



Case Report

Urinary bladder paraganglioma - A rare dreaded tumor

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Abstract

Catecholamine-secreting tumors that arise from chromaffin cells of the adrenal medulla and the sympathetic ganglia are referred to as pheochromocytomas and extra adrenal catecholamine-secreting paragangliomas (extra adrenal pheochromocytomas), respectively. Bladder paragangliomas are rare entities with initial non-specific presenting symptomatology. Differentiation of urinary bladder pheochromocytomas from other bladder tumors has important treatment implications. We have presented here the case of a 55 year old female who presented to our outpatient urology clinic with complains of hematuria for 3 months and headache for 1 month. Cystoscopy revealed diffusely thickened bladder wall with a well circumscribed smooth surfaced mass protruding from the right lateral wall of the bladder. Multiple biopsies were taken and sent for histopathology. After cystectomy, diagnosis of paraganglioma of bladder was done by histopathology and immunohistochemistry.

Key words

Paraganglioma, Urinary bladder, Histopathology, Immunohistochemistry.

Introduction

Catecholamine-secreting tumors that arise from chromaffin cells of the adrenal medulla and the sympathetic ganglia are referred to as pheochromocytomas and extra adrenal

catecholamine-secreting paragangliomas (extra adrenal pheochromocytomas), respectively. The tumors have similar clinical presentations and are treated with similar approaches; many clinicians use the term pheochromocytoma to refer to both adrenal pheochromocytomas and



extra adrenal catecholamine secreting paragangliomas. However, the distinction between pheochromocytoma and paraganglioma is an important one because of implications for associated neoplasms, risk for malignancy, and genetic testing. Pheochromocytomas that originate from the urinary bladder are extremely rare. In most series, bladder pheochromocytomas often cause micturitional attacks. Paragangliomas, which arise from the chromaffin tissue of the sympathetic nervous system in locations outside the adrenal gland, are referred to as extra-adrenal pheochromocytomas. The first case of paraganglioma of the urinary bladder was reported by Zimmerman in 1953 [1]. Paragangliomas of the urinary bladder account for 0.06% of all bladder tumors and 6% of extra-adrenal pheochromocytomas [2].

Uniqueness of the case

Pheochromocytomas are primarily a disease of the adrenals and sympathetic nerve ganglia. It is an unusually rare finding in bladder specimens. Bladder paragangliomas are rare entities with initial non-specific presenting symptomatology. Differentiation of urinary bladder pheochromocytomas from other bladder tumors has important treatment implications.

Case report

We have presented here the case of a 55 year old female who presented to our outpatient urology clinic with complains of hematuria for 3 months and headache for 1 month. There was no history of fever, pyuria, bleeding per vagina, diaphoresis, flushing.

On examination, patient was average build with an unremarkable general examination except for moderate degree of pallor. Per abdominal examination revealed mild tenderness in the hypogastrium and a vague lump of size 3x4 cm in the right half of hypogastrium that moved

very little with respiration. Bimanual examination confirmed the lump to be of origin from the urinary bladder. It was non-ballotable. At time of admission, Pulse was 88/min and BP = 160/100 mm of Hg.

Laboratory investigations

Routine blood and serum work up showed Anemia and raised ESR. Otherwise the patient had a normal biochemical profile. Urine examination showed plenty of RBC's and cytology was negative for malignant cells.

Ultrasound examination showed a heterogeneous polypoid mass lesion of size 4x6 cm in the right wall of urinary bladder with thickened bladder wall suggestive of Neoplastic bladder mass with cystitis. A CECT of abdomen and pelvis was done which showed a contrast enhancing soft tissue mass with central necrotic regions arising from the right lateral wall of urinary bladder but with maintained fat planes. **(Figure – 1)**

A decision of cystoscopic examination was made and patient was posted in the OR. Cystoscopy revealed diffusely thickened bladder wall with a well circumscribed smooth surfaced mass protruding from the right lateral wall of the bladder. Surface appeared to be covered with normal urothelium. **(Figure – 2)** Multiple biopsies were taken and sent for histopathology.

Histopathology revealed characteristic cellular pattern arrangement in nests or alveoli formations known as 'Zellballen', the cells are clustered together with a rim of sustentacular cells at the nest periphery. The cells are polygonal or at times elongated spindle shaped (chromaffin or chief cells). The cell cytoplasm is finely granular eosinophilic, while the nucleus is round to oval with stippled nuclear chromatin (salt and pepper) appearance. **(Figure – 3)**



With such information in our knowledge, the patient was re-evaluated for uncontrolled hypertension and persistent hematuria. Serum metanephrine levels were obtained and found to be high (502 pg/ml). MIBG scan was arranged for the patient (**Figure – 4**) which showed concentration of the radioisotope in the urinary bladder.

