Pheochromocytoma
An unusual cause of angina

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Abstract

A pheochromocytoma is a catecholamine-secreting neuroendocrine tumor derived from chromaffin cells in the adrenal medulla. The annual incidence is two to eight cases per million people, representing a rare cause of secondary arterial hypertension (HTN). These tumors release significant quantities of dopamine, adrenaline and norepinephrine and are responsible for paroxysmal episodes of symptoms like headaches, diaphoresis and tachycardia.

We report the case of a 53-year-old male patient who had a three-year history of self-limited adrenergic symptoms, but whose symptoms on this occasion were coupled with angina, requiring hospitalization. The diagnostic workup led to the incidental finding of a unilateral adrenal tumor on a thoracic computed tomography (CT) angiography, which was completely resected. The patient's condition progressed successfully, and he was discharged. In conclusion, pheochromocytomas are extremely rare tumors that may cause nonspecific symptoms, delaying diagnosis. **(Acta Med Colomb 2024; 49. DOI: https://doi.org/10.36104/amc.2024.2904).**

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Introduction

Pheochromocytomas are neuroendocrine tumors arising from chromaffin cells in the adrenal medulla. The etymology of the word "pheochromocytoma" is derived from the Greek meaning "mass of blackish-brown cells." They are characterized by episodic production of catecholamines from the sympathetic or parasympathetic nervous system (1). The global incidence ranges from two to eight cases per million people, and they affect both sexes equally between the third and fifth decade of life. They account for 23% of adrenal "incidentalomas," and up to 21% are metastatic on presentation (2). Symptoms are characterized by the paroxysmal triad of headache, diaphoresis and tachycardia in 40% of cases, and HTN (occasionally refractory) in 60%. They tend to debut as an incidental finding through x-ray analyses and laboratory tests, and their definitive treatment is surgical (3, 4).

The importance of presenting this case lies in the fact that, since this clinical condition is rare, it is not often suspected when it occurs, thus affecting quality of life and delaying diagnosis until it is found incidentally. Despite this, it has a favorable prognosis and recovery is usually complete. We describe the case of a 53-year-old male patient who consulted due to angina, whose diagnostic workup led to the incidental finding of a pheochromocytoma.

Case presentation

We present the case of a 53-year-old male patient who was a policeman from the northern urban area of Honduras, with a history of HTN and prediabetes diagnosed 17 and three years previously, respectively. He was admitted to the emergency room with a three-year complaint of headaches, palpitations and diaphoresis which self-resolved in minutes. However, on this occasion, they were coupled with angina radiating to the right arm and a feeling of impending doom.

On exam, his blood pressure (BP) was 150/100 mmHg, heart rate (HR) was 115 beats per minute (bpm), respiratory rate was 25 per minute, and temperature was 37 degrees Celsius. He was anxious and diaphoretic but cooperative. He had no jugular distention, and heart and lung auscultation was normal. His abdomen was nonpainful, and normal to palpation, and his extremities were symmetrical, with no edema.

An initial electrocardiogram reported ST segment elevation in the inferior surface and lower lateral leads. His biochemical analysis was normal, except for his troponins and D-dimer reported as 0.037 ng/mL (0-0.014 ng/mL) and 0.60 μg/mL (0-0.5 ug/mL). He was treated as having an acute coronary syndrome with ST segment elevation, with a coronary angiography reporting mildly slow flow in the coronary arteries but no significant lesions.

The patient continued to have pain, and therefore a pulmonary thromboembolism (PTE) was suspected. An angiography tomography was negative for PTE and aortic dissection but revealed a solid heterogenous 66.5 mm x 60.9 mm left adrenal mass (Figure 1).

In light of the electrocardiographic findings, he was seen by cardiology, who performed an echocardiogram showing concentric remodeling of the left ventricle, mild diastolic dysfunction with an 80% ejection fraction, and no motility abnormalities, myocarditis or ischemia.

At the same time, he was evaluated by endocrinology, who ordered measurement of free plasma metanephrine and normetanephrine, a thyroid ultrasound (USG) and thyroid function tests, looking for multiple endocrine neoplasia. They also started him on treatment with terazosin 2 mg/day.

The thyroid USG and thyroid function tests were normal, but the free plasma metanephrine and normetanephrine levels were 0.14 nmol/L (0-0.45 nmol/L) and 28.54 nmol/L (0-0.47 nmol/L), respectively. A triphasic computed tomography of the adrenal glands was performed, as well as abdominal magnetic resonance imaging (MRI), establishing the pheochromocytoma diagnosis. He was then referred to surgical oncology for treatment (Figure 1).

After hemodynamic preparation with terazosin and proper hydration, the patient underwent surgery for complete laparoscopic tumor resection, with no complications (Figure 2). The tumor was sent to pathology, confirming the pheochromocytoma diagnosis (Figure 3).

The patient progressed well and was discharged two weeks later, continuing follow up with oncology, who ordered 30 sessions of radiation therapy and genetic tests, with a reported mutation of the TET2 – S254fs*38 gene.

