CASE REPORT

Pheochromocytoma presenting as an acute coronary syndrome complicated by acute heart failure: The challenge of a great mimic

Giuseppe Damiano Sanna [a,*], Giuseppe Talanas [a], Giuseppina Fiore [a], Antonella Canu [a], Pierfranco Terrosu [a]

[a] Unità Operativa di Cardiologia, Ospedale SS Annunzia, Sassari

[a] Italy

Pheochromocytoma is a rare neuroendocrine tumor with a highly variable clinical presentation. The serious and potentially lethal cardiovascular complications of these tumors are related to the effects of secreted catecholamines. We describe a case of a 50-year-old woman urgently admitted to our hospital because of symptoms and clinical and instrumental findings consistent with an acute coronary syndrome complicated by acute heart failure. Urgent coronary angiography showed normal coronary arteries. During her hospital stay, the recurrence of episodes characterized by a sudden increase in blood pressure, cold sweating, and nausea allowed us to hypothesize a pheochromocytoma. The diagnosis was confirmed by elevated levels of urinary catecholamines and by the finding of a left adrenal mass on magnetic resonance imaging. The patient underwent left adrenalectomy. Therefore, the initial diagnosis was critically reappraised and reviewed as a cardiac manifestation of a pheochromocytoma during catecholaminergic crisis.

Keywords: Acute coronary syndrome, Arterial hypertension, Heart failure, Pheochromocytoma

Introduction

Pheochromocytoma is a neuroendocrine tumor. Clinical presentation is highly variable and pheochromocytoma is often defined as a great mimic.

Case report

A 50-year-old woman was admitted to the Emergency Room for epigastric pain, dyspnea, nausea, emesis, and cold sweating ongoing for 10 hours. Her medical history included arterial hypertension diagnosed 10 years before, poorly controlled despite combination therapy. A few

Disclosure: Authors have nothing to disclose with regard to commercial support.

Received 11 January 2016; revised 30 January 2016; accepted 2 February 2016.
Available online 10 February 2016

* Corresponding author at: Unità Operativa di Cardiologia, Ospedale SS Annunzia, Via Enrico de Nicola, Sassari 07100, Italy.
E-mail address: giuseppedasanna@tiscali.it (G.D. Sanna).

P.O. Box 2925 Riyadh – 11461KSA
Tel: +966 1 2520088 ext 40151
Fax: +966 1 2520718
Email: sha@sha.org.sa
URL: www.sha.org.sa

Peer review under responsibility of King Saud University.
URL: www.ksu.edu.sa
http://dx.doi.org/10.1016/j.jsha.2016.02.002

Production and hosting by Elsevier

days prior to hospital admission, electrocardiogram (ECG) and echocardiogram were normal, and antihypertensive therapy (including an angiotensin-converting enzyme inhibitor and a thiazidic diuretic) was enhanced by adding spironolactone 25 mg/d and atenolol 50 mg/d.

At presentation, physical examination showed cold and sweaty skin, tachycardia, and pulmonary basal rales. Arterial blood pressure (BP) was 170/110 mmHg. ECG showed a sinus tachycardia with negative T waves in precordial leads (Fig. 1A). The echocardiogram showed regional wall motion abnormalities (hypokinesia of interventricular septum, anterior wall, and apex) resulting in severe left ventricular systolic dysfunction (ejection fraction 30%).

The patient was thus admitted to our intensive care unit where the diagnosis of a non-ST elevation myocardial infarction was made due to the presence of ECG abnormalities together with increased cardiac enzymes [troponin I 2.4 ng/mL (normal value 0.00–0.15 ng/mL)]. An urgent invasive strategy was planned. Coronary arteries were normal angiographically (Fig. 1B and C).

After a first period of clinical stability, the recurrence of paroxysmal episodes characterized by a sudden increase in BP, cold sweating, and nausea allowed us to hypothesize a pheochromocytoma. This diagnostic hypothesis was first supported by elevated urinary catecholamines [noradrenaline 2433 μg/24 h (normal value 15–80 μg/24 h)]. Magnetic resonance imaging showed a left adrenal mass consistent with a pheochromocytoma (Fig. 2A). An alpha-adrenergic blocker (doxazosin 4 mg/d) was added to the patient therapy. Thereafter, a progressive improvement of clinical status was observed; left ventricular systolic function returned within normal limits (ejection fraction 55%) and ECG normalized (Fig. 2B). The patient underwent left adrenalectomy (Fig. 2C). Intraoperative management was based on the lessening of sympathetic tone, avoiding some drugs, and blunting the sympathetic response during anesthesia induction and tracheal intubation. Minor changes in systemic hemodynamics occurred during surgical manipulation of the tumor and they were easily managed. The postoperative hospital stay was uneventful and BP normalized without the use of any drug.

