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PHEOCHROMOCYTOMA AND THYROID STORM PRESENTING AS ST-ELEVATION MYOCARDIAL INFARCTION IN A PATIENT WITH NON-OBSTRUCTIVE CORONARY ARTERIES

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ABSTRACT

Introduction: Pheochromocytomas can present as a diagnostic challenge, given their diverse clinical manifestations. Though classically taught as presenting with headaches, palpitations and paroxysmal hypertension, only 1 in 4 present with such a triad. Catecholamines affect the myocardium in various ways, ranging from beta-adrenergic receptor-mediated myofibril dysfunction to direct myocardial injury by catecholamine oxidation products.

Case description: We report the case of a 41-year-old female with no significant past medical history, who presented with acute coronary syndrome. She was found to have myocardial infarction with non-obstructive coronary arteries (MINOCA), and her clinical course was complicated by erratic blood pressure management. Laboratory findings and imaging findings confirmed the diagnosis of pheochromocytoma. Post-cardiac catheterisation, she developed a thyroid storm and fatal cardiac arrest.

Conclusions: The combination of hyperthyroidism with pheochromocytoma is rare but often fatal; iodinated angiography contrast likely precipitated her thyroid storm. This case underscores the importance of considering pheochromocytoma early in patients with MINOCA, particularly in those with erratic blood pressure. Pheochromocytomas have been reported to be associated with MINOCA in rare cases and have significant mortality. Current guidelines do not include pheochromocytoma as a possible differential diagnosis; recognition and early diagnosis are crucial for improved outcomes.

KEYWORDS

MINOCA, pheochromocytoma, thyroid storm, non-obstructive myocardial infarction, STEMI

LEARNING POINTS

- Pheochromocytoma and thyroid disease should be added as recommended differential diagnoses in patients with myocardial infarction with non-obstructive coronary artery disease (MINOCA) despite current guidelines not including them in the routine work-up.
- For patients with erratic blood pressure and MINOCA, the possibility of a pheochromocytoma should be considered early, as a prompt diagnosis can result in favourable outcomes.

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INTRODUCTION

Pheochromocytomas are rare, benign neuroendocrine tumours originating from the neuroectodermal chromaffin cells; they synthesise, store and release catecholamines and have 0.1–0.6% prevalence in the hypertensive population[1]. The majority of the cases of these tumours arise from the adrenal medulla, and around 10–20% are extra-adrenal paragangliomas; of these, 10–20% can become malignant[1]. Though classically taught as presenting with headaches, palpitations and paroxysmal hypertension, only 1 in 4 present with such a triad[2]. Catecholamines affect the myocardium in various ways, ranging from β-adrenergic receptor-mediated myofibril dysfunction to direct myocardial injury by catecholamine oxidation products[2]. Clinically, manifestations range from ST-elevation myocardial infarction to asymptomatic hypertension. Myocardial infarction with non-obstructive coronary artery disease (MINOCA) is defined as the absence of obstructive coronary artery disease on angiography (i.e. stenosis ≥50%) in any potential infarct-related artery in a patient meeting the acute myocardial infarction (AMI) criteria[3].

CASE DESCRIPTION

A 41-year-old non-smoking, non-alcoholic female with no significant past medical history presented to the emergency department with sudden-onset substernal chest pain radiating to her left shoulder and jaw. She also reported shortness of breath that had begun 10 minutes before the chest pain. Vital signs revealed a blood pressure of 220/112 mmHg bilaterally in both arms, with a regular heart rate of 121 beats/min. Her respiratory rate was 24 breaths/min, with a normal saturation on room air. On physical examination, she appeared anxious, alert and responsive. The point of maximal impulse was slightly displaced, and auscultation revealed a loud S2 and S4. Lower extremity pulses were equal, and mild basal crackles were noted in the bilateral lower lobes. Her neurological examination was unremarkable. Basic laboratory panels were unremarkable, including complete blood count and comprehensive metabolic panel. An EKG revealed ST elevations in the precordial leads, and her first troponin level was elevated at 7.549 ng/ml (reference: 0–0.033 ng/ml). The patient was quickly taken to the cardiac catheterisation laboratory for a left heart catheterisation. Angiography revealed patent coronaries with good blood flow (Fig. 1). She was diagnosed with MINOCA and placed on heparin infusion, an arterial line was placed, and she was transferred to the intensive care unit for blood pressure management. Her blood pressure improved to 160/102 mmHg with intravenous esmolol, and her chest pain began to resolve; an echocardiogram was obtained, which showed a normal ejection fraction. A computed tomography of the abdomen and pelvis with contrast showed a right-sided adrenal mass.

