Urinary Bladder Paraganglioma—A Case Series with Proposed Treating Algorithm Based on Our Experience and Review of Literature

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Introduction

Pheochromocytomas are catecholamine secreting tumors of chromaffin cells. The extra adrenal pheochromocytomas are known as paragangliomas. Paragangliomas of the urinary bladder account for less than 0.06 % of all bladder tumors [1]. It commonly presents between second to fourth decades of life. Most surgeons and anesthesiologists are unfamiliar with paraganglioma of the urinary bladder. Unsuspected paraganglioma greatly increases perioperative morbidity and mortality in patients undergoing even relatively minor surgical procedures.

Material and Methods

Our Experience

We encountered three cases of urinary bladder paraganglioma. All presented with hematuria. None of these had known characteristic symptom of bladder paraganglioma i.e. sharp headache, hypertension, palpitation, sweating, fainting and blurring of vision immediately after voiding and in only one of them, the markers were raised. We found that cystoscopic findings may give an important clue as all three were having similar characteristic

cystoscopic appearance (broad based, solid, submucosal tumor with bluish hue) (Fig. 1). In the first case—a 38 years man, we went for cystoscopic biopsy which resulted in sharp rise in blood pressure and severe chest pain which settled down in short time. The biopsy report came out to be paraganglioma. This experience restrained us from conducting biopsy in the next case who was a 46 years old male having similar cystoscopic finding. The third, a 30 years man also didn't have any characteristic symptom. After cystoscopy, we went for serum and urinary markers which were raised.

MIBG scan was done in all cases which showed increased uptake in urinary bladder. CT scan was done which ruled out any extra vesical extension in all cases (Fig. 2). Each one was managed by partial cystectomy. The size of the tumour was 2.5 cm, 2 cm and 1.5 cm in diameter respectively.

Review of Literature

We searched the database of pub med and biomed central using keywords—urinary bladder paraganglioma or pheochromocytoma in order to go through the available literature on such cases. We found about 200 case reports of urinary bladder paraganglioma. But there are no definite guidelines regarding diagnosis and treatment of such cases.

Results

Partial cystectomy was done under general anaesthesia with proper preparation. We gave alpha blocker (phenoxybenzamine) to all our patients preoperatively. The surgery and follow up was uneventful. The histopathology report was paraganglioma in all three cases (Fig 3 a, b).

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Fig 1 Cystoscopic view showing broad based, solid, submucosal tumour with bluish hue

In review of literature, most of the cases were diagnosed either on the basis of characteristic symptoms or raised markers. Mostly, they were managed by open partial cystectomy. Though there are case reports of transurethral resection [2], laparoscopic excision of bladder paraganglioma [3] and robotic assisted laparoscopic partial cystectomy [4].

Discussion

Urinary bladder paragangliomas are extremely rare and high index of suspicion is needed to correctly diagnose these cases. The characteristic symptoms of these tumors are present only in about 50 % of cases [5]. These are due to increased catecholamine release in association with bladder contraction during micturition. However, approximately half of the patients, but as in all of our cases, lack these typical symptoms, a reason responsible for a large number

of such cases being incidentally discovered. Thus the clinician must be aware of the adrenosympathetic syndrome of headache, hypertension or blurring of vision with detrusor activity. Gross or microscopic hematuria may be present in about 50–65 % cases [6]. On cystoscopy, the characteristic findings are presence of a broad based, solid, submucosal tumor with bluish hue due to increased vascularity, usually supratrigonal in location. The cystoscopic findings may provide an important clue towards the diagnosis especially when the markers are not raised. The 24 hours urinary metanephrines and VMA are positive in about 88 % and 71 % cases respectively whereas serum catecholamines are positive in about 88 % cases [7]. On ultra sonogram, a solid mass with mixed echogenicity is present in the supratrigonal area and near dome in 40 % cases [5]. CT scan shows a solid lesion with intense contrast enhancement. It is more relevant for staging and to rule out pelvic lymphadenopathy. On MRI, a homogeneous T1 hyperintensity is present [8]. It shows presence of necrosis and lower apparent diffusion coefficient. It may prove to be better than CT in localizing tumor and differentiating it from surroundings. I ¹²³ labeled MIBG scan is more specific than CT/MRI and especially valuable in detecting extra adrenal cases, several locations and skeletal metastasis. Use of other modalities such as mass spectroscopy, PET scan using various nucleotides such as FDG or Ga 68–DOTANOC (whereas the latter is considered to be more accurate) and combination of PET and CT may be helpful when MIBG is negative but is not routinely recommended.

