BLADDER PARAGANGLIOMA
A Case Report

INTRODUCTION
Paragangliomas or extra-adrenal pheochromocytomas arise from sympathetic paraganglias and account for less than 0.05% of bladder tumors. Patients present usually with hematuria and micturition attacks characterized by hypertension episodes during micturition with systemic symptoms of headache, blurred vision and palpitation due to elevated plasma catecholamines [1, 17]. We present a case of bladder paraganglioma that was treated with partial cystectomy.

CASE REPORT
A 32-year-old male patient presents with nine months history of dyspnea, headache, and palpitations directly following micturition. He does not report obstructive or irritative lower urinary tract symptoms. Medical history is positive for controlled dyslipidemia. Vital signs assessment shows a blood pressure of 130/80 mmHg with heart rate of 75 beats per minute (bpm). Physical exam is unremarkable. He has no history of dyspnea upon exertion or at rest. He also does not report orthopnea or paroxysmal nocturnal dyspnea. Family history is not indicative of any related condition.


RÉSUMÉ : Nous rapportons le cas d’un homme âgé de 32 ans présentant une dyspnée post mictionnelle. L’analyse des urines révèle une hématurie. Une échographie pelvienne et un CT scan abdomino-pelvien révèlent la présence d’un polype vésical gauche confirmé par une cystoscopie qui montre une masse sous-muqueuse pulsatile. Le dosage des métanéphrines plasmatiques libres confirme une élévation en faveur d’un paragangliome vésical. Par contre, le dosage des métanéphrines et des catécholamines urinaires montre une valeur normale. Une scintigraphie à la méta-iodobenzylguanidine (MIBG) est également normale. Le patient subit une cystectomie partielle avec disparition de ses symptômes. La pathologie montre une excision complète d’un paragangliome. L’évaluation, le diagnostic et le traitement seront discutés.

Patient is examined after voiding and is found to have an elevated blood pressure of 170/100 mmHg along with tachycardia (100 bpm). Urinalysis shows microscopic hematuria. Pelvic ultrasound reveals a left bladder wall polyp measuring 35 x 23 mm observed on cystoscopy to be a submucosal pulsating mass around 3 cm in size (Figure 1a).

Computerized tomography of the chest, abdomen and pelvis confirms the presence of a 3 cm well circumscribed homogeneously enhancing soft tissue tumor arising from the left lateral wall with a convex outer border possibly involving the muscularis layer but with preservation of the...
perivesical fat and with no lymphadenopathies or distant metastatic disease (Figure 1b).

Biochemical assessment reveals elevated plasma free normetanephrine (1.90 nmol/l; N : < 0.93), 348 ng/l (N < 170). However this value was not obtained directly post micturition. 24 h urine catecholamines and metanephrines were within normal limits.

Iode 131-MIBG (methyl-iodobenzylguanidine) scintigraphy shows normal signal with no focal accentuation relative to the urinary content. Patient’s clinical symptoms along with the presence of a bladder polyp and elevated plasma metanephrines suggest the presence of secreting bladder paraganglioma thus partial cystectomy is planned. Patient is prepared for surgical intervention by being put on an α-adrenergic blocker (doxasocin 1 mg, 2 tabs twice daily) along with vigorous intravenous (IV) hydration before surgery. Intra-operatively, care is taken to prevent hypertensive crisis and intravenous nitroglycerin is prepared. Partial cystectomy is performed under spinal anesthesia with meticulous technique and care is taken not to manipulate the mass and to leave an excision margin of around 0.5-1 cm. There is no recorded intra-operative increase in blood pressure or heart rate and surgery is uneventful. Besides severe bladder spasms, the patient has a smooth postoperative recovery. Macroscopic description of the specimen shows an encapsulated, well demarcated, beige brown soft nodule. Microscopically, completely excised paraganglioma is identified with a minor ganglioneuroma component. Immunostain shows strong positivity for synaptophysin and chromogranin in favor of a paraganglioma. On follow-up patient reports disappearance of his presenting symptoms.

