

Malignant Pelvic Paraganglioma with Bladder Invasion

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We report a case of malignant pelvic paraganglioma invading the urinary bladder with malignant ascites. The computed tomography revealed a pelvic mass adjacent to the urinary bladder. The patient had hypertensive crisis while receiving cystoscopy for tumor evaluation. After thorough preoperative preparation, the patient underwent exploratory laparotomy with removal of pelvic tumor and partial cystectomy with reimplantation of right ureter. Malignant paraganglioma is not established upon the pathology, but upon local invasion to bladder and malignant cells in the ascites collected during the operation.

Key words: malignant, paraganglioma, pheochromocytoma, bladder invasion

INTRODUCTION

Paragangliomas are neuroendocrine tumors that arise from sympathetic nerve ganglia. They can develop anywhere from the neck to the pelvis, but are most commonly found in the abdomen, particularly at the aortic bifurcation or in the peri-aortic region. Paragangliomas are rare tumors that arise from extraadrenal chromaffin cells, which are reported at an incidence of 2-8 cases/million/yr.¹

Paraganglioma are histologically identical to pheochromocytomas that arise from the adrenal medulla. Malignancy is more common in paragangliomas (30%-50%) than in pheochromocytomas (10%-15%), with local invasion, destruction of adjacent vertebrae, and distant metastases to lungs, lymph nodes, and bones. The malignancy of paraganglioma is established upon the presence of local aggressive behavior or distant metastasis. About 36% to 60% of paragangliomas are functional and secrete nor-epinephrine and normetanephrine. Thus, patients may be hypertensive or normotensive. However, paragangliomas do not ordinarily secrete epinephrine and are less likely

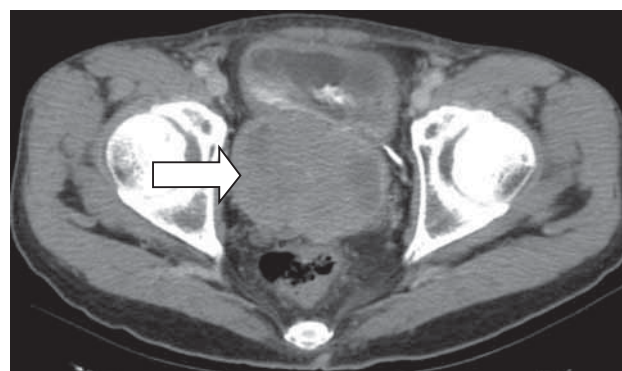


Fig. 1 Abdominal CT revealed a huge pelvic tumor mass with extrinsic compression of the posterior urinary bladder wall.

to cause the severe symptom complex seen in patients with pheochromocytomas.²

CASE REPORT

A 53-year-old man presented with poor intake, fatigue, body weight loss (>10kg in 4 months), and general weakness in the recent 3 months before admission. Abdominal sonography performed by gastroenterologist incidentally found a pelvic mass. Then abdominal CT revealed a huge pelvic tumor mass with contrast enhancement and extrinsic compression of the posterior urinary bladder wall. (Fig.1). Therefore, the patient was referred to our clinic for further evaluation. After admission, CT-guided needle aspiration biopsy of the pelvic tumor was

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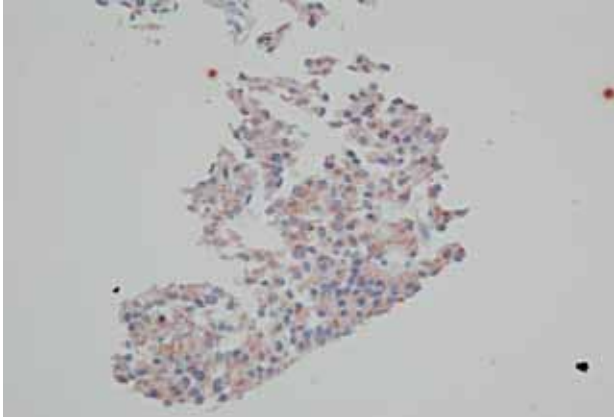


Fig. 2 Tumor, CK stain

performed and neuroendocrine origin was suspected. Furthermore, the patient had hypertensive crisis (systolic pressure: 250 mmHg) while undergoing cystoscopy for tumor evaluation.

Because respiratory failure developed, caused by general weakness, malnutrition (serum albumin: 1.8 g/dL) and severe hypokalemia (1.5mEq/L) as well as endotracheal intubation with ventilator support was administered. Neurological examination revealed no neuromuscular disease. Then the patient had successful weaning of ventilator after nutritional support and correction of electrolyte imbalance. High levels of urine catecholamines were found. (Dopamine: 588.3 mcg/L [normal range <450mcg/24hrs]; Norepinephrine:249.5 mcg/L [normal range <85mcg/24hrs]; Epinephrine 30.3 mcg/L [normal range <22.5 mcg/24hrs]). Thus, paraganglioma was highly suspected as the nature of the tumor. After preoperative preparation with alpha blocker, the patient underwent exploratory laparotomy with removal of the pelvic tumor and partial cystectomy with reimplantation of the right ureter.

