Paraganglioma of the Bladder – A case report and review

I McKenzie

Citation

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Abstract

Paraganglioma of the urinary bladder is a rare tumour. Failure to diagnose pre-operatively can have serious intra-operative consequences. We present a case of bladder paraganglioma and review of literature regarding frequency of typical symptoms.

INTRODUCTION

Phaeochromocytoma is a tumour of chromaffin cells derived from the embryonic neural crest[1]. Whilst usually derived from the adrenal medulla, approximately 10% of these tumours occur at extra-adrenal sites[2]. Extra-adrenal phaeochromocytomas are known as paragangliomas. The majority of extra-adrenal tumours occur intra-abdominally (85% occur below the diaphragm[3]) along the sympathetic chain or from the organ of Zuckerkandl.

Primary paraganglioma of the urinary bladder is rare making up less than 0.05% of all bladder neoplasms[4]. It has been postulated that bladder paragangliomas arise from embryonic rests of chromaffin cells within the bladder wall. They are most commonly situated at the dome or the trigone of the bladder[25].

The position of these tumours within the bladder cause a characteristic symptom complex most commonly related to micturition or over-distension of the bladder causing catecholamine release. The most common symptoms are paroxysmal hypertension, headache, sweating and palpitations[6]. The other symptom commonly reported is haematuria (55-60% cases[7]) though this is not specific for paraganglioma. Pre-operative diagnosis is usually suspected on the grounds of the typical clinical symptoms and signs above and further confirmed by measurement of biogenic amines in both urine and plasma[8].

Here we present a case of bladder paraganglioma without typical symptoms.

CASE REPORT

A 55 year old man presented initially with a history of frank haematuria. He had no other symptoms or past medical history of note. Routine blood tests and physical examination were unremarkable. Cystoscopy revealed a smooth, well vascularised, submucosal mass on the dome of the bladder without signs of surface ulceration. On attempted trans-urethral resection, the patient became severely hypertensive with systolic blood pressure rising to 260mmHg. This episode was controlled with intraoperative intravenous antihypertensives. After biopsies of the lesion were obtained, the procedure was abandoned.

Histological examination of the biopsy specimen showed neuroendocrine cells with some typical ‘Zellballen’ appearance. There was no evidence of stromal invasion. These features were consistent with paraganglioma. Staining was strongly positive for synaptophysin and chromogranin. S-100 staining was non-contributory.

A more focussed post-operative history revealed no symptoms suggestive of the presence of paraganglioma. In particular, neither hypertension nor micturition syncope were present. Interestingly the patient did complain of headaches in the years prior to presentation however these occurred infrequently and appeared to bear no relation to micturition or bladder distension.

The immediate post-operative course was complicated by a persistent, severe headache. This settled over the subsequent 2 weeks.

More detailed investigations were performed post-operatively including plasma and urinary biogenic amines. These investigations were all normal. CT-scans revealed no evidence of distant metastases. 131-I MIBG scans were performed and revealed no deposits of secreting tissue other than the bladder mass.

Surgical removal was via partial cystectomy. Pre-operative preparation was via -adrenergic blockade in the form of Phenoxybenzamine at 10mg BD. Adequate pre-operative -blockade was made difficult by the patient's pre-treatment normotension resulting in significant symptomatic orthostatic hypotension with minimal doses.

After 5 weeks of -adrenergic blockade and 1 week of -adrenergic blockade, a partial cystectomy was performed without complication. Histopathology of the operative specimen confirmed the original diagnosis and showed clear surgical margins with no evidence of lymphovascular invasion. The patient made a full recovery and is due for repeat cystoscopy in 3 months to assess progress. All pre-operative anti-hypertensives were ceased during the immediate post-operative period without complication.

DISCUSSION

Paraganglioma of the bladder is a rare condition. Approximately 10% of bladder paragangliomas are malignant with one or more of local invasion, regional lymph node metastasis or distant spread[4]. One of the difficulties with phaeochromocytoma is in diagnosing malignancy. Histologically there are no definitive characteristics which reliably distinguish benign from malignant tumours[9]. A review of studies looking at other factors (including biochemical and genetic markers) for determination of malignancy by Pattarino et al (1996) came to the conclusion that metastatic dissemination is the only real proof of malignancy[10].

Both CT scanning and MRI are useful in the localisation of both the primary tumour and any metastases however scanning with ^{131}Iodine metaiodinebenzylguinidine (MIBG) has been shown to have a very high sensitivity and specificity for phaeochromocytoma detection[4].

Given the relatively low incidence of malignant bladder paragangliomas, complete surgical resection of the tumour can be curative in many cases[9]. The procedure of choice is complete or partial cystectomy if tumour position within the bladder allows. Pre-operatively the patient requires -adrenergic blockade (usually with phenoxybenzamine or prazosin) and volume expansion. These measures have been shown to significantly reduce peri-operative mortality and morbidity[1]. Life-long clinical and biological follow-up of patients is essential as dissemination or local recurrence of malignant paragangliomas can occur very late in the clinical course following removal of the tumour[4,10]. Radiotherapy and chemotherapy have shown limited effectiveness in the treatment of locally recurrent and metastatic paraganglioma [4,9].

The interesting feature of the case presented above is that the patient reported none of the micturition-induced symptoms of catecholamine release typical of primary paraganglioma of the bladder. In this case it led to an unexpected intra-operative hypertensive crisis that could have had far more serious outcomes. It has been quoted that 83% of bladder tumours of this type are hormonally active[2]. Given this high figure, we decided to look into how many of the reported cases available actually described symptoms which would suggest the presence of vesical paraganglioma pre-operatively. If these tumours are suspected the patient can be appropriately prepared pre-operatively with adequate -blockade and volume expansion to assist in preventing hypertensive crises and their resulting haemodynamic consequences.

A literature review of available case reports of primary bladder paraganglioma was performed looking for the incidence of these tumours in the absence of the typical symptoms described above. 50 Case Reports were reviewed which included a total of 80 cases of bladder paraganglioma. Of these 80 cases, 51 patients (63.75%) had reported at least 1 of the typical symptoms or signs (not including haematuria).

Of the 51 patients reporting typical symptoms, it was interesting to note that a significant proportion had their symptoms revealed retrospectively after a tissue diagnosis had already been made. Given the rare nature of this type of bladder tumour, most clinicians would not specifically seek the symptoms of micturition-related catecholamine release in initial history taking of a patient presenting with a likely bladder tumour. As shown above however, over one third of primary bladder paragangliomas actually produce no symptoms or signs considered typical for this type of tumour. As a result, even if these symptoms were sought more often by clinicians, it is likely that a pre-operative provisional diagnosis of primary bladder paraganglioma would still not be possible.

In the case presented above, catecholamine release and hypertensive crisis was only provoked by tumour manipulation intra-operatively. Given that this patient fitted into the 36% of patients without typical symptoms, a pre-operative diagnosis was not made. This is problematic in that no pre-operative preparation with anti-hypertensive

cover can be made to prevent the potentially significant consequences of intra-operative hypertensive crises. Clues to early diagnosis may perhaps include a characteristic cystoscopic appearance though this has not been specifically investigated in the literature to date. Due to the low prevalence of these tumours this is something that will likely rely on further assessment of case reports in the future to establish.

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Author Information

Ian McKenzie, MBBS (Hons)
Registrar Surgery, Department of Urology, Royal Brisbane Hospital