Non-Functioning "Malignant" Paraganglioma Of The Urinary Bladder

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Citation

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Abstract

Paraganglioma of urinary bladder is a rare tumor and assessing its malignant potential is a challenging issue. We present a case of paraganglioma of urinary bladder treated with partial cystectomy along with a review of literature on histological and immunohistochemical features.

INTRODUCTION

Paragangliomas, also called extra-adrenal pheochromocytomas, arise from chromaffin tissue in the sympathetic ganglia. They are derived from the embryonic neural crest cells. Paragangliomas that account for 10% of pheochromocytomas may arise anywhere, including carotid body, along the aorta and within the urinary bladder. Paragangliomas of urinary bladder represent less than 1% of bladder tumors and 6% of all paragangliomas. ([1]) Of these, only 10% show malignant behavior. ([2]) There is neither exact histological proof nor are there immunohistochemical features for a diagnosis of malignancy. The only absolute criterion for malignancy is the presence of secondary tumors in sites where chromaffin cells are usually absent and visceral metastases.

CASE REPORT

A 25-year-old gentleman presented with a history of an episode of hematuria 5 years back that subsided with medications. He was not evaluated further. In March 2007, he had dysuria with increased frequency of micturition. He underwent transurethral resection of bladder tumor (TURBT) at a private hospital and was referred to our institute with a diagnosis of poorly differentiated carcinoma of urinary bladder.

The slides were reviewed and showed a "cellular neoplasm"; S-100, chromogranin and neuron-specific enolase were strongly positive on immunohistochemistry. With a few areas showing "Zellballen" appearance in addition to immuno-histochemical presentation, paraganglionoma was diagnosed. Tumor was found infiltrating muscularis propria.

Cystoscopy revealed resected tumor bed in the left lateral wall of the bladder close to the left ureteric orifice. Computed tomography of the abdomen and pelvis showed thickening of the posterolateral wall of the bladder with perivesical stranding and suspicious infiltration of the left seminal vesicle. 24-hours urinary VMA was 36.7ng/ml. Periodic blood pressure measurements revealed the non-functioning status of the tumor.

The patient underwent partial cystectomy with left seminal vesiculectomy and left pelvic lymph nodal dissection. As the tumor was in the base of the bladder close to the left ureteric orifice, the lower end of the left ureter was resected and the ureter was re-implanted. Histopathology of the lesion revealed an atypical "Zellballen" appearance of the tumor (Figure1). The muscularis propria was deeply infiltrated by the tumor (Figure 2). The seminal vesicle was found to be free, so also the resected lymph nodes. There was evidence of vascular invasion by tumor (Figure 3). The presence of vascular invasion prompted the pathologist to caution the clinicians about a case of malignant paraganglioma.

