Case Report

A Case of Metastatic Extra-Adrenal Pheochromocytoma
12 Years after Surgery

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At the age of 53, a 65-year-old man had been diagnosed with extra-adrenal pheochromocytoma in the retroperitoneum and underwent total tumorectomy. Afterward, he had his serum catecholamine periodically measured in an outpatient clinic. In February 1999, 12 years after surgery, he complained of lower left abdominal pain. Computed tomography and magnetic resonance imaging revealed an osteolytic lesion in thoracic vertebrae 11Th (Th 11). Although his basal serum and urine catecholamines were at normal levels, glucagon injection increased blood pressure and plasma catecholamine levels. 131I-metaiodobenzylguanidine (MIBG) scintigraphy was specifically taken up to Th 11. By bone biopsy, the osteolytic lesion in Th 11 was finally diagnosed with metastasis of pheochromocytoma. For post-operative pheochromocytoma, long-term follow-up involving biochemical tests, including serum catecholamines, and MIBG is needed. *(Hypertens Res 2002; 25: 141–144)*

Key Words: metastasis, glucagon test, 131I-metaiodobenzylguanidine scintigraphy (MIBG), long-term follow up

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Introduction

Pheochromocytoma, a catecholamine-secreting tumor, is a rare, curable cause of hypertension. However, pheochromocytoma can recur as a benign or malignant tumor. Pheochromocytoma is diagnosed as benign or malignant according to the existence of distant metastasis in which chromaffin tissues are absent (1). Because clinically malignant behavior is difficult to predict based on the tumor’s histologic appearance, there has been some controversy regarding pheochromocytoma’s prognosis following surgery. The 5-year survival rate from the first operation is 84% to 96% for patients with benign pheochromocytoma, and about 40% for those with malignant pheochromocytoma (2, 3). Recently, benign pheochromocytomas have been reported to recur during a follow-up period from several months to sixteen years (4, 5).

We report a case of extra-adrenal pheochromocytoma, which recurred in the thoracic vertebrae, twelve years after the initial operation.

Case Report

First Admission

A 53-year-old man was admitted to our hospital in August 1987 for extra-adrenal pheochromocytoma. His blood pressure was 156/84 mmHg and his pulse rate was 84/min on admission. His systolic blood pressure periodically elevated up to 200 mmHg. Concentrations of serum adrenaline and noradrenaline were 31 pg/ml (normal range: 0–120 pg/ml) and 3,670 pg/ml (normal range: 40–360 pg/ml), respectively. Urine adrenaline, noradrenaline, and vanillylmandelic acid (VMA) was 112 µg/day (normal range: 0–12 µg/day), 655 µg/day (normal range: 10–90 µg/day), and 12.9 mg/day (normal range: 2.5–9.5 mg/day), respectively. Computed to-
mography (CT) and magnetic resonance imaging (MRI) showed a para-aortic tumor (9 cm × 9 cm × 6 cm) between the second and fourth lumbar vertebra in the retroperitoneum. 131I-metaiodobenzylguanidine (MIBG) scintigraphy revealed positive uptake in this tumor (Fig. 1). Distant metastases were not observed by MIBG, gallium, or bone scintigraphy. The patient had undergone a total tumorectomy in September 1987. The resected tumor was confirmed to be an extra-adrenal pheochromocytoma by pathological examination. No residual tissues were founded by CT or MIBG after surgery.

Second Admission

After surgery in 1987, the patient had been seen in an outpatient clinic, periodically, to follow-up serum catecholamine levels. In February 1999, he had left abdominal pain, which had been gradually worsening. He was admitted to Yawatahama City General Hospital where an osteolytic lesion was detected in thoracic vertebrae 11 Th (TH 11) by CT. He was readmitted to our hospital in May 1999 for further evaluation. His blood pressure was 80/52 mmHg and his pulse rate 72/min. CT revealed an osteolytic lesion (3 cm × 4 cm × 2 cm) at Th 11 (Fig. 2). MRI showed the bright lesion at the same site on T2-weighted images, which was enhanced by gadolinium diethylene triamine-pentaacetic acid (Fig. 3A, B). MIBG had highly accumulated at this lesion (Fig. 4); however, his catecholamine levels were normal in both serum and urine. Serum neuron-specific enolase (NSE) was significantly elevated to 21.5 ng/ml (normal: < 9.2 ng/ml). Because his basal catecholamine levels were normal, a glucagon test was carefully performed with blood pressure monitoring. After injection of 1 mg of glucagon, blood pressure was elevated from 88/56 mmHg to 126/83 mmHg, and serum adrenaline and noradrenaline were increased from 34 pg/ml to 86 pg/ml and from 249 pg/ml to 1,120 pg/ml, respectively. The tissue specimen taken by a tumor biopsy revealed a zellballen pattern appearance and positive chromogranin A staining. He was finally diagnosed with bone metastasis of pheochromocytoma and transferred to another hospital for radiation therapy.

