Journal of Taibah University Medical Sciences (2020) 15(3), 244–248

Taibah University

Journal of Taibah University Medical Sciences

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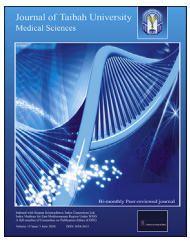

Case Report

Congestive heart failure and upper extremity deep vein thrombosis: A rare presentation of a pheochromocytoma

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Received 19 September 2019; revised 15 March 2020; accepted 18 March 2020; Available online 1 May 2020

الملخص

ورم القواتم هو ورم نادر يفرز هرمونات الكاتيكولامين ويحدث في حوالي ٠.١-٠.٥٪ من مرضى ارتفاع ضغط الدم. تشمل علامات ورم القواتم وأعراضه عادة ارتفاع ضغط الدم ونوبات من الصداع والتعرق والخفقان. في حالات نادرة قد يشكو المريض من أعراض وعلامات أقل شيوعا من الأعراض التقليدية لورم القواتم.

في هذا التقرير نناقش حالة سيدة كانت أعراض شكواها الأساسية فشل القلب الاحتقاني وجلطة في الأوردة العميقة للبد اليمنى، ثم تم تشخيصها بورم القواتم. مع العلاج الطبي والجراحي تم شفاء اعتلال عضلة القلب بالكامل وتم علاج الجلطة بأدوية منع تخثر الدم.

يعتبر ورم القواتم أحد العلل المسببة لفشل القلب المفاجئ وغير المبرر و/أو سبب لجلطة الأوردة العميقة.

يمكن شفاء اعتلال عضلة القلب الناجم عن ورم القواتم بالعلاج الطبي والجراحي.

الكلمات المفتاحية: ورم القواتم؛ فشل القلب الاحتقاني؛ جلطة في الأوردة العميقة؛ ارتفاع ضغط الدم؛ أورام مفرزة للكاتيكولامين

Abstract

Pheochromocytomas are rare catecholamine-secreting neoplasms, occurring in approximately 0.1–0.5% of the patients with hypertension. Typically, a pheochromocytoma presents with hypertension, a paroxysm of headaches, sweating, and palpitation. However, patients may also present with atypical clinical manifestations on rare occasions. This report presents a case involving a young woman who presented with two rare manifestations of pheochromocytomas: congestive heart failure and right upper extremity deep vein thrombosis (DVT). Her cardiomyopathy was completely resolved by surgical and medical therapy, while DVT was resolved with anticoagulation. Pheochromocytoma should be considered in case of sudden and unexplained cardiac failure and/or DVT. Pheochromocytoma-induced cardiomyopathy can be reversed with medical and/or surgical therapy for pheochromocytomas.

Keywords: Catecholamine-secreting neoplasms; Congestive heart failure; Deep vein thrombosis; Hypertension; Pheochromocytoma

Introduction

Pheochromocytomas are rare catecholamine-secreting neoplasms, occurring in approximately 0.1–0.5% of the patients with hypertension.[1] The incidence of pheochromocytomas is equal among men and women and pheochromocytomas usually manifests in the third to fifth decades of life.[2]

Catecholamine secretion due to pheochromocytoma may occur either intermittently or continuously. Alpha-adrenergic receptor stimulation causes increased blood pressure (BP), enhanced cardiac contraction, gluconeogenesis, and glycogenolysis, whereas beta-adrenergic receptor stimulation causes increased heart rate and contractility.[3]

Patients with pheochromocytoma usually present with hypertension and spells or paroxysms of headaches,

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Peer review under responsibility of Taibah University.

ELSEVIER Production and hosting by Elsevier

 https://doi.org/10.1016/j.jtumed.2020.03.010

sweating, pallor, tremor, and palpitation.[4] Hypertension may be sustained or paroxysmal and associated with occasional orthostatic hypotension.[2] In some patients, the BP may be normal, particularly if a pheochromocytoma is diagnosed in an early stage.[2] Other clinical manifestations of pheochromocytoma include anxiety, panic attacks, hypertensive retinopathy, constipation, weight loss, hyperglycaemia, and diabetes mellitus. Rarely, pheochromocytomas may be asymptomatic despite high catecholamine levels.[2]