Discussion

Pheochromocytomas are rare neuroendocrine tumors secreting catecholamines that arise from chromaffin cells of the sympathetic nervous system. Common clinical manifestations include hypertension, tachycardia, and feelings of panic or anxiety, while nausea, fever, and flushing are less common [1]. Cardiovascular complications include myocardial infarction, cardiac arrhythmias, and heart failure due to toxic cardiomyopathy [2]. Although the prevalence of pheochromocytomas in hypertensive patients is reported to be 0.1–0.6% [3], the relatively higher prevalence in necropsy findings suggests that many tumors are undiagnosed.

We would like to draw attention to certain key aspects of our report, first of all the medical history of the patient. Arterial hypertension was not adequately investigated at the moment of initial diagnosis (the patient was hurriedly labeled as having a primary arterial hypertension). Moreover, the poor BP control during the follow up should have inspired a critical reappraisal of the initial diagnosis.

The second aspect is related to the changes in drug therapy during the last follow-up visit prior to hospital admission when atenolol and spironolactone were added to the patient therapy. Because atenolol has been introduced, we may presume its pathogenic role in triggering a catecholaminergic crisis. In this setting it is reported that blockade of β-adrenoceptors should never be initiated before blockade of α-adrenoceptors, because the loss of β-adrenoceptor mediated vasodilatation leaves α-adrenoceptors stimulation unopposed resulting in hypertensive crises [1].

Whatever the trigger mechanism of catecholaminergic crises may be, our patient suddenly experienced symptoms consistent with an acute coronary syndrome complicated by a dramatic reduction in left ventricular function (normal before hospital admission). Coronary arteries were normal.

The recurrence of a sudden increase in BP, nausea, and cold sweating led us to hypothesize a catecholamine excess, confirmed by both elevated levels of urinary catecholamines and by the finding of a large left adrenal mass during magnetic resonance imaging. Therefore, the initial diagnosis of acute coronary syndrome was critically reviewed as a cardiac manifestation of a pheochromocytoma during a catecholaminergic crisis, as previously described by other authors [4–6].

Although the majority of patients with pheochromocytoma have a normal echocardiogram, the pattern of left ventricular dysfunction may be different, sometimes resembling a takotsubo or a reverse takotsubo cardiomyopathy [7,8]. Similarly to takotsubo syndrome, left ventricular dysfunction is transient and usually recovers

