Diagnosis and Treatment of Malignant Extra-adrenal Pheochromocytoma with Presentation of Bone Pain and Low Urinary Tract Symptoms: A Case Report

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This report describes an extremely rare case of malignant extra-adrenal pheochromocytoma of urinary bladder with multiple bone metastases in a hormonally inactive 38-year-old man, who initially presented as right shoulder pain, frequency, dysuria and microhematuria. A combined-modality treatment plan of partial cystectomy with post-operative palliative radiotherapy for bone pain and subsequent systemic chemotherapy with cyclophosphamide, vincristine, and dacarbazine (CVD) was performed. Although the patient survived the surgical intervention and the cytotoxic chemotherapy for at least 9 months, the bone metastatic lesions showed unsatisfied response after undergoing 3 courses of CVD chemotherapy. **(JTUA 20:184-6, 2009)**

Key words: extra-adrenal pheochromocytoma, bladder tumor, chemotherapy.

INTRODUCTION

Malignant extra-adrenal pheochromocytoma is a rare disorder with only a few of case reports or analyses in the recent decades. It is easily misdiagnosed if the tumor releases less catecholamines, which usually result in elevated blood pressure, headache, flush, etc. We present here a hormonally inactive malignant pheochromocytoma involving the urinary bladder with multiple bone metastases.

CASE REPORT

A 38-year-old man with slight hypertension for 2 years suffered from right shoulder pain, which progressed to right arm weakness under complementary and alternative medicine therapy, for 6 months. Subsequently, frequency and mild dysuria developed. Then microhematuria was detected and the abdominal sonography examination revealed one 6-cm echoic mass lesion over dome area of urinary bladder. Cystourethroscopy disclosed a huge wide-based tumor mass with a reddish nodule on the surface over dome area (Fig. 1).

At the same time, the right shoulder x-ray showed a significant osteolytic bone lesion whereas the Tc99m

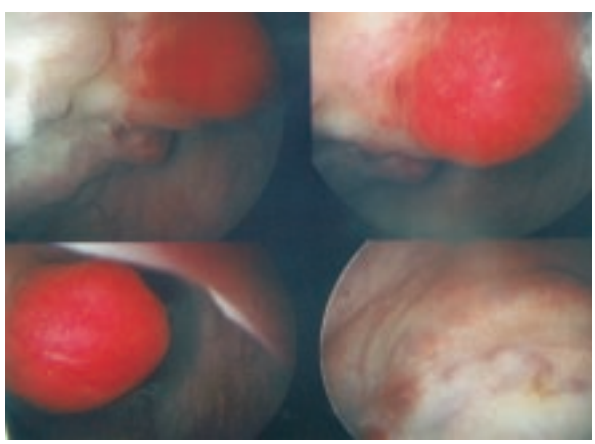

Fig. 1. Cystourethroscopy disclosed a huge wide-based tumor mass with a reddish nodule lesion on the surface over the dome area of urinary bladder.

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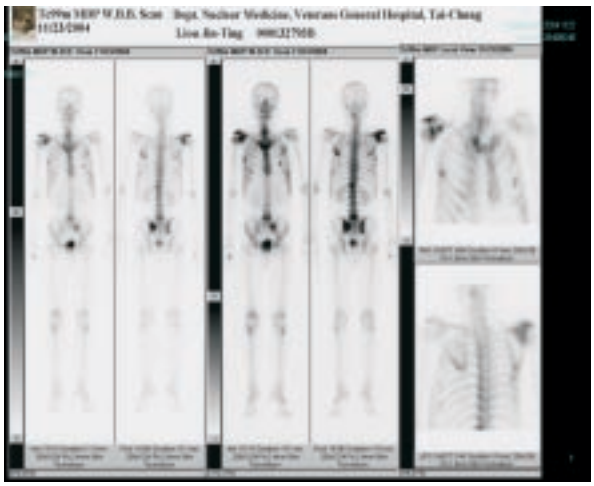

Fig. 2. Whole body bone scan showed multiple bone metastasis.

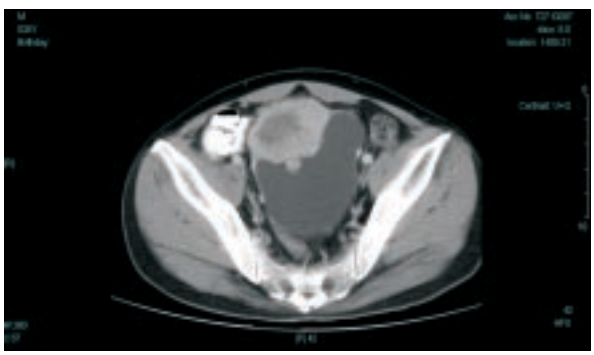

Fig. 3. Abdominal computer tomography scan showed a 6-cm contrast-enhanced bulging tumor with central necrosis over the dome area of urinary bladder.