Intervention

Under careful and complete anesthetic and endocrinological critical care, the patient was planned for cystectomy under GA. A low midline approach was used and the tumor was resected *en bloc* with the urinary bladder. Reconstruction was done using Ureterosigmoidostomy. (**Figures - 5A to D**)

The resected specimen on the whole was subjected to histopathology and immunohistochemistry. Grossly the tumor was well circumscribed with a fibrous capsule partially surrounding it (Pseudo capsule), the soft tissue mass was pushing into the bladder musculature, the size of the tumor mass being 6x5x4 cm, and the weight was around 600 gms, Cut section showing homogenous, solid areas with tan appearance. Very few areas of necrosis hemorrhage and cystic changes were evident.

Immunohistochemistry revealed a strongly positive stain for Chromogranin and Synaptophysin. (**Figure – 6, Figure – 7**)

Response to treatment

The patient was discharged uneventfully on day 14 of surgery and is doing well one year after surgery.

Discussion

Pheochromocytoma is rare tumor of adrenal medulla, occurring in less than 0.1% of hypertensive population [3]. Extra-adrenal pheochromocytomas are rarer still (10% of all

pheochromocytomas) and are usually seen in the second and third decades and both sexes are equally affected [4]. They are often multi centric and more likely to be malignant than those of adrenal origin. Amongst the extra adrenal sites the organ of Zuckerkandl, is the common site along with bladder [4]. The origin of pheochromocytoma of the urinary bladder is unclear with a female preponderance (female/male ratio is 3: 1) during the second to fourth decades of life [5]. The case described in our report was a 55 year old female. The patients may present with headache, palpitations and paroxysmal hypertension due to catecholamine excess, especially during micturition. Our patient presented with only hematuria and headache and no other features that would suggest a biologically functional tumor, making it a diagnostic challenge. So when the presence of pheochromocytoma of the urinary bladder is suspected, endocrine tests should be performed, including vanillyl mandelic acid (VMA) in 24 hour urine sample, serum metanephrine and so on. With the advances in imaging technology, ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) may be useful in localizing the tumor, while I131-methylidobenzylguanidine (I131-MIBG) and positron emission tomography (PET)-CT help to evaluate its function. Cystoscopy has got limited value and biopsy is usually not recommended since the tumor is mostly located in the sub mucosa with an intact surface, and it may notoriously provoke a hypertensive episode in patients who have not had proper medical treatment. Additionally, artifactual changes in a small biopsy may confuse diagnosis [6]. Yet in some asymptomatic bladder paragangliomas like in this case, histological and immunohistochemical diagnosis become the last choices and cystoscopy becomes necessary. Pheochromocytomas of the urinary bladder show histological features similar to adrenal pheochromocytomas. The



tumor cells usually grow in a nested, zellballen pattern or a diffuse pattern with delicate fibrovascular stroma [7]. Immunohistochemistry gives a definitive diagnosis. Chromogranin, synaptophysin and NSE can help to identify neural tissue and neuroendocrine cells. Treatment modalities include transurethral resection and partial or total cystectomy combined with pelvic lymph node dissection, especially in the presence of proven metastasis which speaks of malignant nature of the tumor [8, 9]. Our patient had no evidence of metastasis and histology showed a benign paraganglioma. For patients who had characteristic paroxysmal hypertension during micturition, it is necessary to stabilize hypertension before the operation by using alpha-blocking agents for about two weeks and expanding the blood volume, which is similar to treatment for other pheochromocytomas. There is always a danger of insufficient preparation that may lead to hypertensive crisis during surgery [10]. With the improvements seen in laparoscopy technique, laparoscopic partial cystectomy becomes the treatment of choice [11].

Conclusion

Extra-adrenal pheochromocytomas though rare in the urinary bladder, pose a diagnostic and therapeutic challenge to the surgeon. Surgeons need to be clinically suspicious of such rare tumors especially when radiological findings are not consistent with a known common disease. Managed appropriately, patients with pheochromocytomas enjoy a long disease free life with no further medical hassles in life. We emphasize that patients with hematuria and urinary bladder mass complaining of other systemic symptoms, should be thoroughly evaluated to exclude such life threatening yet benign conditions.

