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Case Report

Malignant Metastatic Pheochromocytoma: Case Report and Clinical Course

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Abstract: Pheochromocytoma is a rare neuroendocrine tumor that arises from chromaffin cells of the adrenal medulla and secretes excess catecholamines. Clinically, it presents with various symptoms, with a hallmark of treatment-resistant hypertension, often accompanied by paroxysmal episodes of headache, sweating, and palpitations. Although its overall incidence is low, pheochromocytoma should be considered in the differential diagnosis of young patients with refractory hypertension despite the use of multiple antihypertensive agents, particularly when secondary hypertension is suspected. We present the case of a patient who developed a hypertensive crisis and hemodynamic angina, ultimately diagnosed with malignant pheochromocytoma with hepatic and pulmonary metastases.

Keywords: Pheochromocytoma, Catecholamines, Arterial Hypertension, Diagnosis, Case Report.

INTRODUCTION

Pheochromocytoma is a catecholamine-producing neuroendocrine tumor derived from the chromaffin cells of the adrenal medulla [1]. It was first described in the 19th century by pathologist Max Schottelius [2].

Its incidence ranges from 2 to 8 cases per million population per year, with a peak presentation between the ages of 40 and 50. A high hereditary component is present in 30–40% of cases, associated with germline mutations in susceptibility genes [3].

Due to its diverse clinical presentation, pheochromocytoma must be considered in the evaluation of secondary hypertension. Catecholamine hypersecretion from these tumors can mimic over 30 different pathological conditions, including panic attacks, thyrotoxicosis, and hypoglycemia [2-4].

We report the case of a patient with a history of systemic arterial hypertension and type 2 diabetes mellitus who presented with a hypertensive crisis and hemodynamic angina, ultimately diagnosed with a malignant pheochromocytoma. Hepatic and pulmonary metastases were identified during evaluation, leading to multiple complications and surgical interventions. This case highlights the importance of a thorough evaluation for secondary hypertension and early suspicion of pheochromocytoma.

CASE PRESENTATION

A 47-year-old male emergency medical technician with a 10-year history of systemic arterial hypertension, poorly controlled for the past year despite multiple antihypertensives, with blood pressure readings up to 220/110 mmHg. He also had a one-year history of tachyarrhythmia and type 2 diabetes mellitus.

He presented to the emergency department with severe oppressive precordial chest pain (10/10 on the pain scale), radiating to the left arm, accompanied by palpitations and diaphoresis. On admission, his blood pressure was 200/110 mmHg and heart rate 122 bpm. Physical examination was unremarkable. A 12-lead ECG revealed sinus tachycardia. Cardiac enzymes were within normal limits. Cardiology was consulted and adjusted antihypertensive therapy. Due to clinical suspicion of an aortic syndrome, a thoracic CT angiography was performed. Incidentally, it revealed a heterogeneous, bilobed left adrenal mass measuring 12 × 10 × 12 cm.

Despite optimized treatment, the patient continued to exhibit hypertensive episodes with blood pressure >180/110 mmHg and signs of hemodynamic angina. He was transferred to the intensive care unit (ICU) for intravenous antihypertensive therapy, achieving symptom resolution and blood pressure control. He was then admitted to the Internal Medicine service for continued evaluation.

Given the clinical picture and CT findings, secondary hypertension work-up was initiated with suspicion of pheochromocytoma. A 24-hour urine collection revealed elevated metanephrines (1,116 µg/24h), free metanephrines at 142 nmol/L, free normetanephrines >20,000 pg/mL, and total normetanephrines of 20,142 pg/mL, confirming the biochemical diagnosis.

The Medical Oncology service requested a PET-CT with FDG, which revealed a left adrenal mass infiltrating the upper pole of the left kidney and a hypermetabolic lesion in the liver.

A multidisciplinary team (surgical and clinical) decided to proceed with left adrenalectomy and nephrectomy. Given the high likelihood of metastatic spread, a distal pancreatectomy, splenectomy, and diaphragmatic repair were also performed to reduce catecholamine burden, alleviate symptoms, and obtain tissue for biopsy.

Histopathology confirmed an 11.2 × 8.5 cm hemorrhagic carcinoma of the left adrenal cortex with vascular invasion. The tumor capsule showed no invasion; ureter, pancreas, and spleen were free of tumor infiltration.

Due to hepatic metastases detected on PET imaging, a partial hepatectomy (segments IVB and V) and cholecystectomy were performed. A follow-up 24-hour urine collection showed a significant decrease in metanephrine levels (399 µg/24h).

The patient was monitored with annual PET/CT using Ga-68 DOTANOC. One year later, the scan revealed increased somatostatin receptor expression with a rise in the number and size of cervical, mediastinal, and retroperitoneal lymph nodes, along with paravertebral thickening—findings consistent with disease progression. Robotic-assisted para-aortic lymphadenectomy and resection of level IV and V tumors in the left neck were performed.

Subsequent Ga-68 DOTANOC PET/CT revealed new hypermetabolic bilateral pulmonary nodules, predominantly in the right lung, consistent with metastatic deposits. A 200-millicurie dose of Lutetium-177 DOTATATE was administered.