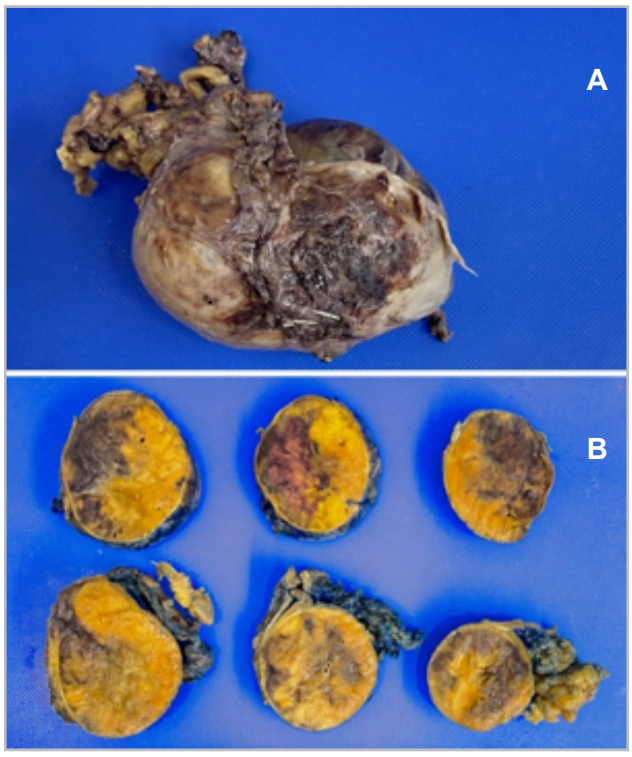

Figure 2. (A) *A vascularized tumor with a brown surface measuring 7.5 x 7 x 5 cm and weighing 123 grams.* **(B)** *A heterogenous yellowish surface with violaceous areas with a hemorrhagic appearance and scant residual peripheral adrenal parenchyma.*

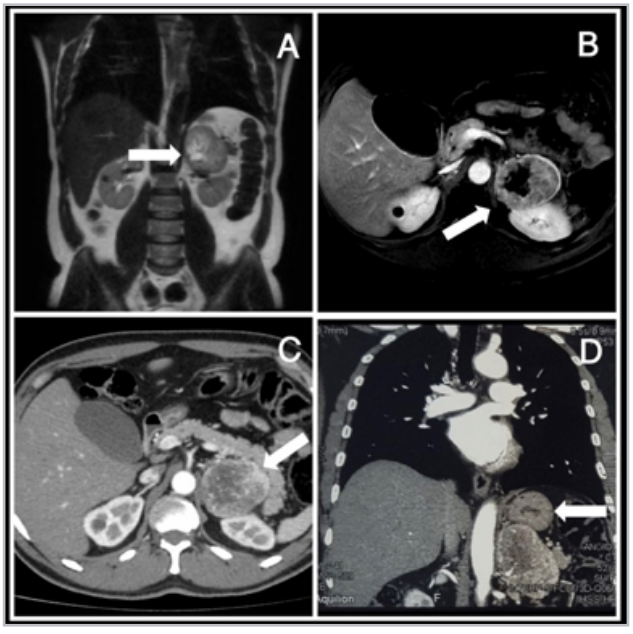

Figure 1. A, B: *An abdominal MRI in the arterial phase.* **C:** *A triphasic abdominal CT.* **D:** *CT angiography of the chest showing a heterogenous left adrenal mass with areas of necrosis and hemorrhage, measuring 66.5 mm x 60.9 mm.*

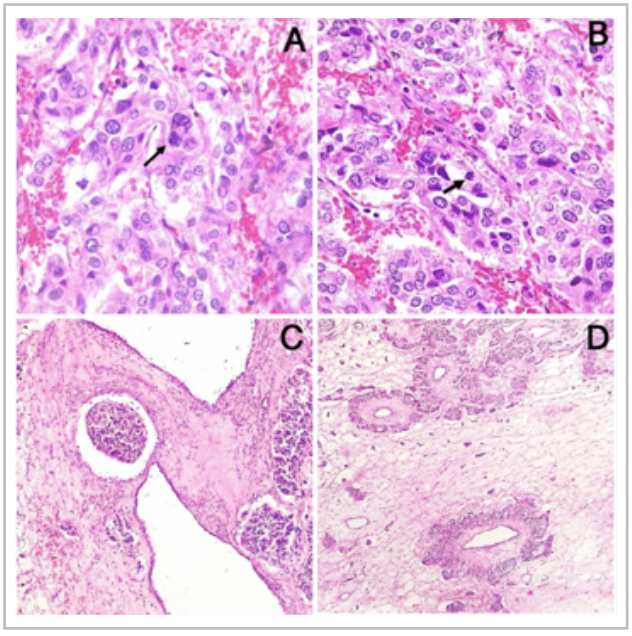

Figure 3. *Microscopic excisional biopsy. A, B, C, D. Hematoxylin eosin staining, showing cells with abnormal mitotic activity scattered in various-sized nests with granular eosinophilic cytoplasm, round nuclei and granular chromatin. There are also necrotic foci with myxoid degeneration and vascular invasion. (A, B: 400x) (C, D: 100x).*

