American Journal of Emergency Medicine xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Case Report

A peculiar etiology of acute heart failure: adrenergic myocarditis☆

Pheochromocytoma can occur with a variety of cardiovascular signs and symptoms, and this tumor can also precipitate an acute heart failure associated with the typical clinical and instrumental findings of myocarditis. This peculiar etiology of acute myocarditis, known as "adrenergic myocarditis," should be suspected when specific "red flags" of pheochromocytoma such as headache, palpitations, diaphoresis, hypertension, orthostatic hypotension, and left ventricular dysfunction suggesting Takotsubo syndrome are detected. In fact, its diagnosis allows a specific targeted therapy.

We report the challenging case of a 24-year-old man admitted to our hospital for acute heart failure secondary to adrenergic myocarditis.

Acute myocarditis recognizes a number of causes and, in some cases such as immune-mediated forms, allows specific treatment. The myocardial tissue characterization with invasive and noninvasive methods shows a peculiar diagnostic pattern of myocarditis but often is not able to detect the specific etiology. Therefore, the therapy is often only supportive.

We report the case of a 24-year-old man without cardiovascular risk factors or history of heart disease, admitted to our emergency department for dyspnea, palpitation, diaphoresis, and vomiting. A blood pressure of 95/50 mm Hg, heart rate 130 beats/min, Spo_2 73%, and partial pressure of oxygen of 44.7 mm Hg revealed an acute respiratory failure associated with hemodynamic instability. Therefore, a prompt support therapy with continuous positive airway pressure and aggressive fluid and inotropic agent infusion was started. Blood examinations showed the following: troponin I, 68 (normal values, 0-0.1) ng/mL; creatinine, 3.66 (normal values, 0.7-1.3) mg/dL; blood nitrogen, 102 (normal values, 10-50) mg/dL; glutamic oxaloacetic transaminase, 335 (normal values, <41) U/L; glutamic-pyruvic transaminase, 369 (normal values, <45) U/L; white blood cells, $26.95 \times 10^3/\mu L$ (normal values, 4,50-10.00 $\times 10^3$) with a prevalence of neutrophils (87% at leukogram; normal values, 40%-75%); hemoglobin, 18 (normal values, 13-16) g/dL; C-reactive protein, 8.6 (normal value <0.5) mg/dL; and erythrocyte sedimentation rate, 22 (normal values, <12) mm/h. A thoracic computed tomography (CT) showed multiple and bilateral air space consolidations, especially in the posterior areas of the apical and middle lobes (Fig. 1A). Transthoracic echocardiography (TTE) documented a severely reduced (25%) left ventricular (LV) ejection fraction (EF) with diffuse hypokinesia and normal ventricular volumes. The patient was immediately transferred to the intensive care unit where the temperature raised to 39°C and a further marked reduction of the blood pressure precipitating a cardiogenic shock required the implantation of an intra-aortic balloon pump; furthermore, the patient underwent orotracheal intubation and mechanical ventilation. Meanwhile, on the basis of blood examinations and CT evidence suggestive of pneumonia, an empiric broad-spectrum antibiotic therapy was started. The next day, the intra-aortic balloon pump was removed due to the markedly increase of blood pressure (150/95 mm Hg) and the clinical evidence of ischemia of the right lower limb requiring angiography, which showed a femoral artery dissection, surgically treated without delay. Afterward also mechanical ventilation was interrupted. During the hospitalization, the patient was subsequently referred for a cardiac magnetic resonance (CMR) study. The LV cine images confirmed the depressed LV function observed by TTE, and the myocardial tissue characterization with T_2- and T_1-weighted imaging demonstrated edema of the inferior and lateral walls (Fig. 1B) and subepicardial late gadolinium enhancement (LGE) in the inferior, lateral, and anterior walls (Fig. 1C), respectively, suggesting an acute myocarditis. In the following days, the clinical symptoms as well as instrumental and laboratory parameters improved; therefore, after 40 days in the intensive care unit, the patient was discharged with an EF of 53% and a final diagnosis of acute myocarditis. Within 15 days after discharge, the patient was admitted again for the same clinical symptoms characterized by dyspnea, palpitation, and diaphoresis, but this time, the blood pressure was very high (220/100 mm Hg) and TTE showed a reduced LVEF of 30% secondary to akinesia of the midwall and apical segments associated with hyperkinesia of the basal segments, resembling the typical apical ballooning pattern of the Takotsubo cardiomyopathy. On the basis of these findings, the hypothesis of pheochromocytoma was considered and, in fact, a 24-hour urine test for total catecholamines resulted to be positive with a concentration of free norepinephrine of 122.4 (normal values, 12.1-85.5) μg/d and free epinephrine of 91.2 (normal values, of 1.7-22-4) μg/d. Therefore, the patient underwent contrast-enhanced abdominal CT scan showing an oval hypervascular lesion with a maximum diameter of 5 cm in the right adrenal gland suggestive of pheochromocytoma (Fig. 1D) also confirmed by metaiodobenzylguanidine scintigraphy. Therefore, alpha-lytic therapy in association with β-blockers was administrated and the patient subsequently showed a good recovery. Afterward, the mass was removed by laparoscopic approach and the diagnosis was confirmed by histology. After surgery, the patient had a good clinical course. At 6-month follow-up, TTE showed a full recovery of LV contractility and CMR confirmed a good EF with no edema in T_2-weighted sequences (Fig. 1E) and poor residual LGE (Fig. 1F).