Untreated pheochromocytomas may lead to hypertensive crisis, encephalopathy, pulmonary oedema, cardiac arrhythmias, or even death.[5] The five-year survival for benign tumours is approximately 95%, and the recurrence rate is <10%. Effective surgical removal can treat hypertension in most patients.[5]

Cardiac manifestations of pheochromocytoma include hypertension, tachycardia, left ventricular hypertrophy, arrhythmias, acute coronary syndrome, and heart failure.[6] Cardiomyopathy and congestive heart failure (CHF) are relatively rare and are, thus, frequently missed by clinicians.[7–14] Although cardiomyopathy worsens the prognosis of a pheochromocytoma and increases the surgical risk, it may be totally reversible with tumour resection.[11,15]

Venous thromboembolism is a very rare complication of pheochromocytoma with few reported cases.[16–20]

In this report, we discuss an interesting case involving a young woman who presented with two rare presentations of pheochromocytoma, namely, CHF and upper extremity deep vein thrombosis. Her cardiomyopathy was completely reversed with medical and surgical therapy for the pheochromocytoma, and the DVT was resolved with anticoagulation.

Case report

A 34-year-old woman without a medical or surgical history presented to the emergency department with painful right upper limb swelling for 2 days. Additionally, she complained of dyspnoea, orthopnoea, dry cough, bilateral lower extremity oedema, palpitation, and low exercise tolerance that have been ongoing for a few weeks before admission. She had no history of chest pain, haemoptysis, joint problem, or skin changes. She admitted that she had lost some weight recently and had no history of recent travel or immobilisation. The patient was a mother of three children and had a regular menstrual cycle without a history of abortions. Her family history was negative for cardiac or pulmonary diseases and malignancy.

On presentation, the patient was ill-looking, thin lady, afebrile, tachycardic at 120 BPM, and BP 140/82 mmHg. The physical exam revealed right upper limb swelling with some tenderness but without skin changes, decreased breath sounds in her chest with bilateral basal crackles, and bilateral pitting lower extremity oedema. Other examination results were unremarkable.

Upper extremity duplex was positive for venous thromboembolism in the right subclavian, axillary, and brachial veins.

Electrocardiogram on admission revealed sinus tachycardia, without ischaemic changes. Echocardiogram showed global hypokinesia without wall thickening or concentric hypertrophy, and an estimated left ventricular ejection fraction (LVEF) of 15% with moderate mitral and tricuspid valve regurgitation and a small pericardial effusion. (The patient had no previous history of cardiac disease.)

CHF was treated with anti-failure medications: furosemide, spironolactone, perindopril, digoxin, and carvedilol. DVT was initially treated with subcutaneous low-molecular-weight heparin and then oral warfarin that continued for 3 months.

Subsequently, an abdominal ultrasound was performed, revealing an incidental partially solid mass at the upper pole of the left kidney, measuring 5.0 × 4.8 × 3.8 cm. Abdominal magnetic resonance imaging showed a left adrenal gland mass with high signal intensity (a 'light-bulb' bright lesion) (Figure 1).

An endocrine referral was performed to evaluate the adrenal incidentaloma. Further examinations revealed no history of hypertension, spells of headache, sweating, or tremor. No clinical manifestations of Cushing's syndrome or hyperandrogenism were observed. Family history was negative for any endocrine disease. Laboratory investigations revealed serum cortisol level of 703 nmol/l, and 1 mg of dexamethasone suppressed to 54 nmol/l. A 24-h urine for metanephrine excretion was 9.5 (reference range, 0–1.49) umol/day, and normetanephrine excretion of 3.83 (reference range, 0–3.43) umol/day, which confirmed the pheochromocytoma diagnosis.

The patient was started on phenoxybenzamine, which improved her LVEF to 20–25% within days. She was discharged from the hospital in a stable condition with planned surgical intervention after heart failure stabilisation.

Four months after her presentation, laparoscopic adrenalectomy was performed after an adequate preoperative preparation, including BP control with alpha (phenoxybenzamine 10 mg three times a day) and beta-blockers (carvedilol 12.5 mg twice a day) and correction of fluid volume with isotonic sodium chloride solution. Surgery was successful without significant complications. Histopathological examination confirmed the diagnosis of pheochromocytoma with a size 7 × 4 × 3 cm but without capsular or vascular invasion.

