Management of a Rare Case of Adrenergic Myocarditis Complicated with Cardiogenic Shock

CASE REPORT

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Abstract

A 41-year-old female was referred to our clinic with progressive dyspnea and a syncope, preceded by angina. On admission she was in cardiogenic shock. ECG showed diffuse repolarization changes and cardiac enzymes were elevated. The echocardiogram revealed severe left ventricular dysfunction with basal and medium walls hypokinesia. After stabilizing the patient, a coronary angiography was performed which revealed normal epicardial arteries. In the next days her clinical status was marked by severe hypertensive episodes with flash pulmonary edema and low responsiveness to therapy. Cardiovascular magnetic resonance showed myocardial edema and intramyocardial late gadolinium enhancement. An abdominal ultrasound raised suspicion of a pheochromocytoma due to an abnormal mass with cystic areas found on the right suprarenal gland. Elevated urinary free catecholamines and fractionated metanephrines confirmed the diagnosis. Further on, a CT scan better identified the heterogeneous tumor and the patient was referred for a right laparoscopic adrenalectomy. Follow-up at 1 month reported full recovery of the systolic function. The particularity of the case is represented by the difficulty of diagnosis of adrenergic myocarditis, as well as the management of cardiogenic shock induced by it.

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Introduction

Adrenergic myocarditis is a very rare presentation of pheochromocytoma and a particular cause of acute heart failure. Acute myocardial infarction, acute pulmonary edema, cardiac arrhythmias or

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cardiomyopathies are only few of myocardial dysfunctions seen in this pathology. Myocarditis, as a clinically significant condition, is extremely rare in pheochromocytoma, and most likely is provoked by a direct myocardial injury caused by catecholamines [1]. Adrenergic myocarditis complicated with cardiogenic shock is a therapeutic challenge due to the important limitations of disease pathogenesis.

Case report

A 41-year-old female, former smoker (12 pack-years), was referred to our clinic with 2 days progressive dyspnea and a syncope preceded by chest pain. She had a personal history of hypertension for 1 year and she took nebivolol 2.5 mg and lisinopril 10 mg, daily. On arrival, the patient was polypneic (24 breaths/minute), orthopneic, SpO₂ =88% with oxygen therapy and a FiO₂ of 0.45, heart rate was 110 b.p.m. and blood pressure was 70/50 mmHg on both arms. Cardiac auscultation revealed a systolic murmur in mitral area and pulmonary auscultation was specific with acute pulmonary edema – diffuse crackles in all lung fields. She had a BMI of 24 kg/m² and was afebrile.

An ECG (**Figure 1**) was obtained showing sinus rhythm of 110 b.p.m.; intermediate heart axis and

normal conduction times; 1 mm concave ST-segment elevations in lead aVR; 3 mm ST - segment depression in leads V4-V6, negative T wave in lead aVL and flat in D1.

The initial etiological differential diagnosis for the cardiogenic shock included acute coronary syndrome, myocarditis/Takotsubo syndrome, acute mitral regurgitation, aortic dissection.

Laboratory analyses exposed elevated cardiac enzymes (hs-cTnI =244ng/L, TGO 69 U/l, CK MB 76 U/l), normal lipid and renal profile, mild normochromic normocytic anemia (Hg=11.8g/dl) but with normal iron levels. An echocardiogram was performed which revealed non dilated cardiac chambers: parasternal long axis view (PLAX): LV diastolic dimension = 45 mm, LV systolic dimension= 39mm; left atrium volume = 20ml (Simpson biplane method), parasternal short axis view (PSAX): RV diastolic dimension = 28mm, mild hypertrophy: PLAX: interventricular septum and posterior wall of 13 mm but with severely left ventricular systolic dysfunction (ejection fraction of 15% with Simpson biplane method), with akinetic basal walls and medium walls hypokinesia, moderate mitral regurgitation (PLAX: vena contracta = 5 mm) with no pericardial effusion or aortic dissection.

We admitted the patient in the Intensive Cardiac Care Unit and began to treat accordingly the cardiogenic shock with acute pulmonary edema. We started with a continuous intravenous inotropic dobutamine support in dose of 5 micrograms/kg/min which was progressively increased to a dose of 20/micrograms/kg/min in 40 minutes in absence of not targeting a value of 65 mmHg for the mean arterial pressure (MAP). At that time, we considered it necessary to initiate norepinephrine as a vasopressor adjunct to inotropic therapy in a dose of 2 micrograms/minute and we reached a MAP of 70 mmHg with a dose of 5 micrograms/minute (after 25 minutes). Nitroglycerine (5-15 micrograms/min) and furosemide (100 mg over 100 minutes) in continuous infusion protocol were also

Figure 1: ECG showed sinus rhythm, with diffuse repolarization changes.

started along with morphine (single dose of 2 mg) and unfractionated heparin (initial i.v. bolus of 60 units/kg (4000 units), then i.v. infusion of 12 units/kg/hr). Our main diagnosis at the arrival time was an acute coronary syndrome without ST- segment elevation and for this reason we also gave aspirin (250mg) and ticagrelor (180mg) in loading doses with atorvastatin 80mg. After a few hours, we observed a moderate improvement in the patient clinical status (remission of acute pulmonary edema: respiratory rate of 18/min, $\text{FiO}_2 = 0.3$, presence of diuresis, hemodynamic stability: MAP = 65-70 mmHg, normal pulmonary auscultation) so it was decided to continue with a coronary angiogram to exclude or treat significant obstructive coronary artery disease. Coronary angiography did not show obstructive coronary artery disease (**Figure 2 & 3**), and a left ventriculography (**Figure 4**) disclosed apical contractility but with mid-ventricular and basal akinesia, which raised suspicion of an inverted Takotsubo syndrome, although we did not have any information about a triggering stress event.