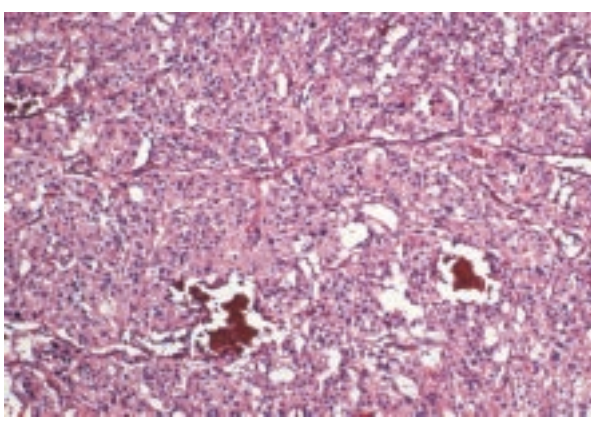

Fig. 4. Microscopically, tumor cells were stained positively for NSE, synaptophysin, S-100 protein, chromogranin.

MDP whole body bone scan suspected multiple bone metastasis including right shoulder (Fig. 2). The further abdominal computer tomography (CT) scan (Fig. 3) revealed a contrast-enhanced bulging tumor, 6 cm in diameter, with central necrosis over the dome area of urinary bladder. Transurethral resection of urinary bladder tumor for the nature determining was performed followed by computer tomography (CT)-guided biopsy for the osteolytic bone lesion over right shoulder. Both pathologic reports were confirmed to be metastatic extra-adrenal pheochromocytoma (Fig. 4).

Fortunately, no fluctuating blood pressure during the peri-operative period was noted and the post-operative 24-hour urinary vanillylmandelic acid (VMA) level was within normal range. Meta-iodo-benzyl-guanidine labeled with 131-iodine [(131)I-MIBG] scan result was compatible with the pathologic reports and there's no primary lesions over bilateral adrenal glands.

The patient turned to the traditional Chinese herb and other alternative therapies after partial cystectomy and subsequent palliative radiotherapy for the major metastatic bone lesions. He hesitated about systemic chemotherapy initially. However, due to the deteriorated bone pain, systemic chemotherapy consisting of cyclophosphamide at 750 mg/m(2), vincristine at 1.4 mg/m(2), and dacarbazine at 600 mg/m(2) on Day 1 and dacarbazine at 600 mg/m(2) on Day 2, every 21 days was accepted 4 months after partial cystectomy. He only underwent three courses of chemotherapy, because the bone metastasis progressed according to the repeated whole body bone scan at the end of the 3rd course. Unfortunately, the patient lost follow-up 9 months later.

DISCUSSION

Extra-adrenal malignant pheochromocytoma is a rare disease with a high mortality. Pheochromocytoma of the urinary bladder is generated from chromaffin tissue of the sympathetic nervous system within the layers of the bladder wall. It accounts for less than 0.06% of all urinary bladder tumors and less than 1% of all pheochromocytomas. The diagnosis is strongly based on the clinical symptoms related to catecholamine hypersecretion. In some cases however, the tumor is hormonally inactive and may go undetected for years, such as the case we illustrate here. This patient had neither fluctuating blood pressure nor episodic headache but presented with bone pain followed by frequency and dysuria. Reviewing the literatures, patients with pheochromocytoma in urinary bladder frequently present with painless hematuria but none of the characteristic symptoms of pheochromocytoma.[1]

According to one of the recent studies, combination chemotherapy with CVD produced a complete response rate of 11% and a partial response rate of 44% for the malignant pheochromocytoma while the median survival was 1.8 years for patients whose tumors did not respond to that. The authors conclude that CVD therapy is not indicated in every patient with metastatic pheochromocytoma.[2] Except for the surgical debulking, pharmacological control of hormone-mediated symptoms, targeted methods such as external irradiation, and systemic antineoplastic therapy, the alternative strategy established best is [131I]meta-iodobenzylguanidine (MIBG) therapy, which is well tolerated[3] although hematologic complications are the most common side effects.[4]

The present case demonstrates the hormonally inactive extra-adrenal pheochromocytoma in urinary bladder could be silent initially. It may be difficult to be diagnosed in the early stage if the patient pays less attention to the minimal change of his voiding habit. This patient delayed the diagnosis of his illness for several months due to he received complementary and alternative medicine therapy for the bone metastasis related right shoulder pain. Although he then underwent combination therapy and survived more than 9 months, loss of follow-up makes no possibility of the salvage MIBG therapy for the progressed multiple bone metastases.

REFERENCES

1. Siatelis A, Konstantinidis C, Volanis D, et al. Pheochromocytoma of the urinary bladder: report of 2 cases and review of literature. Minerva Urol Nefrol 2008;60:137-40.
2. Huang H, Abraham J, Hung E, et al. Treatment of malignant pheochromocytoma/paraganglioma with cyclophosphamide, vincristine, and dacarbazine: recommendation from a 22-year follow-up of 18 patients. Cancer 2008; Sep 8.
3. Scholz T, Eisenhofer G, Pacak K, et al. Clinical review: current treatment of malignant pheochromocytoma. J Clin Endocrinol Metab 2007;92:1217-25.
4. Gedik GK, Hoefnagel CA, Bais E, et al. 131I-MIBG therapy in metastatic phaeochromocytoma and paraganglioma. Eur J Nucl Med Mol Imaging 2008;35:725-33.