Serial follow-up at the outpatient clinic revealed normal BP with progressive improvement in the left ventricular systolic function. Her echocardiogram at 5 months

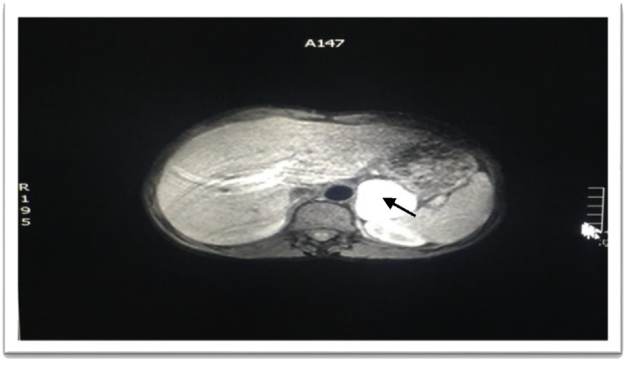

Figure 1: Magnetic resonance imaging of the abdomen showing the left adrenal gland mass (arrow) with high signal intensity (a 'light-bulb' bright lesion).

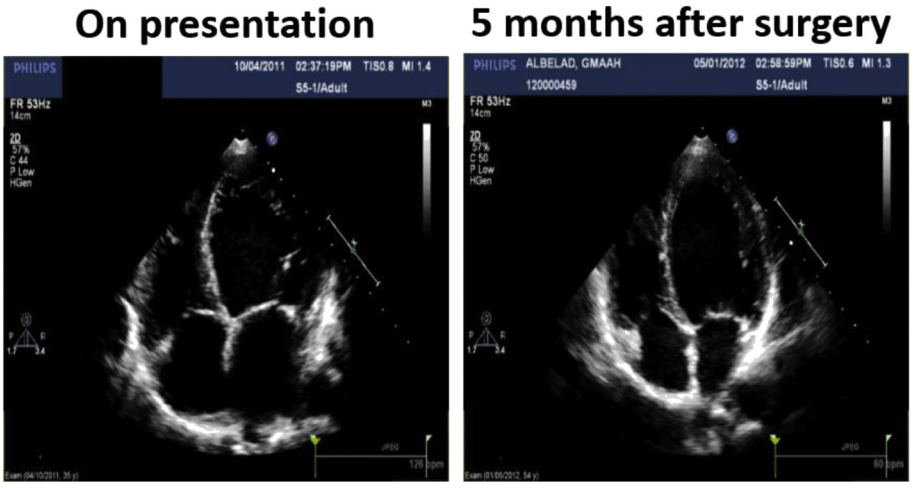

Figure 2: Four-chamber echocardiogram showing dilated heart on presentation and recovery 5 months post-surgery.

postoperatively showed an improved LVEF of 60%. The patient was completely asymptomatic, and hence, her anti-failure medications were gradually discontinued. The DVT was resolved with anticoagulation administered for 3 months.

Discussion

This is an interesting case because the patient did not present with usual manifestations of pheochromocytoma but presented with two unusual presentations: heart failure and venous thromboembolism, both of which were reported rarely in patients with pheochromocytoma.[2–14] However, to the best of our knowledge, this is the first case report describing the two rare manifestations in a single patient.

While pheochromocytoma often causes hypertension and episodic triad of headaches, sweating, and palpitation, these clinical features are not essential for its diagnosis. Hypertension is present in at least 90% of patients and is most commonly sustained with episodic severe hypertension and occasional orthostatic hypotension. Paroxysms of hypertension occur in approximately 30–50%. Some patients may be completely normotensive.[2] In the setting of decompensated heart failure, BP might decrease due to low cardiac output, which could contribute to the apparently normal BP in this patient.