Ten hours into her hospitalisation, her blood pressure became difficult to control, reaching 206/116 mmHg with a heart rate of 125/min and a temperature of 38.6°C. A bolus of esmolol (250 mcg/kg) was administered, followed by an esmolol infusion at 50 mcg/kg/min. This resulted in a drastic drop in blood pressure to 60/31 mmHg, necessitating the immediate cessation of the esmolol infusion. Despite efforts, her blood pressure continued to fluctuate. Norepinephrine was initiated to address hypotension, but with a low dose of norepinephrine infusion her blood pressure suddenly increased again to 180 mmHg systolic; ultimately, her blood pressure stabilised on 25 mcg/kg/min of esmolol.

Laboratory investigations were requested, including thyroid-stimulating hormone, free T4 and T3, renin/aldosterone ratio, morning cortisol, blood cultures, urine analysis, plasma metanephrine and normetanephrine levels. Her thyroid-stimulating hormone was undetectable, free T4 was 4.65 ng/dl (reference: 0.75–1.46 ng/dl) and free T3 was 35 ng/dl (reference: 2.15–4 ng/dl). The aldosterone-renin ratio was 17 (normal < 25) and AM cortisol was 11.7 mcg/dl (reference: 5–25 mcg/dl). Plasma metanephrine was elevated at 2.18 nmol/l (reference: <0.5 nmol/l) and plasma normetanephrine was 3.02 nmol/l (reference: <0.9 nmol/l). Given these findings, suspicion of a thyroid storm with underlying pheochromocytoma was high. A Burch-Wartofsky score was calculated, yielding an elevated score of 60 points.

At this point, the patient was started on hydrocortisone and propylthiouracil, followed by Lugol's iodine; her esmolol infusion was continued. While the patient's condition initially stabilised over the next day, overnight she experienced a

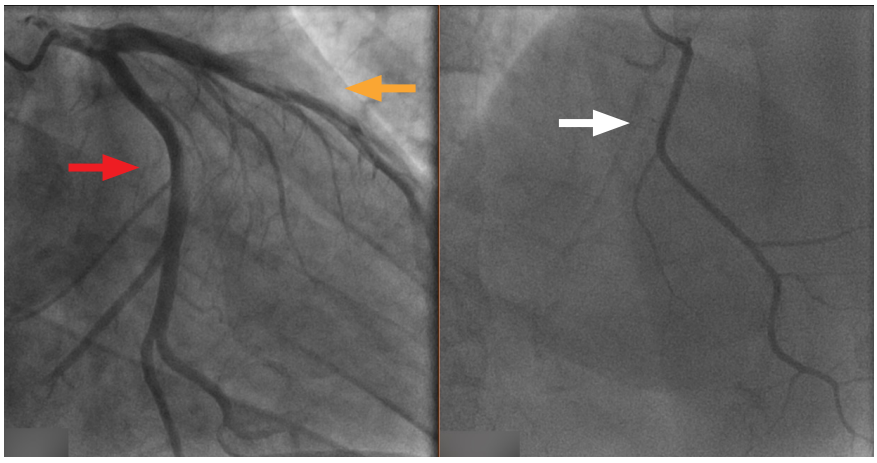


Figure 1. Patent flow in the left anterior descending (yellow arrow), left circumflex (red arrow) and right coronary artery (white arrow).

cardiac arrest with ventricular fibrillation. Despite multiple rounds of cardiopulmonary resuscitation and defibrillation, regrettably, she did not revive and passed away.

