PHEOCHROMOCYTOMA OF URINARY BLADDER:
REPORT OF A CASE AND BRIEF REVIEW OF THE
LITERATURE

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ABSTRACT

A case of pheochromocytoma of the bladder is presented with a review of the
literature. We discuss general management principles of bladder pheochromocytoma.
Successful diagnosis and treatment of this lesion requires a high index of suspicion
based upon the patient's symptom complex, allowing preoperative preparation prior
to surgical treatment.


INTRODUCTION

Pheochromocytomas are chromaffin cell tumors that are derived from neuroectodermal tissue of the adrenal
gland and sympathetic paraganglia. These tumors can arise anywhere in the body from the skull (glomus and carotid
bodies) to the bladder and prostatic glands. Pheochromocytomas of the urinary bladder are rare tumors,
accounting for approximately 1% of extraadrenal pheochromocytomas and 0.06% of bladder tumors.

We report a case of vesical pheochromocytoma in a patient with a twelve year history of post-micturitional
palpitation and anxiety and other related symptoms such as blurred vision, headache and occasional dysuria which was
mismanged for a long time before correct diagnosis.

The symptom complex, radiographic diagnosis and subsequent treatment of this entity are reviewed.

Case report

A 25 year old male was admitted to our department because of anxiety and palpitations associated with micturition. He had a twelve year history of post-micturitional throbs in the chest. At the time after each voiding he developed headache, diaphoresis, flushing, light-headedness, chest pain and palpitations. These symptoms occurred as paroxysms with a few minutes' duration. He experienced these attacks sometimes after defecation and on some occasions, spontaneously. In this regard he sought medical attention frequently and had taken different medications for controlling headache and chest discomfort but the symptoms were not improved. There was also a history of periodic presence of dysuria, frequency and dribbling. He said the severity of each attack was distinct from others. The above problems continued until 2-3 years ago, when he noticed a slight decrease in intensity of symptoms. In the few previous months, anxiety, blurring of vision, and postural dizziness and fainting after micturition (or with no precipitating cause) had been the chief complaints.

The past medical history was negative other than redness of the eyes and conjunctival congestion during the past 10 years. He had never had high blood pressure, and he smoked five cigarettes per day over a period of seven years. In his close relatives, family history was negative and his wife and child are both healthy.

His blood pressure was 150/90 mmHg and pulse rate
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was 72 bpm at rest. After micturition it increased to 180/110 mmHg and heart rate dropped to 64 bpm (Fig. 1). In the head and neck the only positive finding was conjunctival congestion. Examination of the heart and chest was unremarkable. The abdomen was normal without any palpable mass. After deep palpation of the abdomen the blood pressure was not changed. Digital rectal examination was negative. Laboratory data revealed normal urinalysis, blood counts and chemical values. Routine X-ray showed normal findings. Sonography of the abdomen and pelvis was unrevealing. Successive 24-hour urine collections showed vanillylmandelic acid values of 14.5 mg per day and 15 mg per day. (normal: 0.5-12 mg/day). Electrocardiography at rest was normal but after voiding the normal sinus rhythm changed to junctional rhythm, T waves became negative in leads V2-V4, and the heart rate decreased to 40-50 bpm. The arrhythmia disappeared without any intervention in a few minutes.

For further evaluation intravenous pyelography was done. The radiologist reported that the left wall of the bladder had a filling defect (Figs. 2,3). Computerized tomography was performed with contrast agent which indicated the presence of a pelvic mass adjoining to the bladder wall (Fig. 4).

Regardless of the classic clinical findings and revealing laboratory and imaging techniques, with the probable diagnosis of vesical pheochromocytoma, the patient was placed on phenoxybenzamine for 10 days and then propranolol was added. He was prepared for operation with prophylactic antibiotics, hydration, large bowel enema and reservation of blood. Ten minutes after the induction of anesthesia, he had a hypertensive crisis which was managed with a change in dosage of halogenated anesthetics and nitroprusside. Abdominal and pelvic exploration via midline incision showed a mass completely attached to and infiltrating the bladder wall. Partial cystectomy was performed. A smaller tumor was found in the draining lymphatic system of the bladder. Both masses were excised
and sent for pathologic diagnosis (Figs. 5,6). The first tumor was 4x5.5x7 cm in size and weighed 60 gr and the second was 2x3x4.5 cm in size and weighed 15 gr. During the first postoperative day, the patient experienced a gradual drop in blood pressure which was corrected with administration of crystalloid fluids (Fig. 7). Two weeks after operation the patient was discharged from the hospital in excellent health. He did not return for follow up.

DISCUSSION

Zimmerman, Biron and MacMahon reported the first case of pheochromocytoma of the urinary bladder in 1953.34 Thirty years later, in 1985, Das, Lowe and Bulusu raised the number of reported cases to 100 by introducing three new patients.5 In 1991 Sweetser, Ohl and Thompson reviewed the literature and increased the number of cases to 168,25 after collecting the dispersed cases.6 Despite other cases being reported thereafter, the number of reported cases has not exceeded 200 so far.26

