

Lesson of the Month

Urinary Bladder Pheochromocytoma: A Good Lesson

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Abstract

We report a case of urinary bladder pheochromocytoma in a normotensive 45-year-old female with lower urinary tract symptoms who presented with headache and palpitations after voiding. A bladder tumor was found on radiological imaging and cystoscopy. A pheochromocytoma was suspected by clinical presentation and cystoscopy and confirmed by histopathology examination following the removal of the mass. The clinical symptoms, diagnosis, and treatment of bladder pheochromocytomas are reviewed.

Keywords: urinary bladder, bladder neoplasm, pathology, pheochromocytoma, diagnosis, therapeutics, surgery

Introduction

Pheochromocytoma is a neoplasm, which develops from cells of the chromaffin tissues that are derived from the ectodermic neural system and mostly situated within the adrenal medulla. Only approximate 15%

of pheochromocytoma develops from extra-adrenal chromaffin tissue (also known as paragangliomas), in which pheochromocytoma of the bladder is rare and accounts for less than 0.06% of all bladder neoplasms and less than 1% of all pheochromocytoma (1).

Pheochromocytoma of the urinary bladder is a rare but well known clinical entity.

We are presenting a new case, discussing its mode of presentation, clinical manifestations, diagnosis, and treatment along with a brief review of the literature.

Case Report:

A 45-year-old female, normotensive patient with unremarkable past history presented with pollakuria and urgency. Detailed evaluation revealed excessive sweating with headache and palpitations during and after defecation and micturition. She was asymptomatic in between these episodes.

On clinical examination; she was asymptomatic with a



Figure 1. Intravenous urography: normal upper urinary tracts with a unique bladder filling defect.



Figure 2. Bladder ultrasonography: hypoechoic tumor arising from the posterior wall of the urinary bladder measuring 15 mm

regular pulse 86 beats per minute and blood pressure of 120/80 mm/ Hg. There was no abdominal mass or bruit. The urinary bladder was not palpable.

A provisional clinical diagnosis of pheochromocytoma or reno-vascular hypertension was made. Vanillylmandelic

acid (VMA) levels (collected on three consecutive days) were within normal limits (the only test available in our institution at that time) as well as renal chemistry.

An intravenous urography (IVU) showed normal upper urinary tracts with a unique filling defect of the bladder

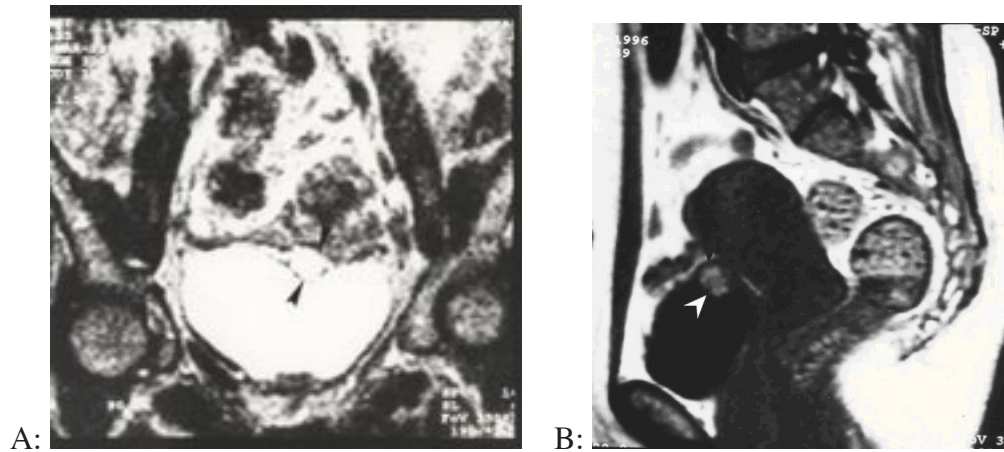


Fig. 3: MRI: A. MRI T1. Well-circumscribed isointense mass at the bladder dome B. MRI T2. Enhancement of the mass.

suggestive of bladder tumor (**Fig. 1**).

Ultrasonography showed a mass in the posterior wall of the urinary bladder measuring 15 mm (**Fig. 2**). MRI showed a round mass covered by intact urothelium with smooth capsules (**Fig. 3**). The adrenal glands were normal.