Pheochromocytoma diagnosis is often difficult due to the similarity to many other acute cardiac syndrome such as myocarditis or Takotsubo syndrome [1,2]. In this report, we describe the peculiar case of an acute myocarditis precipitated by pheochromocytoma, so-called adrenergic myocarditis.

In our patient, despite a mild increase of inflammatory biomarkers, the clinical onset with vomiting and fever combined with the lung impairment at CT was suggestive of an infection involving the

☆ No conflict of interest to declare.

http://dx.doi.org/10.1016/j.ajem.2015.07.025

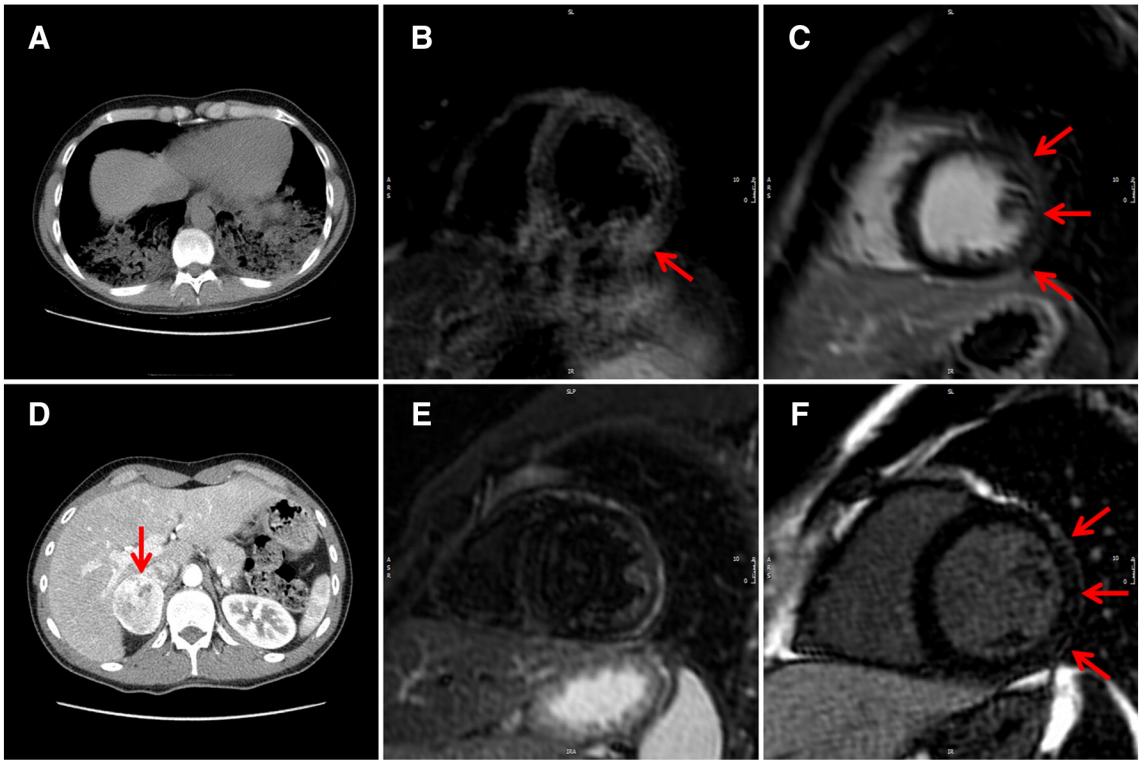

Fig. 1. A, Thoracic CT scan showing bilateral airspace consolidations in the posterior pulmonary quadrants. B, T_2-weighted imaging by basal CMR demonstrating regional myocardial edema of the inferolateral wall of the left ventricle (red arrow). C, Subepicardial LGE in the inferolateral and anterolateral walls (red arrows) in a postcontrast T_1-weighted image. D, Abdominal contrast-enhanced CT scan showing a voluminous mass in the right adrenal gland (red arrow). E, T_2-weighted imaging by follow-up CMR demonstrating the resolution of previously detected myocardial edema. F, Postcontrast T_1-weighted image showing limited residual LGE (red arrows).

gastrointestinal tract, lungs, and myocardium complicated by cardiogenic shock and multiorgan failure. Moreover, the CMR evidence of myocardial signal intensity increase in T_2-weighted images, suggestive of edema, and the LGE distribution in T_1-weighted sequences with a nonischaemic regional pattern were diagnostic for acute myocarditis according to the Lake Louise criteria [3]. Therefore, at the first admission, the pheochromocytoma was not recognized. During the second hospitalization, the recurrence of symptoms associated with high blood pressure and TTE evidence of TTS-like LV dysfunction led us to suspect a pheochromocytoma precipitating an acute adrenergic myocarditis. We also realized that the chest CT findings of the previous hospitalization were secondary to an acute respiratory distress syndrome in the context of a multiorgan failure and not to a pneumonia.

Pheochromocytoma is known as "the great masquerader" because of the great variability of the clinical onset. In fact, it can occur with a variety of cardiovascular symptoms ranging from hypertensive crisis, palpitations, chest pain, diaphoresis, headache, up to acute heart failure [4–6]. Also, the evidence of fever, although generally suggestive of infection, can occur in pheochromocytoma secondary to the cytokine production by the mass [7]. Similarly, nausea, vomiting, and leukocytosis may be present [4].

