Neurofibromatosis type 1 associated with pheochromocytoma: A case report and a review of the literature

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ABSTRACT. Pheochromocytoma (PHEO) occurs in 0.1-5.7% of patients with neurofibromatosis type 1 (NF1). We report a case of adrenal PHEO in a patient with NF1. A 30-yr-old Turkish man was admitted to our hospital for further examinations of a right adrenal mass, that was incidentally discovered by abdominal ultrasonography during examinations for acute hepatitis B infection in another hospital. In his past medical history, the patient had only had one palpitation, sweating and headache episode 4 yr before. On admission, his blood pressure was 110/70 mmHg. Physical examination revealed signs of NF1. He had multiple neurofibromas over the entire skin, café-au-lait spots on the trunk and extremities and skinfold freckling. Bilateral ophthalmic examination revealed multiple Lisch nodules. The 24-h ambulatory blood pressure monitoring revealed paroximal hypertension attacks (190/148 mmHg). Urinary catecholamines were markedly increased. Magnetic resonance imaging (MRI) revealed a solid round tumor approximately 5 cm in diameter, located in right adrenal gland. A ¹³¹Iodine-metaiodobenzylguanidine (¹³¹I-MIBG) scan showed uptake in the right adrenal gland. The pre-operative treatment with an α-blocker (phenoxybenzamine) was performed. Right adrenalectomy was performed; the surgical specimen revealed PHEO. Urine catecholamines and their metabolites returned to normal ranges on post-operative day 7. In conclusion, an adrenal mass can be incidentally discovered in any patient. After diagnosis of NF1, patients who have episodes of hypertension, sweating, headache and palpitation should be evaluated for PHEO.


INTRODUCTION

Pheochromocytomas (PHEOs) are rare tumors of the adrenal gland that arise from chromaffin cells of the adrenal medulla (1-3). In general outpatient clinics, the prevalence of PHEO in patients with hypertension is 0.1-0.6% (1), with an incidence in the general population of 1 in 200,000 (4). Approximately 10-15% of cases of PHEO have been thought to be due to hereditary causes. Hereditary PHEO occur in multiple endocrine neoplasia type 2, von Hippel-Lindau syndrome, neurofibromatosis type 1 (NF1) and familial paragangliomas (5, 6).

NF1, also known as von Recklinghausen disease, is a common autosomal dominant genetic disorder occurring in about one per 3000-4000 individuals and the male to female ratio is 3:1 in all races (7). The NF1 gene has been localized to chromosome 17q11.1. Molecular genetic testing for mutations in NF1 is available, but the diagnosis is typically made on a clinical basis. NF1 is characterized by multiple café-au-lait spots, neurofibromas, Lisch nodules (iris hamartomas), skinfold freckling (especially axillary and/or inguinal), optic glioma, and specific osseous...
dysplastic lesions (1, 2, 8). Patients with NF1 have an increased incidence of other tumor types, including malignant peripheral nerve sheath tumors, PHEO and leukemia (9).

In 1910, Suzuki (10) first recognized the association of PHEO with NF1. PHEOs occur in 0.1-5.7% of patients with NF1 and in 20-50% of NF1 patients with hypertension, as compared with 0.1% of all hypertensive individuals (11, 12). However, when NF1 patients are examined at autopsy, the prevalence of PHEO is slightly higher (3.3-13.0%) (13).

Here, we describe a case of adrenal PHEO in a patient with NF1. To our knowledge, this is the first case from Turkey.

**CASE REPORT**

A 30-yr-old Turkish man was admitted to our hospital for further examinations of a right adrenal mass, that was incidentally discovered by abdominal ultrasonography during examinations for acute hepatitis B infection in another hospital. From past medical history, the patient had only once had an episode of palpitation, sweating and headache 4 yr before. His family had no history of hypertension and associated familial disorders, including NF1 and multiple endocrine neoplasia type 2 syndromes. On admission, his blood pressure was 110/70 mmHg. He had multiple neurofibromas (>2) over the entire skin (mainly in the trunk and upper extremities), multiple café-au-lait spots (>6 and approximately 4-5 cm in diameter) on the trunk and extremities and skinfold freckling (especially axillary) (Fig. 1). Bilateral ophthalmic examination revealed multiple Lisch nodules (>2) (Fig. 2). Twenty-four-h ambulatory blood pressure monitoring revealed paroximal hypertension attacks (190/148 mmHg). Urinary norepinephrine was 353 µg/24 h (N: 8-100), urinary epinephrine 375 µg/24 h (N: 0.5-20), urinary normetanephrine 3280 µg/24 h (N: 88-444), urinary metanephrine 7684 µg/24 h (52-341) and urinary vanillylmandelic acid 27.7 mg/24 h (N: 3-9). The levels of serum cortisol, calcitonin, intact PTH, carcinoembryonic antigen, α-fetoprotein, serum aldosterone concentrations, plasma DHEA-S and plasma renin activity were within normal range. Abdominal magnetic resonance imaging (MRI) revealed a well-demarcated hyperintense mass measuring 50×45 mm, located in the right adrenal gland, on T2-weighted sequences (Fig. 3). Out of phase, MR image did not show significant signal loss in the

Fig. 1 - Cutaneous neurofibromas and multiple café-au-lait spots on the skin of the trunk.

Fig. 2 - Multiple Lisch nodules (iris hamartomas) on ophthalmic examination (arrows). Panel A, right eye; panel B, left eye.