Cystoscopic examination showed a submucosal hypervascular solid mass in the dome of the bladder measuring 1.5 x 2 cm, with ill-defined margins, continuous mucosa, and smooth surface. This tumor was far from ureteral orifices.

During cystoscopy, the patient's blood pressure rose to 200 mm/Hg. She reported headache and palpitations. A decision for open laparotomy was made. The bladder was approached through a midline infra-umbilical incision. A firm mass 1.5 x 2 cm was felt towards the dome of the bladder. The bladder was opened and the mass excised along with a 1.5 cm margin. She underwent a partial cystectomy. During these manipulations of the tumour, the patient's BP rose to 200-220 mm/Hg systolic which then dropped to 80 mm/Hg after excision of tumour. This led us to clinically suspect this tumour to be pheochromocytoma.

We did not perform a frozen section of the specimen. The formal histopathology study showed positive dichromatic reaction, large polygonal and spindle cells arranged in sheets and packets separated by a thin vascular stroma. The cells showed vesicular nuclear, abundant cytoplasm and scanty mitoses. The final histopathology concluded pheochromocytoma. The post-operative period was uneventful and the Foley catheter was removed two

weeks post-operatively. At five years, the patient remains asymptomatic and normotensive.

Discussion:

Zimmerman published the first case of pheochromocytoma of urinary bladder in 1953 (2). Fewer than 200 cases have been reported to date (3). Urinary bladder pheochromocytoma is similar to adrenal pheochromocytoma, most of which can secrete catecholamines. Although urinary bladder pheochromocytoma is now considered to be a well recognized entity, the presenting features are still regarded as clinically challenging and unusual. Though the exact etiology is not understood, it is accepted that pheochromocytoma arises from the chromaffin tissues (paraganglia) of the sympathetic nervous system within all the layers of the bladder wall (4, 5).

A bladder pheochromocytoma is a rare tumor accounting for less than 1% of all pheochromocytomas (1). It accounts for about 0.06% of all bladder tumors (1). The tumor has an equal distribution among males and females. It is most commonly diagnosed in the 4th and 5th decades of life (6). We usually associate symptoms of the pheochromocytoma and bladder tumors, which are continuous or paroxysmal, and are often associated with urination, as in our case, and hematuria (7). In recent years, misdiagnosis has decreased apparently, although asymptomatic bladder pheochromocytoma is almost impossible to diagnose pre-operatively. Main symptoms include: Main symptoms include tachycardia, pallor, headache, sweating, and

hypertension during the filling of bladder and are most prominent after urination (4). The hypertensive crises result from excessive catecholamine secretion usually accompanying voiding (8) due to increased catecholamine release in association with bladder contraction during micturition. Pressing on the abdomen or bi-manual examination may induce similar symptoms on occasion. Hematuria is described as a common presenting symptom in about 50% of all cases over the age of 50 (7). The patient may have difficulty urinating when the tumor is in trigone, and if the patient urinates with straining. Even one complete episode of acute urinary retention was reported (3).

In our case, the patient was totally asymptomatic even during bimanual examination of the bladder. Catecholamine and vanillylmandelic acid levels in the urine, or catecholamine levels in the plasma, help with a diagnosis of a symptomatic pheochromocytoma. However, the biochemical profile can only confirm the presence of a pheochromocytoma, it cannot locate the tumor. Measurements of 24-hour urine excretion of catecholamines and their metabolites are available in its qualitative screening (1). These measurements were normal in our case.

Only 17% of bladder pheochromocytomas are hormonally nonfunctional (9). Preoperative location and qualitative analysis are very important in confirming the diagnosis. Intravenous urography can show bladder filling defects, but it is nonspecific. Ultrasound, CT, and cystoscopy are utilized to locate the tumors. On ultrasonography, the tumors appear as a submucosal homogeneous solid mass, having clear outline, continuous mucosa, and may contain foci of hemorrhaging and necrosis (10). Computed tomography (CT) can detect bladder tumors, show the relationship between the mass and the bladder mucosa, muscular, and peri-tissue (10) but its sensitivity is only 82%. Magnetic resonance imaging (MRI) is superior to CT scans in locating tumors and in differentiating the tumor from the surrounding structures. Pheochromocytomas have a typical bright appearance on T2-weighted MRI images. However, cystoscopy is more important in locating and macroscopic diagnosis (11).