Discussion

On the first admission, our patient had a sporadic extra-adrenal pheochromocytoma. Twelve years later, he was diagnosed with metastasis of pheochromocytoma in a thoracic vertebrae. The recurrence rate of pheochromocytoma has been previously reported as 6% to 23% (5–9), and recurrence is frequent in patients with large (> 50 mm) and bilateral or extra-adrenal tumors. At first admission, our patient had a large (9 cm × 9 cm × 6 cm) extra-adrenal pheochromocytoma. Because he was at high risk for recurrence, he made follow-up visits to an outpatient clinic to have his blood pressure and serum catecholamine level measured, and these were normal. In addition, he was asymptomatic in terms of catecholamine excess during the follow-up period. On the second admission, his urine catecholamine and its metabolites were still within the normal ranges. Elevated plasma catecholamine levels have been seen in 90–95% and 88% of pheochromocytoma patients and extra-adrenal pheochromocytoma patients, respectively (10). More than 95% of patients with pheochromocytoma have shown elevated total urinary catecholamine levels. In patients with extra-adrenal pheochromocytoma, 88% have been seen to have positive urinary metanephrine, 71% have had positive VMA, and 67% have had elevated urinary catecholamines (10). At the first admission, our patient had elevated urine and serum

Fig. 1. 131I-metaiodobenzylguanidine scintigraphy revealed positive uptake in a para-aortic tumor in the retroperitoneum.

Fig. 2. Computed tomography showing a solitary mass in thoracic vertebrae 11 Th. Arrow indicates metastasis of pheochromocytoma.
catecholamines. However, in the period following surgery, our patient had not revealed elevated urine and serum catecholamines, indicating the inadequacy of following-up post-operative pheochromocytoma patients only in regard to serum and urine catecholamines.

The glucagon stimulation test is the most specific provocation test for pheochromocytoma (11). The sensitivity and specificity of the glucagon test have been reported to be 81–83% and 95.5–100%, respectively (11, 12). We performed the glucagon test for our patient carefully with blood pressure monitoring, because basal urine and serum catecholamine levels were normal. Mannelli et al. (13) reported that 11.3% of pheochromocytoma patients were found to show normal plasma catecholamine, whereas the glucagon test gave a positive response in 80% of these pheochromocytoma patients. In our patient, the glucagon test was positive, and proved useful in arriving at his diagnosis. Neuropeptide Y and NSE are also useful markers for diagnosis of neuroendocrine tumors, including pheochromocytoma (14, 15). Our patient revealed elevation of serum NSE level. Baudin et al. (15) reported that serum NSE were elevated in 38% of neuroendocrine tumors (50% of pheochromocytoma), and that NSE levels were exclusively associated with poor tumor differentiation. Schlumberger et al. (16) reported that 61% of patients with malignant pheochromocytoma showed elevated NSE. As a biochemical diagnosis for pheochromocytoma, the glucagon test and measurement of serum NSE, in addition to measurement of serum catecholamines, should be performed in the follow-up period.

CT and MRI yield excellent imaging of abdominal and thoracic pheochromocytoma (17, 18). However, the sensitivity of CT for extra-adrenal pheochromocytoma is lower than that for adrenal pheochromocytoma (82% vs. 94%) (11). The sensitivity and specificity of MIBG scintigraphy is reported to be 87.4% and 99%, respectively (19). MIBG scintigraphy is the most valuable tool in detection of extra-adrenal pheochromocytoma and its metastases, especially when CT and MRI findings are negative. In our case, MIBG scintigraphy could specifically detect the metastasis in the thoracic...
vertebrae (Fig. 4).

Currently, the long-term postoperative outcome of pheochromocytoma is considered to be not very good (4, 5). Plouin et al. reported that of the 113 patients with benign pheochromocytoma at first operation, 15 patients (13%) experienced recurrence in the form of a benign or malignant tumor between 17 and 194 months after the initial operation (4). Our patient experienced recurrence in the form of the malignant metastasis of pheochromocytoma 12 years after the initial operation. Long-term follow up for post-operative pheochromocytoma by biochemical tests, including the glucagon test and NSE as well as serum catecholamine level, and if possible by MIBG, is needed.

References


