

Case report

Pheochromocytoma with hypertensive crisis due to glucocorticoid administration: a case report and review of the literature

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Abstract

We report a patient who presented with single episode of severe hypertension after intramuscular injection of betamethasone which was given to treat acute exacerbation of bronchial asthma. Episode of severe arterial hypertension was associated with pulmonary edema, acute renal failure and hyperkalemia. Further evaluation by appropriate diagnostic tests revealed that the patient is a case of pheochromocytoma. This neoplasm was excised successfully and the patient is presently asymptomatic. We believe that this episode was initiated by glucocorticoid injection.

Key words: Betamethasone, glucocorticoids, hypertensive crisis, pheochromocytoma.

Introduction

Pheochromocytoma is a rare neuroendocrine tumor derived from chromaffin cells of the sympathetic nervous system. The clinical manifestations of a pheochromocytoma result from excessive catecholamine secretion by the tumor. Catecholamines typically secreted, either intermittently or continuously, include norepinephrine and epinephrine; rarely, dopamine is secreted. The biological effects of catecholamines are well known. Stimulation of alpha-adrenergic receptors results in elevated blood pressure increased cardiac contractility, glycogenolysis, gluconeogenesis, and intestinal relaxation. Stimulation of beta-adrenergic receptors results in an increase in heart rate and contractility.

Catecholamine secretion in pheochromocytomas is not regulated in the same manner as in healthy adrenal tissue. Unlike the healthy adrenal medulla, pheochromocytomas are not innervated, and catecholamine release is not precipitated by neural stimulation. The trigger for catecholamine release is unclear, but multiple mechanisms have been postulated, including direct pressure, medications, and changes in tumor blood flow.

Relative catecholamine levels also differ in pheochromocytomas. Most pheochromocytomas

secrete norepinephrine predominantly, whereas secretions from the normal adrenal medulla are composed of roughly 85% epinephrine. Familial pheochromocytomas are an exception because they secrete large amounts of epinephrine. Thus, the clinical manifestations of a familial pheochromocytoma differ from those of a sporadic pheochromocytoma.

Typically affected patients present with hypertension and the triad of headache, palpitation, and sweating. However, there are many reports of other unusual presentations.¹ Severe paroxysms of pheochromocytoma have been induced by several drugs.

We report an unusual presentation of pheochromocytoma after steroid administration.

Case report

A 47-year-old man was admitted to the hospital with hypertension and respiratory distress. The patient was visited one day before admission in an outpatient department because of persistent dry cough after an upper respiratory tract infection. He had received 4 mg betamethasone intramuscularly as well as an oral antihistamine. The following day

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he developed palpitation, headache, chest uneasiness, nausea and vomiting. He was severely hypertensive with blood pressure of 200/110 mmHg for which he was referred to our hospital for admission.

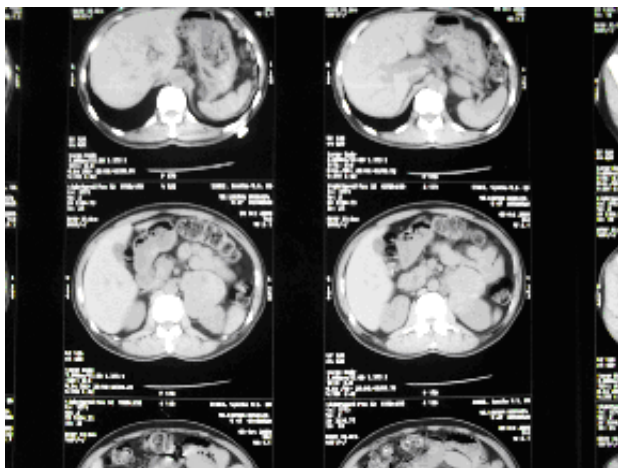


Figure 1: CT scan of Abdomen shows an abnormal image under the left adrenal gland

On admission, he was tachypnic, tachycardic, temperature was 100°F with blood pressure of 200/100 mmHg, and had bilateral crackles over both lung fields. Laboratory findings included the following: Troponine I was negative (0.04 ng/ml), leukocyte count: 13,490 cells/mm³ with 81% polymorphonuclear cells, urea: 75 mg/dL, creatinine: 2.46 mg/dL, erythrocyte sedimentation rate (ESR): 104 mm in 1st hr, hemoglobin (Hb): 12.5 gm/dL, platelet count: 2,01,300/mm³, blood sugar: 10 mmol/L, sodium: 124 mmol/L, and potassium: 6.2 mmol/L. Initial arterial blood gas values were: pH: 7.40, PCO₂: 38.2 mmHg, PaO₂: 88 mmHg, and O₂ saturation: 96% on room air. Chest radiography revealed mild to moderate bilateral pulmonary oedema. Electrocardiography showed sinus tachycardia and Echocardiography showed no regional wall motion abnormality with LVEF was 60%. The patient was treated with intravenous antibiotics with the presumed diagnosis of pneumonia, renal failure and hyperkalaemia. He felt much better on next day with a blood pressure of 137/66 mmHg and O₂ saturation of 96% on room air. After two days of admission, chest radiograph had significantly improved. Further studies showed urine VMA: 26.0 mg/24 hr. Ultrasonography of Whole Abdomen showed renal parenchymal disease with left suprarenal SOL (suspected pheochromocytoma), 24 hours ambulatory blood pressure was recorded which revealed awake time average blood pressure

was 140/90 mm Hg and sleep time average blood pressure was 110/70 mmHg with all antihypertensive medication.