Literally, paraganglia refers to the collection of neural crest cells which are distributed all over the body. These are collateral autonomic ganglia and include the adrenal medulla, chemoreceptors (aortic and carotid bodies), vagal bodies and small groups of cells which are dependent to the neck, chest and abdominal sympathetic ganglia. Functional paraganglion tumors are known as extra-adrenal pheochromocytomas.26 About 1% of all pheochromocytomas occur in the urinary bladder.20 The primary bladder pheochromocytoma is derived from the remainder of the embryonic chromaffin cells in the sympathetic plexus of the bladder wall.13 For pathologic classification of these tumors there is a lack of general agreement, but most researchers favor the classification system proposed by Glenner and Grimley in 1974. Based on this scheme the bladder pheochromocytoma is classified as "visceral-autonomic type". Histologically, paragangliomas including the bladder are composed of two groups of cells: the chief cells (type 1) are round or oval and contain neurosecretory granules in which catecholamines are reserved, and the sustentacular cells (type 2) that are located around the chief cells with less percentage. It must be noted that histological criteria for malignancy in this tumor as other endocrine tumors are not discrete. In paraganglioma and pheochromocytoma, malignant behavior may not be predicted by the presence of nuclear atypia, increased numbers of mitoses or capsular and vascular invasion. The only valuable criterion for diagnosis of malignant nature is existence of paraganglial tissue in areas other than its native places such as lymph nodes, bone, liver and lung.6,23-26 Therefore the presented case in this report can be assigned as malignant due to the invasion by the tumor of the draining lymph nodes.

Based on the afore-said definitions, about 10-15% of pheochromocytomas of the urinary bladder are malignant5,10,22,25 and so far, only 20 cases of malignant tumors of this type have been reported.21 Unlike adrenal malignant tumors, pheochromocytoma of the bladder is seen in association with other diseases such as neurofibromatosis,7 renal cell carcinoma7,24 and transitional cell carcinoma of the bladder.17

The age of onset of the disease is between 11-78 years (mean age 41) and it is distributed evenly among men and women, probably with a slight increase in females. Most of these tumors are hormonally active (38%) and in 34-41% of cases are located in the dome or trigone of the urinary bladder near the ureteral orifice and grow intramurally or submucosally.4,10,12,20,25,26

The release of catecholamines into the circulation during micturition causes a complex of diverse symptoms including headache, palpitation, hypertension, blurred vision and sweating. The most common complaint is painless hematuria and the most common finding in these patients is intermittent hypertension, present in 55-60% and 65-70% of the patients, respectively.2,5,10,12,26 The blood pressure of these patients is often normal between micturitions. Dysuria and suprapubic pain is observed in 9% of the patients. For diagnosis, particularly at the onset of headache, sweating and palpitation following urination, there must be a high index of suspicion. These symptoms may become established after fullness of the bladder, abdominal palpation, defecation, intercourse, rectal examination and sometimes following paroxysmal psychological changes.4,12,19,26,27

The symptoms will be intensified if urination is delayed
due to overdistension of the bladder. Sometimes the onset of hypertension in these patients is associated with appearance of severe headaches and loss of vision. Malignant hypertension and death may occur following the consumption of drugs, use of anesthetics and/or surgery of other parts of the body.\textsuperscript{25} If cases of stable and transient hypertension are considered together, elevated blood pressure will be present in 65-80\% of the patients.\textsuperscript{27}

The diagnosis is confirmed by demonstrating increased urinary excretion of catecholamines (epinephrine and norepinephrine) or their metabolites (metanephrine and vanillylmandelic acid) or increased plasma concentrations of catecholamines, although these tests were negative in a considerable percentage of patients whose disease was proven pathologically, as all urinary bladder pheochromocytomas do not secrete pressoramines.\textsuperscript{11} There is no single best test that can be regarded as ideal for this disease and the priority of the tests is determined by the capabilities of the individual laboratory.\textsuperscript{27}

However, Engelman believes that measurement of urinary catecholamines during a period in which the patient is not taking drugs which interfere with the assays, remains the gold standard for diagnosis.\textsuperscript{8} It is worthy to note that in most cases the release of sympathetic amines occurs following urination and often at other times their level in blood or urine is not abnormal. Therefore, in suspicious cases it can be advised to collect 24-hour urine or to take a spot blood or urine sample immediately after a paroxysm. There are reports of urinary bladder pheochromocytoma with a high catecholamine excretion without hypertension.\textsuperscript{11}

In the plain radiograph of the abdomen it is rare to see ring calcification, which is considered pathognomonic for urinary bladder pheochromocytoma by some investigators. A filling defect and/or ureteral obstruction may be seen in IVP but are non-specific. Ultrasound was used in 1984 for
the first time for diagnosing this disease but this method is very non-specific. 

Since the introduction of computerized tomographic scan it has been selected as the imaging procedure of choice for the localization of pheochromocytoma at many centers. It was revealed in a review that the sensitivity of CT-scan for the diagnosis of tumor in adrenal pheochromocytoma is 94% and for extra-adrenal tumors is 82%. 

It is important to know that in vesical pheochromocytoma, opacification of the bladder after injection of contrast may produce a false negative result. Magnetic resonance imaging was first used in 1987 for localizing pheochromocytoma of the urinary bladder. The image obtained by T2-weighted method makes a very proper spatial contrast and this method is performed successfully for pregnant women. There are a few radioisotope agents which have been used for localizing extra-adrenal pheochromocytomas and among them J131-MIBG and DTPA were more helpful for this purpose. 

It is worthy to note that the physician must be informed about the disturbance produced by this procedure for interpretation of biochemical tests and it is better that they be used after making the definite diagnosis. 

REFERENCES

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