Von Hippel-Lindau Disease with Multiple Spinal Cord Hemangioblastomas, Syringomyelia and Pheochromocytoma

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A 31-year-old blind man presented with numbness and weakness in the left hand, and elevated blood pressure. Multiple hemangioblastomas in the spinal cord associated with syringomyelia were well demonstrated by gadolinium-enhanced magnetic resonance imaging (MRI). He also had pheochromocytoma in the right adrenal gland, which was disclosed by abdominal computed tomography, MRI and 131I-metaiodobenzylguanidine scintigraphy. MRI screening should be considered for patients with von Hippel-Lindau gene to detect the multiple lesions in this disease. (Internal Medicine 34: 216–219, 1995)

Key words: spinal cord tumor, magnetic resonance imaging, adrenal tumor, hypertension

Introduction

Von Hippel-Lindau disease (VHL) is a dominantly inherited disorder characterized by hemangioblastomas of the central nervous system (CNS), retinal angiomas, and multiple cysts and tumors of the viscera (1). Only 25 families have been reported in Japan (2, 3). Clinical diagnosis of VHL is often difficult because of the late onset of symptoms in affected individuals and the variety of organ system involvement (4). Magnetic resonance imaging (MRI) and computed tomography (CT) have enabled early detection of the multiple occult lesions in this disease. We report a case of VHL with pheochromocytoma and multiple spinal cord hemangioblastomas and syringomyelia, which were detected by MRI.

Case Report

A 31-year-old blind man had slowly progressive numbness and weakness in the left hand for 2 years. He had a history of an operation for retinal angioma at the age of 15, when the elevation of his blood pressure was first noticed. His father died of cerebellar tumor and had retinal angiomas. His uncle also had retinal angiomas and spinal cord tumor. No further family history was available. On examination, cranial nerves, except the ophthalmic nerve, were normal. Mild weakness with exaggerated biceps, triceps, and brachioradial reflexes were present in the left upper extremity. Touch sensation, but not pain, temperature, or vibration, was decreased in the left C7-8 dermatomes. Motor function, tendon reflexes and sensation in the other extremities and trunk were normal. No ataxia was found. His blood pressure was 170/110 mmHg. Hematological findings were as follows; hemoglobin of 16.5 g/dl, red blood cell count 548×10⁴/mm³, white blood cell count 7,600/mm³ and platelet 31.5×10⁴/mm³. Blood biochemical findings were normal. Endocrinological analysis revealed an elevated norepinephrine level; 3,849 pg/ml in the plasma (normal: 100–50 pg/ml) and 397.6 μg/day in the urine (normal: 26.0–121.0 μg/day). Epinephrine and dopamine levels in the plasma and urine were normal. Plasma renin activity, aldosterone, and erythropoietin were within normal levels.

Brain CT showed no abnormality. Gadolinium-enhanced MRI demonstrated multiple enhancing lesions in the lower medulla to the lower thoracic spinal cord (Fig. 1). Syringomyelia was also detected through the cervical to thoracic cord (Fig. 1a, b). Abdominal CT disclosed a mass measuring 4 cm in diameter in the right adrenal gland, which contained a solid and cystic component and calcification (Fig. 2a). Blood biochemical findings were normal. Endocrinological analysis revealed an elevated norepinephrine level; 3,849 pg/ml in the plasma (normal: 100–50 pg/ml) and 397.6 μg/day in the urine (normal: 26.0–121.0 μg/day). Epinephrine and dopamine levels in the plasma and urine were normal. Plasma renin activity, aldosterone, and erythropoietin were within normal levels. Pheochromocytoma and adrenal scintigraphy showed a decrease of uptake in the right adrenal region, where 131I-metaiodobenzylguanidine (MIBG) was markedly accumulated.

Hypertension was controlled with 20 mg of arotinolol hydrochloride. The right adrenal tumor was resected, which was histologically determined to be pheochromocytoma with no evidence of malignancy. The blood pressure and catecholamine levels were normalized after operation.

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Fig. 1. a, b) Postcontrast sagittal magnetic resonance images demonstrate multiple enhancing intramedullary tumors in the lower medulla to lower thoracic spinal cord, and syrinx within spinal cord extending from C2 to Th5. c) Postcontrast axial image reveals small vessels (arrow) at the dorsal surface of the enhancing mass.

Discussion

Although at least 25 distinct lesions have been described in VHL, only six frequently cause morbidity: retinal angiomas, cerebellar, medullary and spinal cord hemangioblastomas, pheochromocytoma, and renal cell carcinoma (1). Early detection of asymptomatic lesions is an important factor in the treatment of all six. The present patient had 3 lesion types: retinal angiomas, spinal cord hemangioblastomas, and pheochromocytoma.

CNS lesions in VHL are often overlooked due to the late onset of symptoms and the lack of neurological findings referable to the lesion (5). In the present patient, neurological symptoms and signs were rather mild, as compared with the prominent lesions in the spinal cord. Spinal cord hemangioblastoma has been reported to occur in less than 5% of affected subjects in a clinical series, but autopsy data suggest that the lesions may often go unrecognized during life (1). In fact, recent studies by MRI screening reported a higher frequency (26–44%) of spinal lesions (4, 6, 7). Contrast-enhanced MRI is more useful than noncontrast MRI in lesion detection, particularly, in patients with syringomyelia (7). On MRI the presence of small vessels near the tumor is highly suggestive of

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Fig. 2. a) Abdominal computed tomography (CT) reveals a mass in the right adrenal gland, containing a solid and cystic component and calcification, b) Postcontrast abdominal CT discloses a peripheral and heterogeneous enhancement of the adrenal mass, c) T2-weighted magnetic resonance image shows the tumor as high signal intensity.

hemangioblastoma (8, 9), but has seldom been demonstrated in the literature. We clearly detected the vessels as flow voids in our patient (Fig. 1c). Intramedullary spinal cord lesions are often located in the dorsal half of spinal cord and approximately 66% are associated with syringomyelia (9). However, there are not many reported cases demonstrating multiple spinal hemangioblastomas with syringomyelia on MRI (3, 4, 6–11).

In cases of hemangioblastomatous syringomyelia, several differing opinions have been offered. The first is that cerebrospinal fluid flow obstruction by the tumor causes cavitation (12). A second theory is that the tumor cells form plasma in a manner similar to embryonic angioblasts (13). Finally, it has been suggested that the tumor transudes fluid that dissects through the gray matter alongside the central canal (14, 15).

Pheochromocytoma, which accounts for less than 1% of patients with systemic hypertension (16), is a feature of several disorders with an autosomal dominant pattern of inheritance – multiple endocrine neoplasia type 2, von Recklinghausen’s disease, and VHL. In families with VHL, the frequency of pheochromocytomas ranges from 0 to more than 90% (average, 14%) (17–19), whereas a recent study reported that 19% of unselected patients with pheochromocytoma were carriers of VHL (10). Abdominal MRI is reported to be as sensitive as MIBG scintigraphy (sensitivity; 95%) to detect pheochromocytomas, showing hyperintense lesions on T2-weighted image (10, 20) as seen in the present case.

VHL is a potentially malignant disease. Affected individuals in VHL families directly benefit from screening by early diagnosis and by genetic counseling in the childbearing years. In the future, genetic screening will play a major role in identifying patients with the VHL gene (21). MRI should be considered the best currently available means for detecting lesions in patients with the disease.

References

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