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Figure – 1: CT Pelvis showing tumor mass arising from the bladder.



Figure – 2: Cystoscopy showing the tumor with normal overlying urothelium.

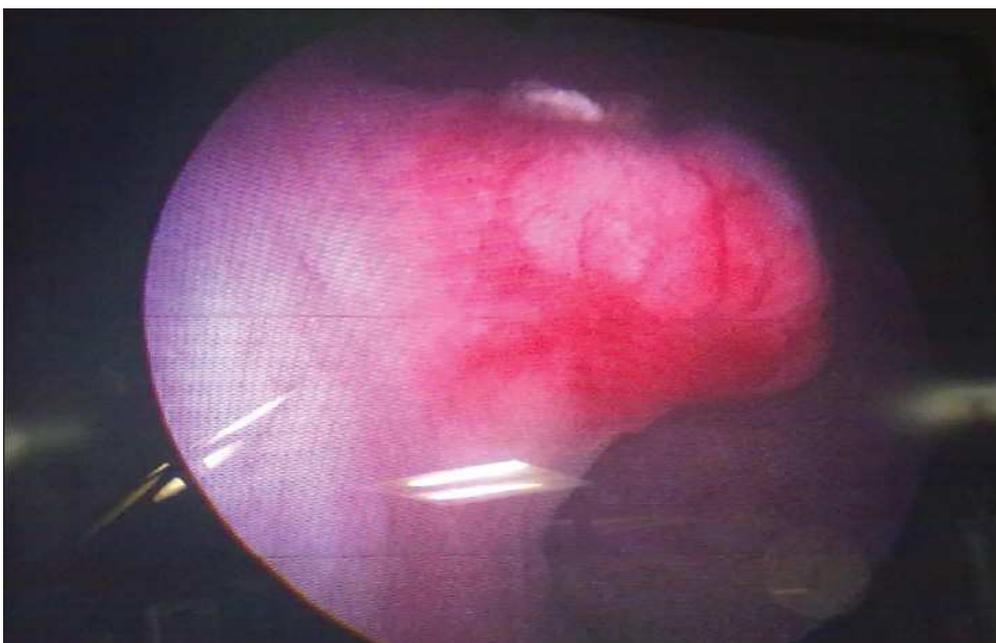


Figure – 3: Characteristic ‘Zellballen’ formation seen on Histopathology.