CASE REPORT

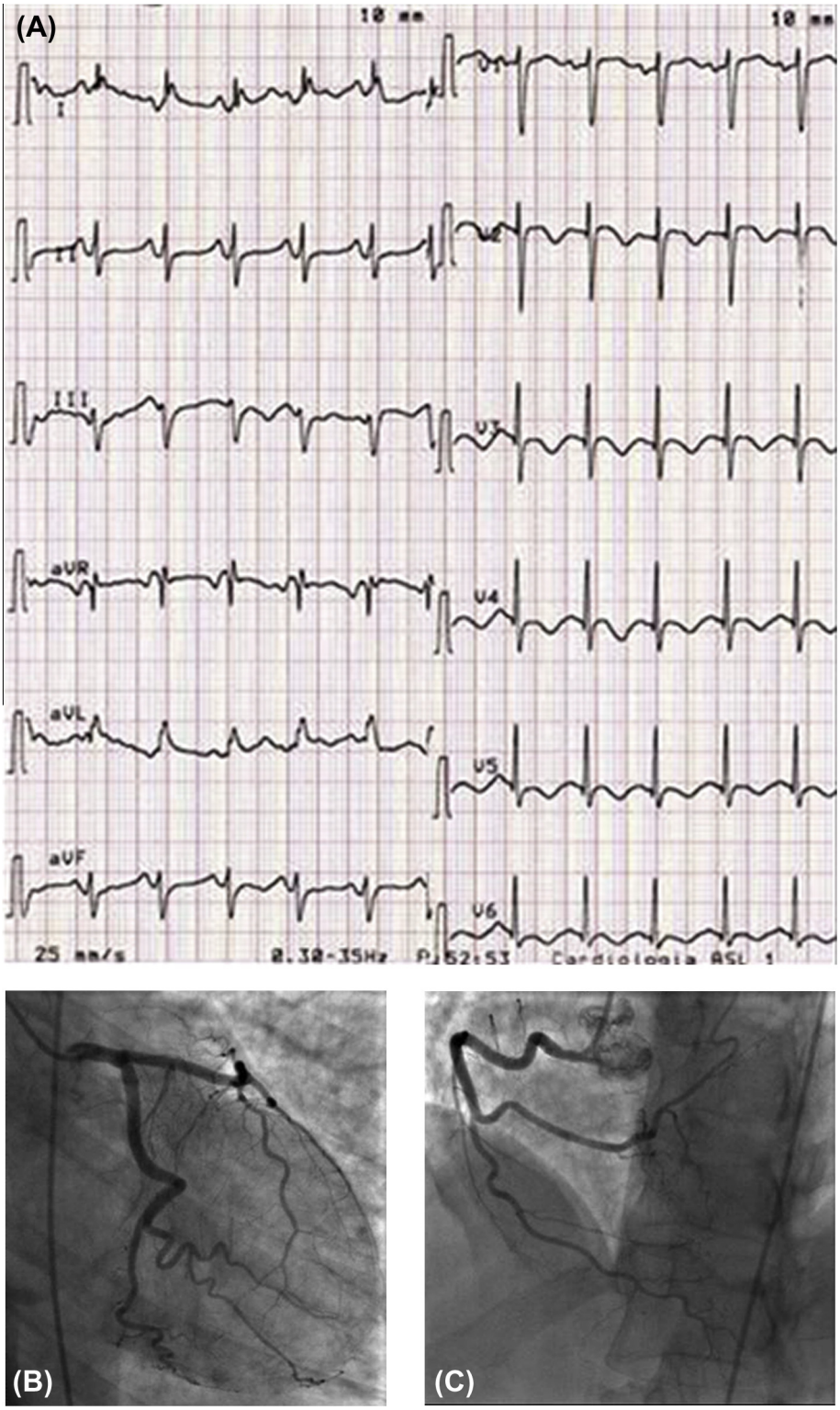

Figure 1. (A) Electrocardiogram at hospital admission showing sinus tachycardia 130 bpm and negative T waves from V2 to V6; (B) left coronary angiogram in the antero-posterior caudal view shows the absence of obstructive coronary lesions; and (C) right coronary angiogram in the left cranial view shows the absence of obstructive coronary lesions.

within several days [7]. The potential mechanisms for transient left ventricular dysfunction during a catecholaminergic crisis include microvascular impairment of the coronary arteries, multivessel epicardial spasm, impaired fatty acid metabolism, myocarditis, and catecholamine-mediated