These tumors are frequently located near the trigone or in the dome (3). The tumors in cystoscopy appear as a globular submucosal mass protruding into the bladder, with a smooth surface, continuous mucosa, and abundant blood supply. In our case, the patient had symptoms during cystoscopy, so when one suspects pheochromocytoma of bladder, one should control the speed of water flush and turn the sheath slowly to reduce irrigation in order to prevent the blood pressure from fluctuating greatly. We take negative attitude on cystoscopy biopsy, because its positive

rate is very low, bleeds easily, and induces blood pressure to fluctuate. Moreover, catecholamine release may have been facilitated when the bladder was distended or when the tumor was excised (12). Methyliodobenzylguanidine (MIBG) scintigraphy has been used to diagnose pheochromocytoma extensively, especially in the extra-adrenal pheochromocytoma. It is accurate for localizing pheochromocytoma. It has a specificity of close to 100% (13) and sensitivity between 85- 100% (14, 15).

Pre-operative confirmed diagnosis and adequate preparation are very important to make the surgery safe (16), especially in cases where blood pressure fluctuates during urination. In order to prevent dramatic intraoperative changes in blood pressure, patients should receive oral α -adrenergic blockers such as phenoxybenzamine for one to two weeks pre-operatively (3), if blood pressure cannot be controlled, Alpha-methyl tyrosine can be added to inhibit the release of catecholamine. When cases present with tachycardia, β -blockade (propranolol) can be added after adequate alpha blockade. Avoiding intraoperative manipulation of the bladder can reduce the risk of hypertensive crisis, which can be controlled with phentolamine or sodium nitroprusside. After removing the tumor, hypotension is common and should be controlled by intravascular volume expansion and pressors (3).

Treatment strategies for these tumours are not well-defined because of their rare incidence. A variety of operative procedures were performed for pheochromocytoma of the bladder like transurethral resection, total cystectomy, partial cystectomy (5) and even laparoscopic partial cystectomy (8). The majority of bladder pheochromocytomas (94%) involve the muscularis propria of the bladder wall. Some experts claim that treatment with transurethral resection is insufficient, and a cystectomy remains the treatment of choice. There are three reasons for this:

1. Transurethral resection (TUR) can irrigate the tumors that are causing the blood pressure to fluctuate, which increase the risks, and is very difficult to control the depth and extent of manipulation.
2. Pheochromocytoma easily recurs if not resected completely. There are clear borders between the normal bladder organism and most of the pheochromocytoma, but the muscular tissues closest to the tumor are often destroyed, so unless the tumor can be resected completely, it will easily recur.
3. The proportion of malignant extra-adrenal pheochromocytoma is > 30% that of adrenal pheochromocytoma, so we should resect the tumor and its peri-tissue completely.

In our case, the tumor was benign; none recurred in our follow-up. Bilateral pelvic lymph node dissection to exclude metastatic disease was suggested by Das, et al., but it remains controversial (9). The histopathological diagnosis may be quite difficult at times. The histological presence of tumour cells in muscle layers indicates the site of origin of the pheochromocytoma and not malignancy (7). The only positive way to diagnose malignant pheochromocytoma is detection of distant metastases. From our literature review, the long-term outcome for each procedure, especially the recurrence rate, has not been well documented. This is perhaps due to its rarity and lack of long-term follow-up of prior cases. It has however been reported that the prognosis is dependent on whether there is evidence of familial endocrinopathy, or the presence of metastases (17). Since histological features are usually unable to confirm malignancy, life-long follow-up is recommended for these patients with yearly endocrine evaluations, I-MIBG scintigraphy, and MR imaging to detect recurrences or metastases (1, 10, 14). In addition, these patients should also be monitored for post-operative complications such as stricture or obstruction at urethral reimplantation site, as hydronephrosis may result.

To date, no specialized protocol has been proposed for asymptomatic bladder pheochromocytomas. We therefore arranged close clinical follow-up with cystoscopy every six months for this case. Local recurrence and metastasis have been reported more than 20 years after initial surgery; and therefore, lifelong follow-up is recommended.

Conclusion:

It is very important to suspect the possibility of pheochromocytoma in cases of bladder tumour associated with hypertension in order to reduce complications and mismanagement. It is usually benign but long term follow-up is mandatory. Urinary bladder pheochromocytoma is a rare tumour of the bladder, which warrants full investigation before embarking on any surgical procedure.

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