At the moment, the patient is free of complaints and recurrences.

Conclusions

Paragangliomas are well-vascularized neuro-endocrine tumours that originate from tissue of the autonomic nervous system, mostly located in the adrenal cortex. Extra-adrenal tumours arise from embryonic nests of chromaffin cells from the sympathetic plexus, for example from the musculus detrusor of the bladder [1]. Paragangliomas can occur at any age, with a median age of 43–45 years at diagnosis and seem to be slightly more common in female patients [2].

Bladder paragangliomas are accountable for less than 0.05% of all tumours of the bladder and constitute less than 1% of all paragangliomas [3]. In the majority, the paragangliomas invade until the muscularis propria. Differentiating between malignant and benign tumours is extremely difficult due to the lack of histological criteria. Malignant nature of a tumour is only certain in the case of metastases [1, 2].

Paragangliomas can be symptomatic due to the production of catecholamines. Eighty-three percent of the paragangliomas in the bladder are hormonally active [1]. Different clinical symptoms can occur, such as headaches, sweating, palpitations, hypertension and paleness. Besides, intermittent hypertension, with hypertension arising during micturition in 50% of cases, and haematuria (33%) can occur [1, 4].

On cystoscopy, these tumours appear as globular submucosal masses that bulge into the bladder, and the surface is intact and covered with mucosa rich in blood supply [1]. Although cystoscopy is the gold standard for the diagnosis of bladder tumours, it can be potentially dangerous in patients with symptomatic paragangliomas because of possible provocation of hypertensive crisis and arrhythmia [4].

The resection of a hormone-producing paraganglioma may lead to a sudden increase in blood pressure. Therefore, it is important to use additional diagnostics prior to resection, for example measuring catecholamines and vanillylmandelic acid in a 24-h urine sample and epinephrine in blood serum [1].

Taking biopsies of a lesion that is suspicious of a hormonally active paraganglioma is not recommended. It has a low positive predictive value. Moreover, it may cause bleeding, can trigger a hypertensive crisis and, therefore, increase the mortality rate [1]. If there is a suspicion of a non-hormonally active paraganglioma, cystoscopy and TUR-B can be performed, but antiadrenergic intervention is advised [4].

It is known that succinate dehydrogenase (SDH) germline mutations are associated with paragangliomas, including paragangliomas of the bladder. When a patient with a primary paraganglioma of the bladder is seen, one should be aware of this mutation especially when the paraganglioma occurs at younger age, there is a large tumour size and higher number of mitoses. The incidence of SDH mutation in paraganglioma of the bladders is reported to be 17%. These mutations can be hereditary. The risk of metastases is higher in patients with paraganglioma of the bladder and the mutation. Consequently, an intensified follow-up and surveillance should be considered when such SDHB mutations are found [5, 6].

The differential diagnosis of the abovementioned bladder lesion may include metastasis of a renal cell carcinoma, prostate carcinoma, urothelial cell carcinoma, rhabdomyosarcoma, haemangioma, leiomyoma, neurofibroma, granular cell tumours, malignant melanoma and cystitis. Current treatment

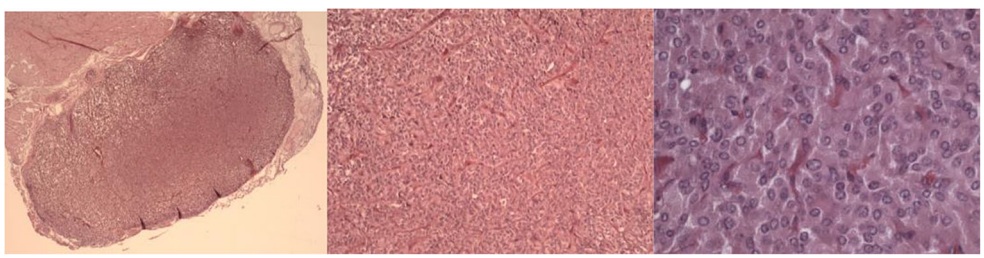

Fig. 2 Vague nodular proliferation of cells with large granular cytoplasm with enlarged nuclei, alveolated chromatin and prominent nucleolus (enlarged resp × 2.5, × 10, × 40)

of paragangliomas of the bladder consists of transurethral resection and partial or total cystectomy. After a TUR-B or partial cystectomy, there is a risk of local recurrence since the paragangliomas tend to grow transmurally [4, 7]. There are no guidelines for long-term monitoring of patients with a paraganglioma of the bladder. The lack of histological criteria for differentiating between benign and malignant paragangliomas affirms life-long monitoring by cystoscopy [1, 4, 7]. Although rare, special attention should be paid when a SDBH mutation is found since the risk of metastases is higher in this group. The follow-up should be intensified [5, 6]

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LA: analysis and wrote the manuscript
JvdL: supervision and conceptualization, supported manuscript writing
HR: supervision and conceptualization, supported manuscript writing

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Declarations

Ethical Approval Not applicable.

Consent to Participate Not applicable.

Consent for Publication Consent for publication was obtained.

Conflict of Interest The authors declare no competing interests.

References

1. Lai Y, Chen D, Yu Z, Ni L, Yang S. Non-functioning paraganglioma of the urinary bladder: a case report and review of the literature. Oncol Lett. 2014;7(3):891–3. https://doi.org/10.3892/ol.2014.1790.
2. Kouba E, Cheng L. Neuroendocrine tumors of the urinary bladder according to the 2016 World Health Organization Classification: molecular and clinical characteristics. Endocr Pathol. 2016;27(3):188–99. https://doi.org/10.1007/s12022-016-9444-5.
3. Elder EE, Elder G, Larsson C. Pheochromocytoma and functional paraganglioma syndrome: no longer the 10% tumor. J Surg Oncol. 2005;89(3):193–201. https://doi.org/10.1002/jso.20177.
4. Lu H, Male M, Jiang K, Ye Z, Song D, Xia D. Clinical significance of functional and anatomical classifications in paraganglioma of the urinary bladder. Urol Oncol. 2019;37(6):354.e9–e17. https://doi.org/10.1016/j.urolonc.2019.01.027.
5. Srirangalingam U, Banerjee A, Patki P, Peters J, George E, Chew SL, et al. Succinate dehydrogenase B (SDHB)-associated bladder paragangliomas. Clin Genitourin Cancer. 2017;15(1):e131–e6. https://doi.org/10.1016/j.clgc.2016.06.006.
6. Park S, Kang SY, Kwon GY, Kwon JE, Kim SK, Kim JY, et al. Clinicopathologic characteristics and mutational status of succinate dehydrogenase genes in paraganglioma of the urinary bladder: a multi-institutional Korean study. Arch Pathol Lab Med. 2017;141(5):671–7. https://doi.org/10.5858/arpa.2016-0403-OA.
7. Chang Y-K CI, Chen C-H, Wang S-M, Lee Y-J, Pu Y-S. Paragangliomas of the urinary bladder: a report of 6 cases and review of the literature. Urol Sci. 2015;26(2):111–4.