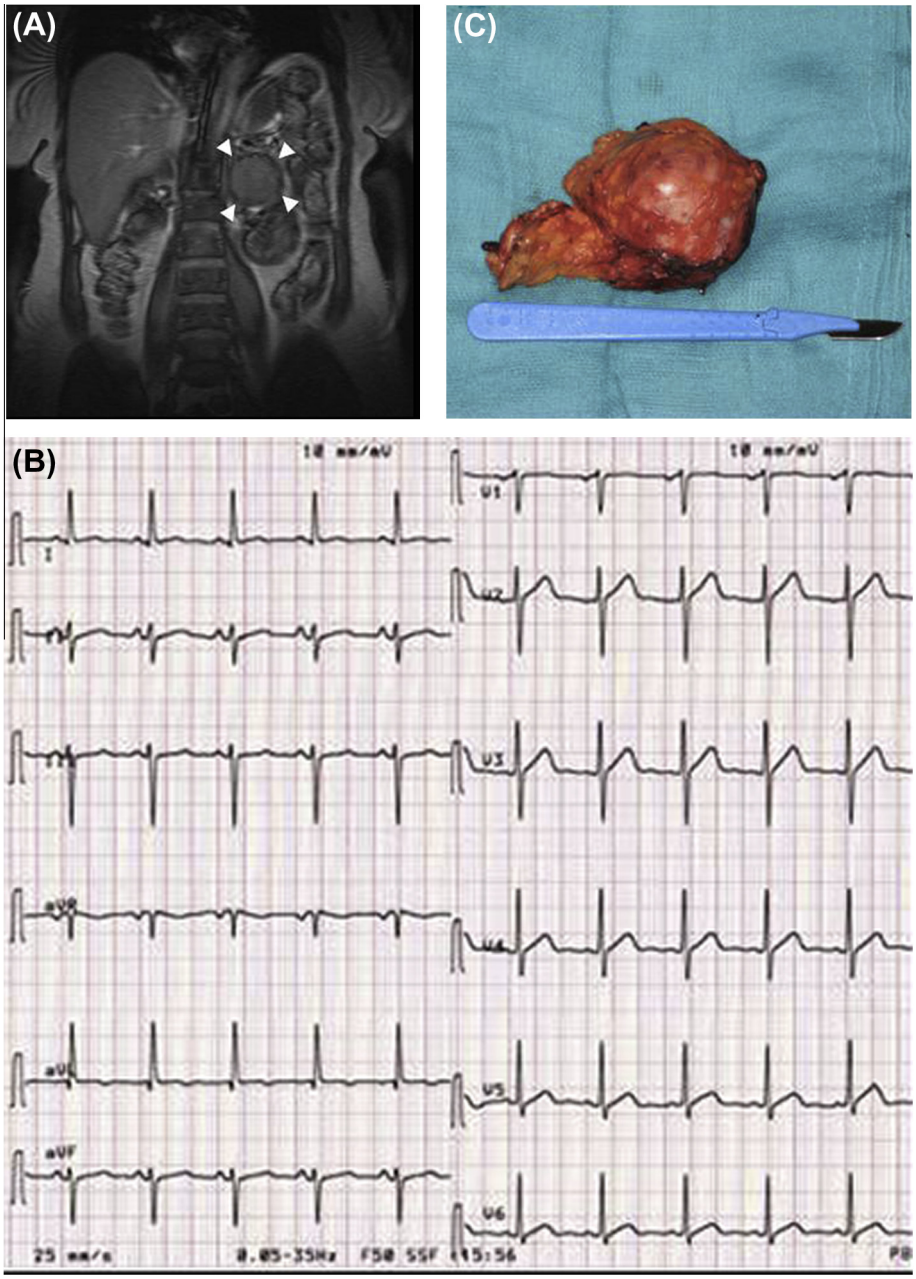

Figure 2. (A) Magnetic resonance imaging showing a huge left adrenal mass (white arrow head) consistent with a pheochromocytoma; (B) electrocardiogram after beginning doxazosin 4 mg/d returns within normal limits; and (C) left adrenalectomy was performed to remove a huge pheochromocytoma.

myocardial dysfunction [8]. Because two patterns of left ventricular dysfunction and a different distribution of sympathetic nerves within the heart have been described, it has been postulated that different segmental involvement may reflect the individual variability in myocardial sympathetic nerve distribution [9].

Finally, we would like to recall some practical aspects concerning the perioperative management of patients with pheochromocytoma. An adequate preoperative pharmacological control of the adverse effects of circulating catecholamines is essential. The most used α-adrenoceptor antagonists include phenoxybenzamine and more recently prazosin, terazosin, and doxazosin, whereas β-adrenoceptor antagonist agents like bisoprolol are preferred over the less selective labetalol and carvedilol. Anesthesia induction is also crucial. The use of drugs that increase sympathetic tone (e.g., ketamine, ephedrine, desflurane, and pancuronium) should be avoided. Anesthesia induction and tracheal intubation must be smooth

in order to avoid and limit a sympathetic response with hypertension and tachycardia. Manipulation of the tumor may cause a brisk hemodynamic response. This is usually a pressure response and phentolamine and labetalol are usually sufficient to control and suppress it. The main postoperative complication of surgery for pheochromocytoma is persistent arterial hypotension, which may be refractory to intravascular volume replacement [10].

We conclude by recalling that in patients with poorly controlled arterial hypertension presenting with an unexpected myocardial event the hypothesis of a pheochromocytoma should be considered in the diagnostic work-up, even in an emergency scenario.

References

[1] Lenders JWM, Eisenhofer G, Mannelli M, Pacak K. Pheochromocytoma. Lancet 2005;366:665–75.
[2] Liao WB, Liu CF, Chiang CW, Kung CT, Lee CW. Cardiovascular manifestations of pheochromocytoma. Am J Emerg Med 2000;18:622–5.
[3] Sinclair AM, Isles CG, Brown I, Cameron H, Murray GD, Robertson JW. Secondary hypertension in a blood pressure clinic. Arch Intern Med 1987;147:1289–93.
[4] Mirza A. Myocardial infarction resulting from nonatherosclerotic coronary artery diseases. Am J Emerg Med 2003;21:578–84.
[5] Darze ES, Von Sohsten RL. Pheochromocytoma-induced segmental myocardial dysfunction mimicking an acute myocardial infarction in a patient with normal coronary arteries. Arq Bras Cardiol 2004;82:178–80.
[6] Lindsey B, Elsner MD, Mitchell HK, Clesham G. Adrenaline rush: an unusual presentation of pheochromocytoma. BMJ Case Rep 2016. http://dx.doi.org/10.1136/bcr-2015-211472 [in press].
[7] Park HJ, Kim KS, Sul JY, Shin SK, Kim JH, Lee JH, et al. Prevalence and patterns of left ventricular dysfunction in patients with pheochromocytoma. J Cardiovasc Ultrasound 2011;19:76–82.
[8] Sharkey SW, McAllister N, Dassenko D, Lin D, Han K, Maron BJ. Evidence that high catecholamine levels produced by pheochromocytoma may be responsible for takotsubo cardiomyopathy. Am J Cardiol 2015;115:1615–8.
[9] Kawano H, Okada R, Yano K. Histological study on the distribution of autonomic nerves in the failing human heart. Heart Vessels 2003;18:32–9.
[10] Prys-Roberts C. Pheochromocytoma-recent progress in its management. Br J Anaesth 2000;85:44–57.