Excessive catecholamine secretions due to pheochromocytoma can damage the cardiac myocytes and causes cardiomyopathy.[21] Pheochromocytoma should be considered as a differential diagnosis of sudden and inexplicable heart failure even though initial presentations are not typical for pheochromocytoma.[7–14] Possible pathogenesis of catecholamine-induced cardiomyopathy includes myocardial fibre injury, coronary vasoconstriction, and tachycardia.[21] Left ventricular hypertrophy and hypertensive cardiomyopathy may occur in patients with chronic hypertension from pheochromocytoma. In addition, the long-term elevation of catecholamine levels leads to significant desensitisation of beta-adrenergic receptors.[10] Oxidised catecholamines may increase the permeability of the sarcolemmal membrane, leading to calcium influx and intracellular calcium overload, which may can result in acute myocarditis, with diffuse interstitial inflammatory infiltrates and myocardial necrosis.[9]

Catecholamine-induced cardiomyopathy may present in several forms.[12,22,23] Zhang et al. assessed the association of pheochromocytoma with cardiomyopathy in a literature review and found "163 cases: 63 with dilated cardiomyopathy, 38 Takotsubo cardiomyopathy, 30 inverted Takotsubo cardiomyopathy, 10 hypertrophic cardiomyopathy, 8 myocarditis, and 14 unspecified cardiomyopathy."[11] Among them, dilated, Takotsubo, and hypertrophic cardiomyopathy are the three main types of catecholamine-induced cardiomyopathy that can complicate pheochromocytoma.[14] In dilated cardiomyopathy, the left ventricle (LV) will be dilated and possibly the right ventricle without or minimal wall thickening and global hypokinesia.[8,12] Takotsubo cardiomyopathy (a stress-induced cardiomyopathy) may typically be induced by stressful emotional or physical experiences (primary Takotsubo cardiomyopathy) but may occur in patients with pheochromocytoma during the time of excessive catecholamine surge. Takotsubo cardiomyopathy is characterised by transient hypokinesia of the left ventricular apex and apical ballooning along with hypercontractility at the base.[24] Reversed Takotsubo cardiomyopathy is characterised by hypokinesia of the basal parts of the left ventricle with hyperkinesia of the apex.[7] The prognosis for Takotsubo cardiomyopathy is generally favourable and resolves within days to weeks.[22,23] In hypertrophic cardiomyopathy, a significant thickening of the LV wall is observed with normal or reduced sizes of the internal cavity. Left ventricular hypertrophy simulating hypertrophic obstructive cardiomyopathy was rarely reported as a complication of pheochromocytoma.[25] The echocardiogram of our patient revealed global hypokinesis without apical ballooning, wall thickening, or concentric hypertrophy; therefore, dilated cardiomyopathy is the likely type of her heart failure. Cardiomyopathy can be totally reversed with medical[26] and/or surgical therapy of pheochromocytoma.[9,19] In the current patient, the ejection fraction increased from 10% to 25% after a few days from starting medical therapy and then increased further to 60% after 5 months postoperatively (Figure 2 and Supplementary material).

Venous thromboembolism has been infrequently described among patients with pheochromocytoma.

Different sites for DVT were reported: intracardiac, inferior vena cava, upper and lower limb veins, and cerebral sinuses thrombosis.[16–20] Arterial thrombosis and systemic embolisation were also reported.[18] The mechanism of thrombosis in pheochromocytoma remains uncertain, but different mechanisms are implicated. Excess catecholamines can directly contribute to hypercoagulability and increase platelet aggregation.[20] Direct vein compression of the mass is another mechanism. Pheochromocytoma can induce polycythaemia due to erythropoietin secretion particularly in case of malignant pheochromocytoma.[19] In addition to pheochromocytoma as a risk for the current patient's DVT, heart failure may boost the risk of increased blood stasis and immobilisation.

Conclusion

Patients with pheochromocytoma may present with atypical symptoms; therefore, a high index of suspicion is required to ensure proper management and avoid complications. Pheochromocytoma should be carefully considered in case of sudden and unexplained cardiac failure and/or DVT. Cardiomyopathy associated with pheochromocytoma can be treated with medical and/or surgical therapy for pheochromocytoma.

Source of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The author have no conflict of interest to declare.

Ethical approval

The Institutional Review Board (IRB), General Directorate of Health Affairs in Almadinah Almunawwarah is fully compliant with the conditions and principles of good clinical practice. The committee is constituted in accordance with the WHO and ICH-GCP guidelines and works according to written Standard operating Procedures.

Acknowledgment

My deep thanks and appreciation to Dr. Faisal Alatawi for providing the video of the echocardiogram of this patient.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jtumed.2020.03.010.

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How to cite this article: Alfadhli EM. Congestive heart failure and upper extremity deep vein thrombosis: A rare presentation of a pheochromocytoma. J Taibah Univ Med Sc 2020;15(3):244–248.