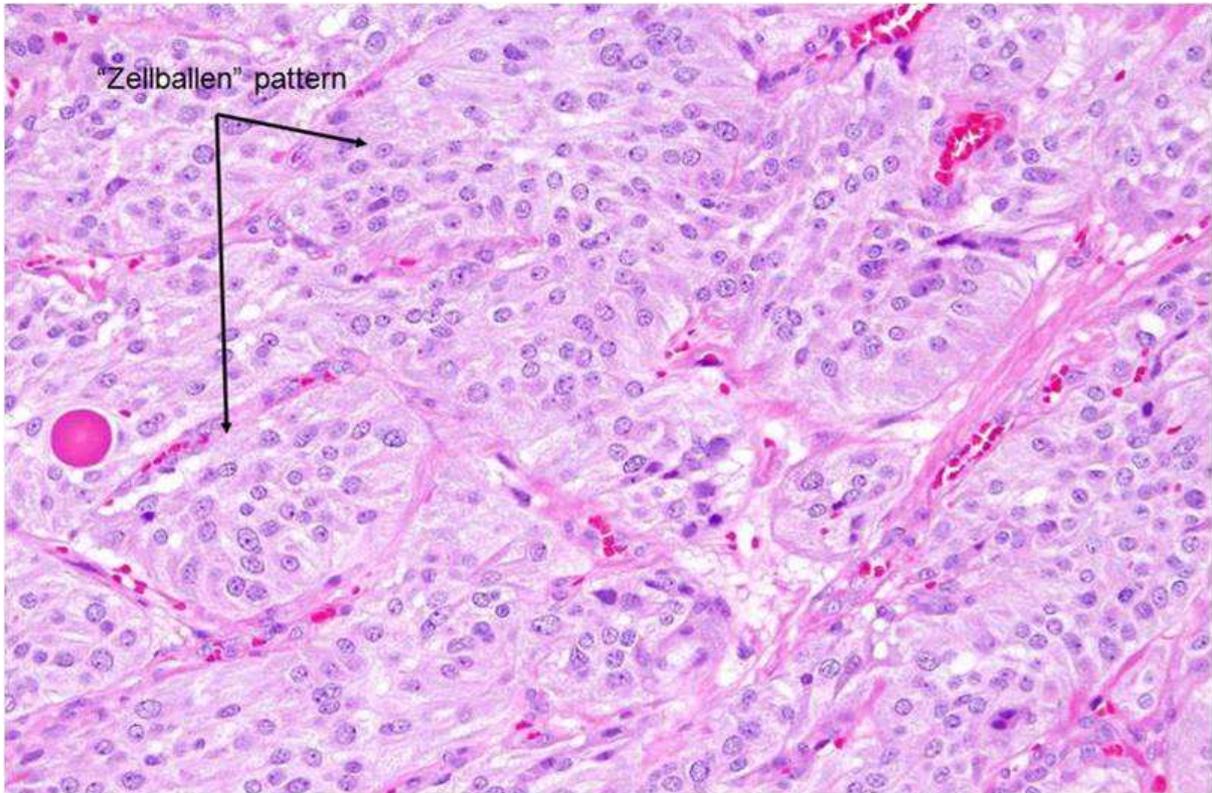
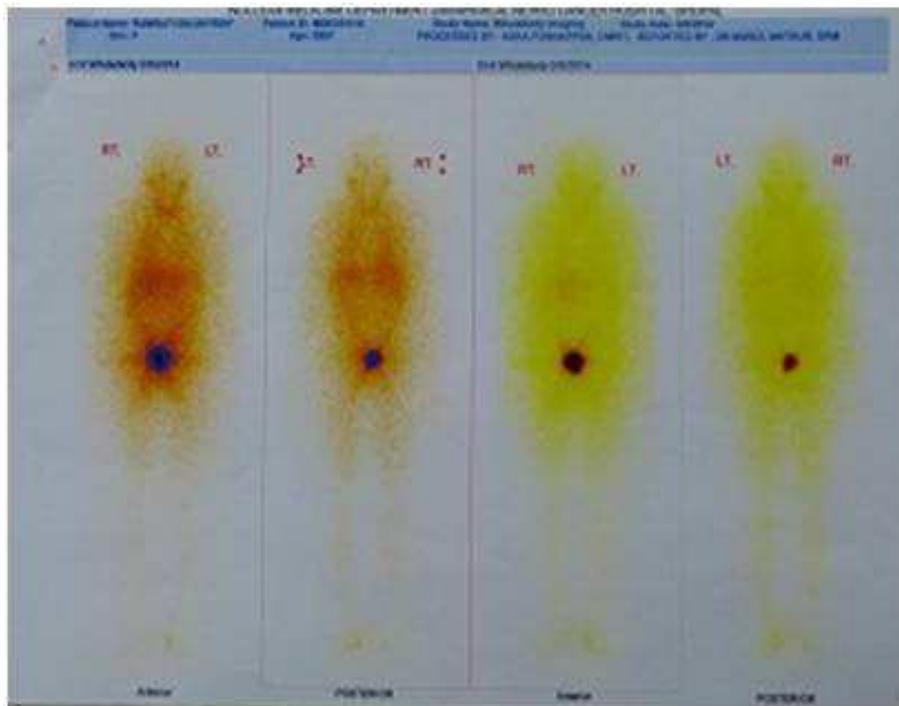
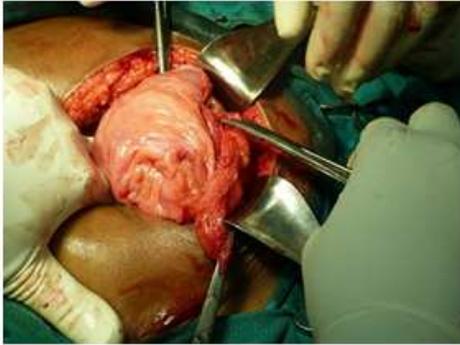


Figure – 4: MIBG scan of the patient.



Figures - 5A to D: Showing the surgical intervention and treatment.