PET-CT and tomography images are not included because the company responsible for performing these imaging studies has changed, and backup is currently unavailable.

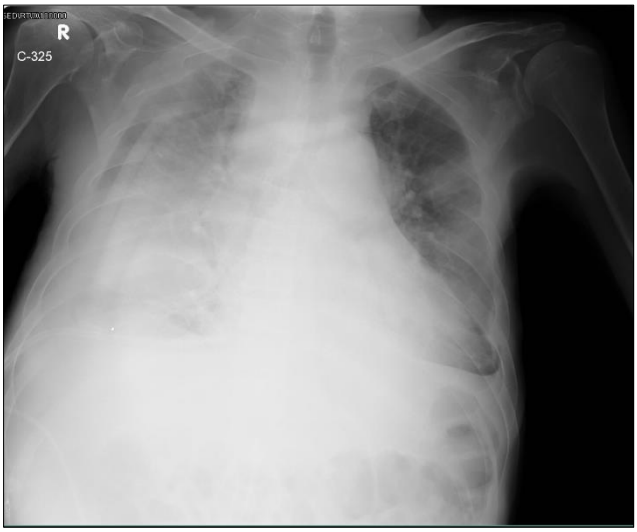

Figure 1: Chest radiograph showing massive malignant right pleural effusion secondary to pulmonary metastasis of pheochromocytoma

Despite radionuclide therapy, the patient presented to the emergency department with dyspnea and oxygen desaturation on room air. Imaging confirmed a large, complex right-sided malignant pleural effusion with septations. Thoracic surgery performed a pleural decortication and chemical pleurodesis. Postoperatively, the patient developed respiratory failure and hemodynamic instability requiring mechanical ventilation. His clinical course deteriorated with the development of pneumonia, ultimately leading to death from septic shock of pulmonary origin.

DISCUSSION

This case describes a rare presentation of malignant pheochromocytoma with hepatic and pulmonary metastases. The patient's age aligns with the typical age of onset reported in the literature (40–60 years), and he exhibited classic symptoms such as palpitations and diaphoresis associated with paroxysmal hypertensive crises [2].

In accordance with international guidelines, the diagnosis of pheochromocytoma requires a specific approach based on clinical suspicion. This includes biochemical testing, typically through plasma or 24-hour urinary metanephrine measurements. In our case, however, the diagnostic process began with the incidental discovery of an adrenal mass on imaging.

Initial evaluation should include plasma metanephrine levels, which offer the highest sensitivity, or alternatively, 24-hour urinary metanephrines. In cases where results are low or borderline, a clonidine suppression test may be performed. Clonidine, an alpha-2 adrenergic agonist, inhibits noradrenergic nerve terminals in the central nervous system. Consequently, normetanephrine levels should also decrease. A reduction of more than 40% in normetanephrine levels indicates a negative test, while a decrease of less than 40% suggests autonomous catecholamine secretion and increases the likelihood of pheochromocytoma.

In this case, additional testing was not necessary due to markedly elevated urinary metanephrines at the time of initial evaluation, confirming the diagnosis both biochemically and through imaging. Following biochemical confirmation, imaging studies are essential for tumor localization.

Genetic testing is also highly valuable, as up to 70% of pheochromocytomas can be classified into three molecular groups based on mutations, which correlate with clinical behavior and prognosis [3-5]. These may include associations with syndromes like von Hippel-Lindau, multiple endocrine neoplasia type 2 (MEN2), and neurofibromatosis type 1 [6].

Surgical resection remains the mainstay of treatment. Due to the high levels of catecholamine production, preoperative alpha-adrenergic blockade for 7 to 14 days is recommended.

In our case, diagnosis was prompted by an incidental imaging finding rather than initial biochemical screening. Nonetheless, elevated urinary metanephrines confirmed the diagnosis. Genetic testing was not performed due to institutional limitations.

Given the presence of a hepatic lesion on imaging and a PASS score of 4, the patient was considered high-risk for metastasis [1]. A PET-FDG scan confirmed hypermetabolic hepatic lesions, justifying an extensive surgical approach including adrenalectomy, nephrectomy, distal pancreatectomy, splenectomy, and hepatic segment resection.

Despite initial control, follow-up PET/CT with Ga-68 DOTANOC revealed progression. Although adjuvant therapies like mitotane have shown potential benefit in recurrent cases, this agent was unavailable in our setting. Additional lymph node resections were performed for disease control.

Progression to the lungs was later confirmed, and the presence of somatostatin receptors enabled treatment with Lutetium-177 DOTATATE radionuclide therapy, currently considered first-line in progressive, receptor-positive disease.

Unfortunately, the patient developed severe complications including a malignant pleural effusion and acute respiratory distress syndrome. Despite surgical intervention and intensive care, the patient succumbed to septic shock.

CONCLUSIONS

This case highlights the diagnostic and therapeutic complexity of malignant metastatic pheochromocytoma. It underscores the importance of early clinical suspicion in patients with secondary hypertension and the necessity of a thorough work-up for timely diagnosis and treatment.

Despite its rarity, the potential for malignancy in pheochromocytomas should always be considered. Early imaging and biochemical testing are crucial for identifying metastases and guiding appropriate multidisciplinary intervention.

Acknowledgments

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