With regard to the imaging techniques, CMR appears to be a safe and noninvasive tool to recognize with adequate accuracy patients with acute myocarditis [8,9]. In fact, evidence of myocardial edema by T_2-weighted images as well as necrosis and subsequent fibrosis by LGE in T_1-weighed sequences depicts the tissue pathology expected in active myocarditis [9]. However, beyond the diagnosis of acute myocarditis, CMR is not able to identify the cause of myocardial phlogosis that can be precipitated by a large variety of conditions such as infection, systemic diseases, drugs, and toxins, and the etiology often remains undetermined [3]. Nonetheless, research of the agents or disease-underlying myocarditis should be as careful as possible because the detection of a specific form of myocarditis allows one to perform an etiology-targeted therapy [3]. The acute adrenergic myocarditis secondary to pheocromocitoma is an uncommon form of acute heart failure that, despite the serious and sometimes life-threatening course, can be treated with an appropriate drug therapy and, after the patient stabilization, radically removed by surgery. Furthermore, the hemodynamic instability occurring during a pheochromocytoma crisis might not respond to standard catecholaminergic inotropic agents (eg, noradrenalin) because of the down-regulation of adrenoreceptors, and requires alternative agents such as vasopressin [4]. Moreover, β-blockers should be avoided in the absence of a combined α-blockade because unopposed α-mediated vasoconstriction may lead to severe hypertensive crisis or pulmonary edema, and precipitate paradoxical reaction [4]. Therefore, for a clear therapeutic and prognostic implication, an early etiologic diagnosis seems fundamental. In our opinion, CMR findings should be always integrated into clinical and instrumental data and pheochromocytoma should be suspected when specific markers (named as "red flags"; Fig. 2, "flowchart") are detected. These red flags include headache, palpitations, diaphoresis, hypertension, orthostatic hypotension, and "Takotsubo-like" left ventricular dysfunction detected as "apical ballooning" on echocardiography. In these patients, the integration of the diagnostic workup with plasma and urine catecholamines and metanephrines followed by abdominal CT and/or eventually magnetic resonance imaging to investigate a possible pheochromocytoma should be considered mandatory.

Evidence of myocardial flogosis, necrosis, and fibrosis characterizing myocarditis at CMR and/or histology may be related to different etiologies and requires further investigations. Although pheochromocytoma

Please cite this article as: Polito MV, et al, A peculiar etiology of acute heart failure: adrenergic myocarditis, Am J Emerg Med (2015), http://dx.doi.org/10.1016/j.ajem.2015.07.025