DISCUSSION

Paragangliomas, or extra-adrenal pheochromocytomas, are tumors that arise from sympathetic paraganglia in rare locations such as the thorax, bladder, or brain. Primary paraganglioma of the bladder, arising from the submucosal paraganglionic cells, makes up less than 0.05% of all bladder neoplasms and less than 1% of all pheochromocytomas with 13 to 15% being malignant recognized by their clinical behavior with their capacity to metastasize [1-3].

They occur in people of all races but less frequently in African-Americans. Incidence peaks in the 3rd to 4th decade with slight female predilection [3-4].

In children, the rate of malignancy is lower accounting for up to 2% of cases [4].

The usual location of these tumors is at the dome of the bladder or near the trigone. Half of the patients present with hematuria [3]. Similar to adrenal pheochromocytoma, they secrete catecholamines resulting into paroxysms of hypertension, headache or syncope upon bladder filling or micturition in two-thirds of patients. The symptoms are mostly pronounced during urination resulting into micturition attacks especially if straining is needed during bladder voiding [5]. Deep palpation over the pelvic area or bimanual exam may reproduce the above mentioned symptoms [6].

These tumors can be sporadic or familial, inherited as part of multiple endocrine neoplasia type 2A or type 2B, neurofibromatosis type 1 and von Hippel-Lindau disease [7].

Imaging studies are necessary in determining tumor locations and to rule out any presence of multifocal lesions or metastases. On ultrasound, bladder pheochromocytomas appear as a well demarcated mass in the bladder wall. If purely solid, they appear homogenous; however, they may contain foci of hemorrhage and necrosis thus giving them a cystic appearance. CT scan with IV contrast has a higher sensitivity, 94% in adrenal and 82% in extra-adrenal pheochromocytomas, in delineating the relationship between the mass and the bladder mucosa, muscularis and perivesical tissue [3, 8]. MRI is more sensitive than both ultrasound and CT scan. Those lesions,
being highly vascular and containing high intracellular water, display high signal intensity on T2-weighted images [9]. MIBG imaging is very accurate for localizing pheochromocytomas with a specificity approaching 100%. The high similarities in molecular structures of MIBG to noradrenaline allow it to be taken up by pheochromocytoma tissue [10]. However, MIBG is negative in 15% of cases of benign pheochromocytoma and in up to 50% of malignant cases [11]. Therefore patients who are suspected to have a pheochromocytoma but have a negative MIBG scan should be subjected to PET scan (18F-dopamine positron emission tomography) for confirmation and to rule out malignancy or metastasis but this is currently not available locally [12].

Biochemical diagnosis of pheochromocytoma includes assessment of plasma free metanephrines which has a sensitivity of 99% and 24 hours urine fractionated metanephrines. Our results confirmed elevated plasma metanephrines but these should have been obtained following micturition or upon micturition attacks.

Other tests include plasma catecholamines and 24-hour urinary catecholamines, total metanephrines and vanillylmandelic acid but these have lower specificity [13]. In our case, urine catecholamines were within normal limits and this can occur in urine paraganglioma especially if urine sample was not taken immediately following micturition [14-15].

Cystoscopy shows typically a submucosal nodule covered by normal urothelium. It provides more qualitative data about the tumor and its location especially if surgery is being planned. Blood pressure fluctuations may occur during cystoscopy, therefore care must be taken not to extensively irrigate the mass under high pressure during the procedure. Biopsies are not encouraged during cystoscopy due to their low positive yield, high bleeding tendencies and risk of hypertensive crisis [2, 6].

Treatment of choice is partial cystectomy with complete excision of the lesion. Transurethral resection is contraindicated mainly because of the high risk of precipitating a hypertensive crisis and the elevated recurrence rate in case of incomplete resection [6]. Care must be taken to ensure adequate pre-operative preparations in order to make the surgery safer [16]. Chemotherapy and radiotherapy have limited effectiveness in the treatment of local recurrence and metastatic disease [3].

CONCLUSION

Paragangliomas of the urinary bladder are rare. Patients might present with typical signs and symptoms but diagnosis is sometimes achieved only after excision and histological examination of the tumor. It is recommended to do a clinical and biological assessment, plasma metanephrines being the biochemical test of choice due to its high sensitivity. Plasma metanephrines have to be measured after a micturition attack or ideally before and after micturition.

REFERENCES