The histological examination revealed that the tumor cells were characterized by nucleus with occasional pseudoinclusion and granular and basophilic cytoplasm with a diffuse growth pattern and focal tumor spindling. Incomplete fibrous capsule and invading to bladder muscle wall were seen. The tumor cells were positive for CK, vimentin, and synaptophysin. (Fig 2,3,4) In addition, tumor emboli were found within the pericapsular vessels. The ascites cytology also revealed many tumor cells with positive immunoreactivity for chromogranin A. The serum and urine catecholamine remained at a high level one week after operation. Massive ascites persisted for 2 weeks after the operation (>200 ml/day), and the amount

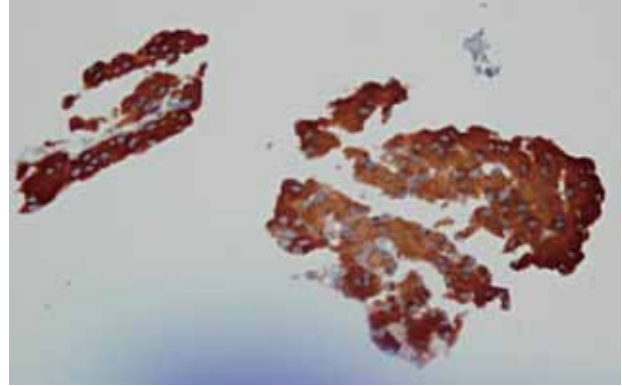


Fig. 3 Tumor, Synaptophysin stain

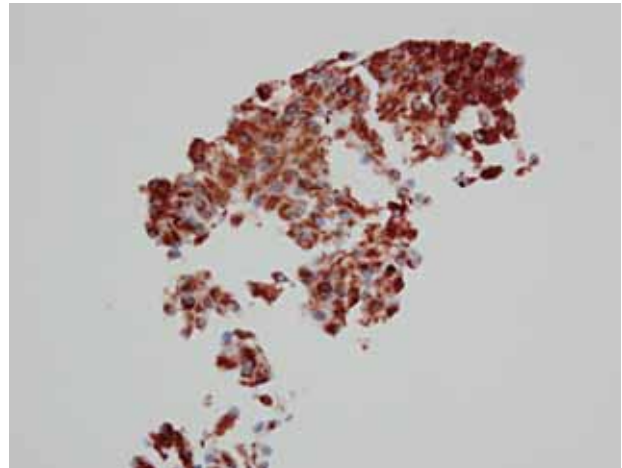


Fig. 4 Tumor, Vimentin stain

decreased after improvement of nutrition status. Liver biopsy revealed chronic inflammation without evidence of malignancy. We follow up the case for about 10 months and there is no evidence of tumor recurrence.

DISCUSSION

Approximately 29-40% of paraganglioma are malignant, which is higher than that of adrenal pheochromocytomas (2-11%).^{3,4} The definition of malignancy is based on biological and clinical behavior and not on histologic features alone.⁵ Surgical resection, chemotherapy or radiation therapy have been reported as the definite treatment for metastatic lesion of paraganglioma, but the efficacy remains unclear and further clinical trials are needed.⁶ Iodine 131 MIBG scintigraphy was suggested as the means of follow up for detecting any recurrence or metastasis.^{7,8}

Pelvic paraganglioma typically presents with hypertensive crises, headache, palpitations, hot flushes and

sweating. Micturition or over-distention of the bladder may trigger hypertensive crisis. In our case, the preoperative diagnosis of pelvic paraganglioma was made on account of the hypertensive crisis occurring during cystoscopy.

Most interesting is that the patient had other non-typical symptoms, such as general weakness, difficult swallowing, and acute respiratory failure caused by malnutrition and hypokalemia. These symptoms were induced by the neuroendocrine secretion of the tumor, which may cause secondary hyperaldosteronism, resulting in increased potassium loss.⁹

Tumor manipulation should be conducted gently and cautiously, and preoperative communication with an anesthesiologist for prevention of hypertensive crisis with nitroprusside during operation is worthwhile to help avoid lethal complications. The diagnosis of malignant paraganglioma was made on account of the tumor's clinical behavior (invasion to the bladder wall and positive finding in ascites cytology). Surgical resection remains the most effective treatment for paraganglioma. In malignant cases, monthly catecholamine determination and image studies every 6 months or annual Iodine-131 MIBG scintigraphy were suggested for postoperative follow-up.^{3,4,10,11} Other treatment options include chemotherapy and radionuclide therapy and radiotherapy. Avertbuch et al. reported that CVD chemotherapy, which is a combination of cyclophosphamide, vincristine, and decarbazine, gave a complete and partial response rate of 57% and that biochemical responses were seen in 79% of all patients.¹²

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