Abdominal computerized tomography scan (CT scan) showed an abnormal mass attached to the inferior border of the left adrenal gland (Figure 1).

The patient underwent left adrenalectomy and the diagnosis of pheochromocytoma was confirmed by pathologic evaluation (Figure 2). Following the surgery, the patient has remained symptom free, although he has not been challenged with high-dose glucocorticoids.

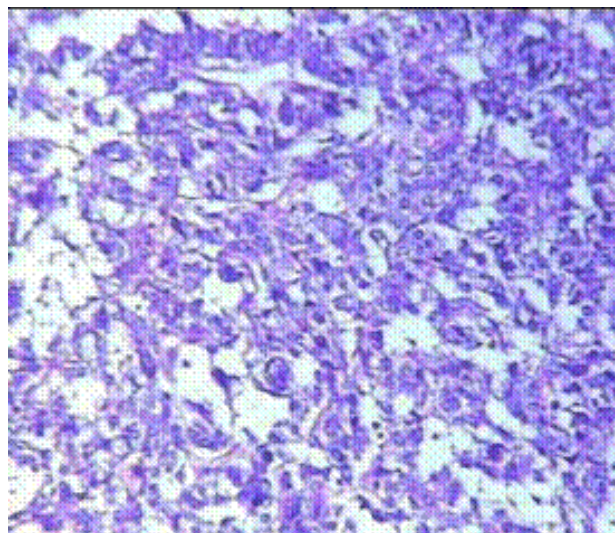


Figure 2: Pathology of the adrenal mass compatible with the diagnosis of pheochromocytoma

Discussion

We present a patient with pheochromocytoma who developed episode of hypertensive crisis 12 hours after steroid administration. Steroids can stimulate enzymes involved in synthesis of catecholamines including tyrosine hydroxylase, dopamine β-hydroxylase, and phenylethanolamine N-methyltransferase (PNMT).²⁻⁴ Steroid administration also augments the release of catecholamines from isolated perfused dog adrenal glands.⁵ Additionally, steroids appear to play a permissive role in the action of catecholamines on peripheral tissues. Administration of ACTH and steroids increases the vasopressor response to infused norepinephrine.⁶

An alternative explanation for clinical presentation of pheochromocytoma after glucocorticoid administration has also been suggested. In adrenal

medulla norepinephrine combines with PNMT to produce epinephrine. A high level of adrenal glucocorticoid is required for PNMT activation, a condition provided by intimate relationship of adrenal cortex to adrenal medulla. So, medullary chromaffin cells are bathed in a sufficiently high level of glucocorticoids to produce epinephrine, provided the adrenal cortex is producing cortisol. Exogenous glucocorticoid administration decreases adrenal steroids production by direct ACTH suppression resulted in decreased PNMT activity and, secondarily, decreased epinephrine production. In patients with pheochromocytoma the vasoconstrictor effect of norepinephrine can be antagonized by epinephrine. By the above-mentioned mechanism, in these patients exogenous glucocorticoid administration would result in increased norepinephrine: epinephrine ratio resulted in unprotected norepinephrine-induced vasopressor effects.⁷

Our patient presented with pulmonary edema, an uncommon manifestation of pheochromocytoma. In such patients pulmonary edema is cardiogenic in origin partially due to severe hypertension. In some patients non-cardiogenic pulmonary edema has also

been reported. This is thought to be due to catecholamine-induced increase in pulmonary capillary pressure and increase in pulmonary capillary permeability.^{8,9} it is difficult to be certain whether pulmonary edema in our patient was cardiogenic or noncardiogenic in origin as pulmonary capillary wedge pressure was not measured.

In our patient presenting features are worth noting. In the admission, fever and leukocytosis raised serum creatinine and high level of serum potassium led to a diagnosis of pneumonia, hyperkalemia, and renal failure. Both diabetic ketoacidosis and lactic acidosis have been reported in patients with pheochromocytoma. The pathophysiology of lactic acidosis in pheochromocytoma is related to increased production of lactate in peripheral tissues or by reduced rate of removal by the liver.¹⁰

In summary, we report a patient with pheochromocytoma who presented with episodes of hypertensive crisis induced by exogenous steroid administration. This presentation, while rare, should alert physicians to the possible presence of pheochromocytoma.

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