DISCUSSION

According to the European Society of Cardiology guidelines, myocardial infarction with non-obstructive coronary artery disease (MINOCA) is defined as the absence of obstructive coronary artery disease on angiography (i.e. stenosis ≥50%) in any potential infarct-related artery in a patient meeting the AMI criteria[3]. MINOCA affects 6–8% of patients presenting with an AMI[3]. Its pathogenesis is heterogeneous and poorly understood; MINOCA is an interim diagnosis requiring additional diagnostic evaluation until a specific aetiology is identified[3].

Current guidelines include coronary artery vasospasm, plaque disruption, coronary venous thromboembolism, coronary dissection, takotsubo cardiomyopathy, unrecognised myocarditis and other forms of type 2 myocardial infarction as common differential considerations in patients with MINOCA[3]. Notably, the guidelines do not include pheochromocytoma as a possible differential diagnosis. An increasing body of literature reports underlying pheochromocytoma associated with MINOCA[4].

All patients with acute coronary syndrome are at increased risk of adverse outcomes, both during and after hospitalisation. Studies specifically evaluating the association between MINOCA and adverse cardiovascular outcomes have yielded conflicting results, with some reporting a more unfavourable prognosis and others reporting an adverse outcome rate approximately half that of those with obstructive coronary artery disease[5]. These patients pose a diagnostic, clinical and therapeutic challenge.

Pheochromocytomas are benign tumours of neuroectodermal origin; chromaffin cells produce and store the catecholamines, which are released in either a continuous pattern or pulsating manner. About half of the adrenal tumours produce a mixture of epinephrine and norepinephrine; however, the rest produce norepinephrine exclusively or occasionally dopamine in conjunction with epinephrine[1]. Generally, norepinephrine is released continuously, resulting in persistent hypertension, whereas epinephrine is released in pulses, resulting in tachyarrhythmias. The effect of these catecholamines is mediated by the α1-, α2- and β1-, β2-adrenoreceptors[1].

Different mechanisms have been postulated for cardiac myocyte injury caused by increased circulating catecholamines. Persistently elevated levels of catecholamines have been related to the downregulation of beta-adrenergic receptors, resulting in myofibril dysfunction and reduction of the contractile units[2]. Catecholamine excess is also linked to increased sarcolemma permeability, elevated cytosolic calcium concentration and even direct myocardial necrosis[2]. Alpha-adrenergic stimulation can result in intense vasoconstriction and coronary vasospasm[2]. Focal degeneration and contraction band necrosis of the myocytes, along with monocytic infiltration, have been reported in 50% of autopsies of patients who died from pheochromocytoma; these findings are likely to cause significant ventricular dysfunction[6].

The combination of hyperthyroidism with pheochromocytoma is rare but can be fatal. Concomitant hyperthyroidism can sometimes mask the underlying pheochromocytoma[1]. Thyroid hormones potentiate the effects of catecholamines on the cardiovascular system[1]. This milieu of high catecholamines and thyroid hormones can become catastrophic for patients, particularly in the context of thyroid storms.

We believe that in our case, the patient had both hyperthyroidism and pheochromocytoma, which were previously undiagnosed. These may have led to an initial hypertensive episode along with the coronary vasospasm, leading to an ST-elevation myocardial infarction. The contrast used in the angiogram may have tipped the patient over into the thyroid storm and to make matters worse, the ongoing beta blockage by esmolol was the possible reason for the second fatal coronary spasm, which led to her unfortunate demise.

For patients with erratic blood pressure and MINOCA, the possibility of a pheochromocytoma should be considered early, as a prompt diagnosis can result in more favourable outcomes. A detailed history, including a history of intermittent symptoms before the index hospitalisation, should be obtained. Biochemical testing for catecholamines and metanephrines should be conducted by measuring plasma levels. If ambiguous, 24-hour urine fractionated metanephrines and catecholamines should be obtained. Imaging of the abdomen and pelvis is also indicated to locate the tumour. Evaluation for pheochromocytoma should be added as part of the routine diagnostic workup for MINOCA.

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