Discussion

This male patient falls within the age range in which most pheochromocytoma cases are diagnosed, usually between the third and fifth decade of life. In a series of 3,783 cases with secondary HTN in Scotland, pheochromocytomas represented 0.1% of all the causes of secondary HTN but, paradoxically, the most frequent clinical presentation was secondary HTN. Therefore, they should be considered as part of the diagnostic workup in patients with secondary HTN (5, 6).

The clinical manifestations may be caused by excess catecholamines, tumor pressure on an organ, or metastasis. The most frequently reported symptoms are paroxysmal tachycardia, pallor, palpitations, headache and diaphoresis. There may also be cardiovascular signs and symptoms like supraventricular arrhythmias, heart failure and sustained HTN in up to 79% of cases, manifesting episodically. Occasionally, HTN can be chronic, damaging organs like the brain, heart and kidneys, altering glucose metabolism and causing prediabetes or diabetes (7, 8).

However, the clinical manifestations will not always be evident, as was the case with our patient, whose clinical diagnosis was masked by the initial suspicion of an acute myocardial infarction, due to the presence of cardiovascular risk factors when he complained of angina. The adrenal tumor was only detected during the search for differential diagnoses.

Due to the increasing availability and use of CTs and MRIs worldwide, 50% of pheochromocytomas are discovered incidentally in asymptomatic patients or during imaging for other reasons (9, 10). Our patient was undergoing a CT angiography in search of other causes of angina when the tumor was detected.

If there are signs and symptoms compatible with catecholamine-secreting tumors, we recommend confirming the excess catecholamines with laboratory tests before ordering imaging studies. This can be done by measuring urinary and/or plasma fractionated metanephrines and catecholamines. The Endocrine Society Clinical Practice Guidelines (ESCPGs) recommend measuring 24-hour urine metanephrines or plasma fractionated normetanephrines, with a cutoff of more than 0.45 nmol/L in 24 hours or more than 0.47 nmol/L, respectively, providing 98% sensitivity and specificity (11). In our patient's case, the mass was confirmed to be adrenal since the plasma normetanephrines were 60 times greater than the normal value.

Once the diagnosis of a catecholamine-secreting tumor has been confirmed, imaging studies must be performed to determine its location, as this provides information regarding the etiology of the tumor. When the tumor is in the adrenal glands, it is classified as a pheochromocytoma; when it has an extra-adrenal origin, this suggests a paraganglioma. Paragangliomas may be located in the upper para-aortic region (46%), lower abdominal para-aortic region (29%), bladder (10%), mediastinum (10%), head and neck (3%), and pelvis (2%) (12).

Regarding imaging studies, a triphasic CT, MRI, 123-metaiodobenzylguanidine scintigraphy, or positron emission tomography are recommended. Computed tomography has a 97-100% sensitivity for locating tumors that are >1 cm. Pheochromocytomas have a particular "imaging phenotype" characterized by being >3 cm, round or oval, with smooth borders, a homogenous texture, areas with cystic degeneration which are usually unilateral, contrast medium uptake, and a radio intensity of >10 Hounsfield units, with < 50% washout. There may be areas of hemorrhage, necrosis or calcifications, with a 1 cm annual growth rate (9, 13). In the presented case, the imaging phenotype was compatible with a pheochromocytoma.

Definitive treatment is complete surgical resection, and the prognosis is generally positive, but requires multidisciplinary management by endocrinology, anesthesiology and surgery to achieve a 76% survival rate (4, 14). Preoperative hemodynamic preparation is necessary, consisting of a pharmacological catecholamine blockade and proper hydration 7-14 days prior to surgery. Catecholamine antagonism is achieved with alpha adrenergic blockers and calcium channel blockers to control BP and HR.

The ESCPGs establish goals for hemodynamic preparation which consist of maintaining the BP at 120/80 mmHg while sitting, a systolic pressure greater than 90 mmHg while standing, and a heart rate between 60 and 80 bpm. A high sodium diet of >5 g per day is also needed, along with optimal hydration. This lowers the risk of intraoperative complications like hypertensive crises (5, 11, 15).

To confirm complete resection, plasma and 24-hour urine metanephrines and catecholamines are measured again two weeks after surgery; if they are normal, the resection was complete. However, if they are still elevated, this indicates residual tumor tissue or occult metastases (6).

Our patient was prepared with terazosin and underwent complete laparoscopic resection with no intraoperative complications, progressing well up to discharge.

In conclusion, this case teaches us that, despite presenting widely recognizable symptoms, the diagnosis requires a specialized approach and a touch of luck.

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