Figure 1

Figure 1: Atypical "Zellballen" appearance

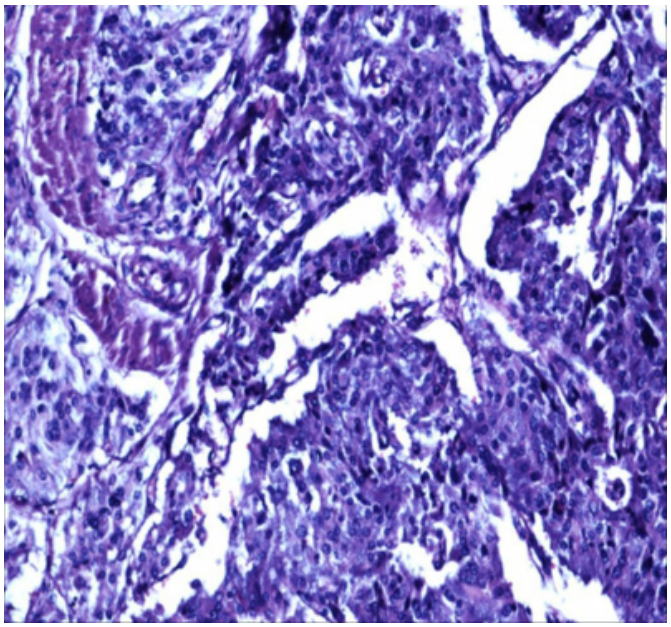


Figure 2

Figure 2: Muscle infiltration by tumor

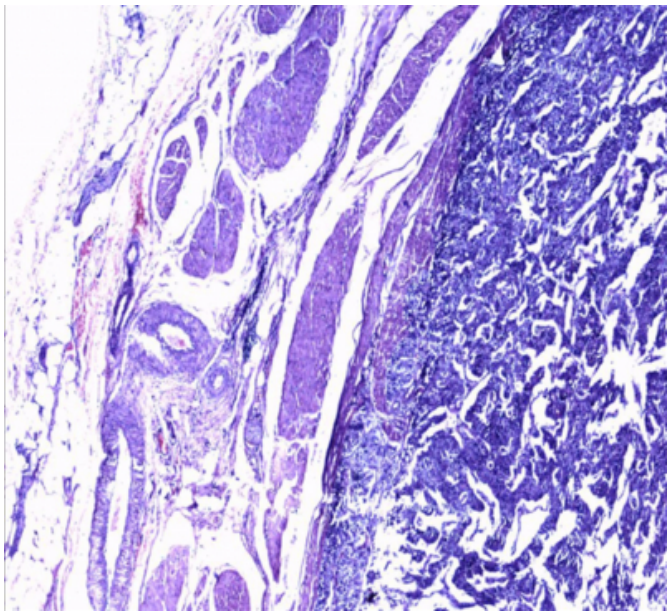
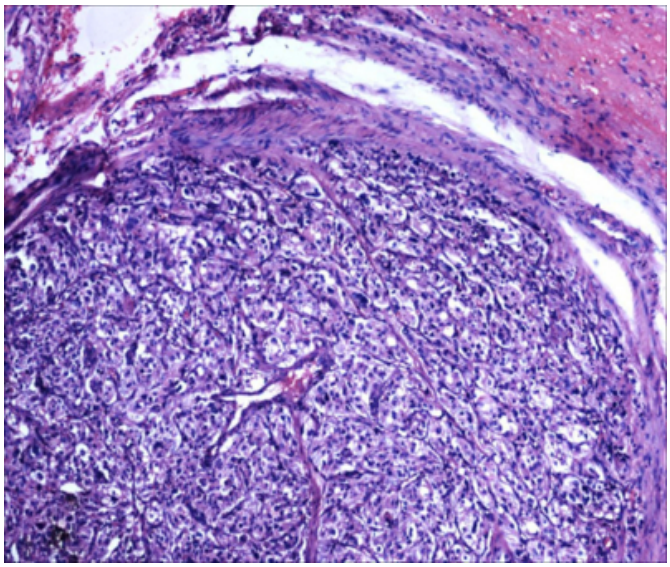


Figure 3

Figure 3: Vascular invasion by tumor



DISCUSSION

Paragangliomas are extra-adrenal pheochromocytomas. Embryologically, primitive neural crest cells migrate to various locations in the body. They differentiate into the neuroendocrine system of the autonomic nervous system. Tumors arising from these cells in adrenal medulla are pheochromocytomas and paragangliomas are their extra-adrenal counterparts. Paragangliomas can arise from orbit, nose, neck, carotid body (termed as chemodectoma), mediastinum, retroperitoneum (a common site being the organ of Zuckerkandl). Most of them are benign, only 10% are malignant with local invasion and spread to lymph nodes, lungs and bone.

Paragangliomas of the urinary bladder constitute 6% of paragangliomas and 0.06% of all bladder tumors. Most often these tumors are found in young adult women and the sex ratio is 1:3. Most of the patients present with irritative voiding symptoms. Only a few present with the classic triad of episodic hypertension, hematuria and post-filling or post-voiding syncope. This typical presentation may be found in functional tumors. These tumors secrete catecholamones, ACTH etc. ($_3$). The typical site of tumor is near the ureteric orifice or trigone.

There is no morphologic criterion to distinguish benign from malignant tumors. Average size of paragangliomas of the urinary bladder is about 2cm (range 0.3 to 5.5cm) ($_4$) Histologically, tumors demonstrate nests of spindle to polygonal cells with granular eosinophilic cytoplasm and hyperchromatic nuclei. Pleomorphism, mitoses and necrosis

may be present in varying proportions in benign and malignant tumors. The classical "Zellballen" (German for "balls of cells") appearance will be present in most tumors. ([5])

Immunohistochemical markers like chromogranin, NSE and S-100 are positive in paraganglionomas. MIB1 and p53 have been studied to assess the malignant potential. Most of the tumors are aneuploid but the same cannot be related to malignant potential.

TURBT is risky in patients with bladder paraganglionoma as hypertensive crisis is a potential hazard. Partial cystectomy is the standard option. Radical cystectomy is reserved for large extensive or multifocal tumors. As these tumors are known to metastasize even after many years, long-term follow-up is advised. Role of chemotherapy and radiotherapy are not well defined.

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