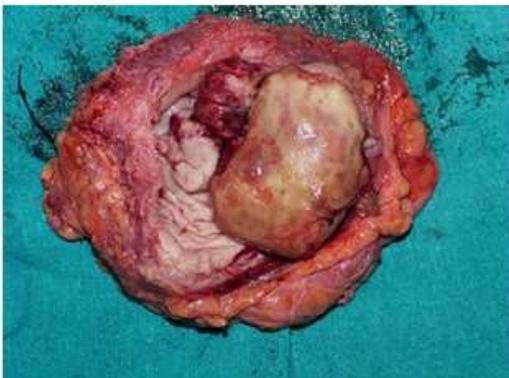
5-A Showing Cystectomy



5-B Showing Ureterosigmoidostomy

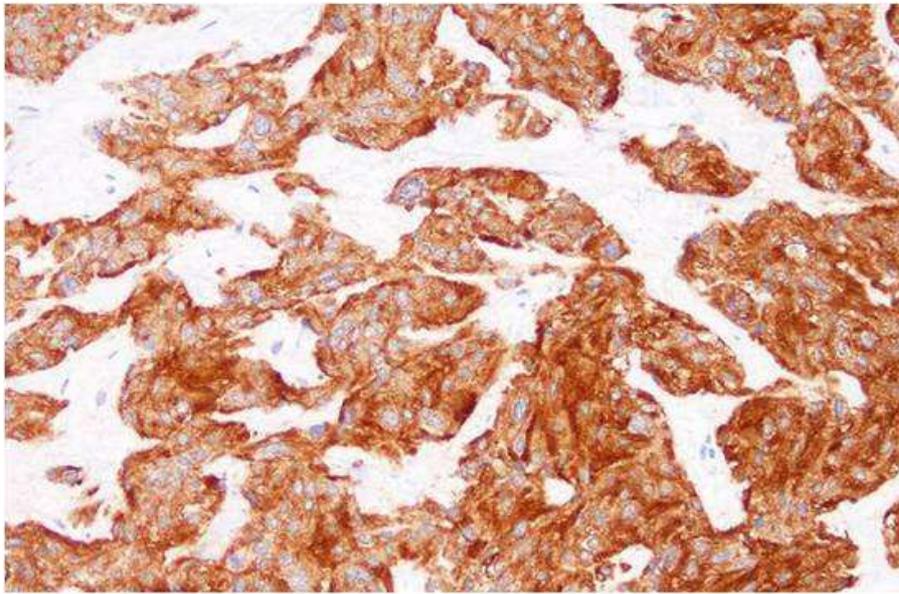


5-C Showing Cystectomy specimen



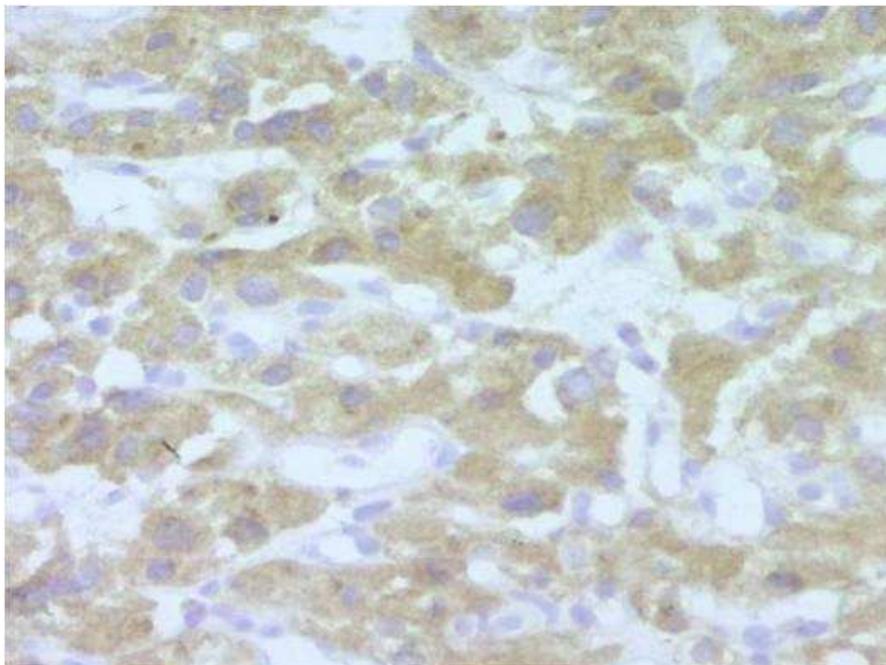
5-D Showing Cut section of bladder with tumor inside

Figure – 6: Immunohistochemistry for Synaptophysin.



Tumor cells positive for Synaptophysin

Figure – 7: Immunohistochemistry for Chromogranin.



Tumor cells Strongly positive for Chromogranin