For the next 36 hours, the patient clinical status improved, with decreasing doses of dobutamine and norepinephrine until cessation.

Figure 2: Coronary angiography: left main coronary artery, left descending coronary artery and left circumflex coronary artery with no lesions.

Figure 3: Coronary angiography. Right coronary artery with no lesions.

Figure 4: Left ventriculography. Apical contractility; mid-ventricular and basal akinesia.

Due to these findings, the diagnosis was unclear and we referred the patient for a cardiovascular magnetic resonance study to better characterize the myocardial tissue. CMR revealed myocardial edema in the mid-ventricular and basal walls (T2-weighted imaging), while T1-weighted late gadolinium enhancement images showed diffuse myocardial enhancement, consistent with a non-ischemic myocardial damage. Taking into consideration the myocardial edema, increased wall thickness with severe hypokinesia and diffuse enhancement, a diagnosis of acute myocarditis was firmly established.

After 76 hours from admittance the patient was again in acute pulmonary edema but with very high blood pressure (250/130mmHg) which required i.v. nitroglycerin in high doses (50 micrograms/minute), furosemide (200mg over 100 minutes), morphine (single dose of 2 mg) and urapidil (intravenous bolus at a dose of 12.5 mg, followed by a continuous infusion at a rate of 10 mg/hr).

We performed a bedside abdominal ultrasound and noticed on the right adrenal gland topography a 50/34 mm tumor with cystic areas inside, highly suggestive of pheochromocytoma (**Figure 5**). Confirmation of diagnosis came when we dosed urinary free catecholamines and fractionated metanephrines on the second episode of flash pulmonary edema. (Urinary - metanephrine 1498 $\mu\text{g}/24\text{ h}$ (N <300); normetanephrine 9720 $\mu\text{g}/24\text{ h}$ (N <400); adrenaline 2 133 $\mu\text{g}/24\text{ h}$ (N <18); noradrenaline 314 $\mu\text{g}/24\text{ h}$ (N <83); dopamine 922 $\mu\text{g}/24\text{ h}$ (N <460).

Taking into consideration all of the above, the positive diagnosis of adrenergic myocarditis due to catecholamine excess was made. A CT abdominal scan better identified the heterogeneous tumor and the patient was referred for a right laparoscopic adrenalectomy. (**Figure 6 & 7**). At that moment, the medical treatment included: alfa blocker (doxazosin 1 mg o.d.), beta blocker (bisoprolol 5mg o.d.), dihydropyridine calcium channel blocker (amlodipine

10mg o.d.), angiotensin-converting-enzyme inhibitor (ramipril 10 mg o.d.), diuretic (indapamide 1.5mg o.d.) and a mineralocorticoid receptor inhibitor (spironolactone 50mg o.d.) .

Follow-up at 1 month reported full recovery of the systolic function (left ventricular ejection fraction of 55%), with minimal antihypertensive therapy required (ramipril 2.5mg/o.d. and nebivolol 5mg/o.d).

Figure 6: Abdominal computed tomography disclosed an oval, well-defined right adrenal mass.

Figure7: Right adrenal gland with a massive tumor, surgically removed.

Figure 5: Abdominal ultrasound revealed a solid, heterogeneous mass in the right supra-renal area.

Discussion

We report a case of acute myocarditis in a young female, complicated with cardiogenic shock and flash pulmonary edema, in the context of an undiagnosed pheochromocytoma. Our case report provides direct evidence supporting the pathogenic role of

excess catecholamine secretion in the development of adrenergic myocarditis.

Pheochromocytoma is a rare catecholamine-producing tumor, emerging from chromaffin cells of the adrenal medulla, with a vast majority of these tumors secreting both norepinephrine and epinephrine [2]. Palpitations, headaches and excessive sweating is the classic triad of this condition. Adrenergic myocarditis is a very rare presentation of pheochromocytoma and a particular cause of acute heart failure, with a pathophysiology which is not fully understood, although some autopsy studies revealed that myocardial inflammatory cell infiltrations and focal necrosis were found in 50% of patients who died from pheochromocytoma [3, 4].

When facing a patient with cardiogenic shock of unknown origin, we must always take into consideration the presence of an underlying pheochromocytoma as a differential diagnosis, as well as other states of adrenergic hyperstimulation [5]. The reversibility of the myocardial affection in this pheochromocytoma-associated cardiomyopathy is common after the tumor resection [6].

At this moment, there is no effective standardized therapy for acute myocarditis, besides the optimal care of heart failure and arrhythmias in accordance with evidence-based guidelines and specific etiology-driven therapy [7, 8].

Conclusion

Adrenergic myocarditis, a rare pathological entity, represents a diagnostic and therapeutic challenge with important prognostic implications.

We believe that a multidisciplinary team (cardiologist, surgeon, radiologist, and anesthesiologist) is imperative in recognizing and managing these extremely difficult cases, while also discussing the therapeutic limitations induced by complications.

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