Intravascular volume is contracted from the chronic sustained effect of the elevated catecholamine levels and should be re-expanded prior to removal of the neoplasm; otherwise, profound postoperative hypotension may result. Blood pressure is first controlled with α -blockade using phenoxybenzamine. β -Blockade may be added to counteract the rebound tachycardia of the former. Certain patients may require calcium channel blockers such as nifedipine to maintain adequate control. Intraoperative intravenous infusions of phentolamine and nitroprusside are kept ready for use in the case of a hypertensive crisis. Strict control of blood pressure is mandatory prior to and during any surgery to prevent the potentially fatal hypertensive crisis.

Surgery provides the best chance of cure for the patient. Although transurethral resection has been reported, such resection rarely excises all tumor deposits as the tumor is intramural in location and sympathetic nerves run through the entire thickness of the bladder wall. Partial cystectomy is the most common procedure performed for this condition [3, 9]. For advanced disease (extravesical extension or pelvic lymphadenopathy), radical cystectomy with pelvic lymph nodal dissection has been advocated. There have been reports of laparoscopic excision of urinary bladder pheochromocytoma [3]. Since histology cannot differentiate between benign and

Fig 2 CT scan abdomen showing intense lesion with contrast enhancement

Fig. 3 **a** Histological section showing sheets of polygonal to oval cells with moderate amount of cytoplasm and central to eccentric nuclei (Haematoxylin & Eosin $\times 400$)
b Histological section from paraganglioma showing diffuse chromogranin positivity in tumour cells (Immunohistochemistry $\times 400$)

malignant pheochromocytoma, follow-up assumes prime importance. Sequential monitoring of blood pressure, urinary catecholamine studies and clinical observation of the persistence or recurrence of headaches may alert the clinician to the possibility of recurrent pheochromocytoma. These studies should be repeated on an annual basis with others recommending the addition of annual MIBG scanning [10]. Options for treating metastatic disease are limited. External beam irradiation, radiofrequency ablation of lesions, combination chemotherapy with cyclophosphamide, vincristine and dacarbazine are treatment alternatives. I^{131}

labelled MIBG therapy is the most important adjunct to surgical treatment.

A treating algorithm can be proposed based on the above mentioned experience and review of literature. Patients of urinary bladder pheochromocytoma can be divided in two groups:

- A. Those who present with characteristic symptoms (sharp headache, hypertension, palpitation, sweating, fainting & blurring of vision immediately after voiding)
- B. Those who present without characteristic symptoms (who present with hematuria)

- A. Treating algorithm for patients of urinary bladder paraganglioma presenting with characteristic symptoms

B. Treating algorithm for patients of urinary bladder paraganglioma presenting without characteristic symptoms

Conclusion

Only half of patients of urinary bladder paraganglioma present with characteristic symptoms and hence the serum and urinary markers carry much importance. But one may come across a case when these are also negative. The characteristic cystoscopic findings may give an important clue when the clinical presentation and markers provide no help. MIBG scan, if feasible, should be done in all cases to establish diagnosis and for localization. As far as possible, cystoscopic biopsy should be avoided and when necessary (when MIBG is negative or not feasible), should be done with proper preparation. Staging of the tumor can be done by either CT or MRI. The aforesaid algorithm may be used for better evaluation. Partial cystectomy is the treatment of choice in most of the cases. As it is difficult to identify malignancy on histopathology, follow up carries prime importance.

References

1. Leestma JE, Price EB Jr (1971) Paraganglionoma of the urinary bladder. *Cancer* 23:1063
2. Persec Z, Buković D, Persec J et al (2012) Paraganglioma of the urinary bladder—clinicopathological, immunohistochemical and electron microscopy analysis—a case report. *Coll Antropol* 36(3):1041–3, 11
3. Kozłowski PM, Mihm FG, Winfield HM (2001) Laparoscopic management of bladder pheochromocytoma. *Urology* 57:365v–vii
4. Kang SG, Kang SH, Choi H et al (2011) Robot-assisted partial cystectomy of a bladder pheochromocytoma. *Urol Int* 87(2):241–4. doi:10.1159/000324269. Epub 2011 May 19
5. Das S, Bulusu NV, Lowe P (1983) Primary vesical pheochromocytoma. *Urology* 21:20–5
6. Attyaoui F, Nouria Y (2000) Le pheochromocytome vesical. *Prog Urol* 10:95–98
7. Goldfarb DA, Novick AC, Bravo EL, Straffon RA, Montie JE, Kay R (1989) Experience with extra-adrenal pheochromocytoma. *J Urol* 142:931–936
8. Haiyi W, Huiyi Y, Zhiwei F et al (2010) Bladder paraganglioma in adults: MR appearance in four patients. *Eur J Radiol* 10:4972–4976
9. Thrasher JB, Humphrey PA, Rajan RR et al (1993) Pheochromocytoma of urinary bladder: contemporary methods of diagnosis and treatment options. *Urology* 41:435–9
10. Lindsey CM, DeHart HS, Glenn JF (1976) Pheochromocytoma of the urinary bladder. *Urology* 7:210–11