



The great mimic: A rare clinical presentation of myocarditis and multi-organ failure secondary to pheochromocytoma

Scaramozzino Marco Umberto ^{1*}, Nassisi Veronica ², Pipitone Vito ³, Guido Levi ⁴

¹ Director of the "La Madonnina" clinic in Reggio Calabria, Head of the thoracic endoscopy service at Villa Aurora Hospital in Reggio Calabria (RC), Italy

² Internal Medicine Unit, Department of Clinical and Experimental Medicine, University of Messina, 98122 Messina, Italy

³ Division of Cardiology, Papardo Hospital, Messina, Italy

⁴ Department of Clinical and Experimental Sciences, Università degli Studi di Brescia, Interventional Pulmonology Unit, ASST Spedali Civili, Brescia, Italy

* Corresponding Author: **Scaramozzino Marco Umberto**

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Abstract

Pheochromocytomas are catecholamine-producing tumours derived from the sympathetic or parasympathetic nervous system. The clinical presentation is variable, ranging from adrenal incidentalomas to patients with hypertensive crisis or, rarely, with myocarditis and multiple organ failure. We present the case of a 54-year-old patient admitted to the emergency room due to sudden onset of dyspnoea and tachycardia; after a few minutes, due to the onset of oxygen desaturation and loss of consciousness, he was intubated; a coronary angiography was performed which revealed no significant stenosis; the diagnostic hypothesis therefore led us to think of a genesis of the clinical presentation due to a myocarditis which was then confirmed by cardiac MRI. The aetiology was also clarified by performing abdominal CT and urinary and serum dosage of catecholamines. Pheochromocytoma confirms itself as an excellent simulator, which is why it is defined as the "great mimic" and is one of the diagnostic hypotheses to think about in young patients with acute multiorgan failure not explained by other causes.

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Keywords: pheochromocytoma, myocarditis, catecholamine, multi-organ

Introduction

Pheochromocytomas are rare catecholamine-secreting neuroendocrine tumours that arise from chromaffin cells within the adrenal medulla or extraadrenal paraganglia, with an annual incidence of approximately 0.8/100,000 person-years ^[1]. The clinical presentation is variable and ranges from adrenal incidentalomas to cardiovascular complications induced by catecholamines which carry a high risk of morbidity and mortality and may include hypertensive crisis, stroke, aortic dissection, myocardial infarction, arrhythmias, stress-induced cardiomyopathy, myocarditis up to multi-organ failure ^[2].

High circulating levels of catecholamines resulting from a pheochromocytoma can cause direct myocardial injury. Focal myocardial necrosis and inflammatory cells are present in 50% of patients who die with pheochromocytoma and may contribute to clinically significant left ventricular failure. Diagnosis is based on documentation of catecholamine excess using biochemical tests and localisation of the tumour using imaging [3]. We report here the clinical case of a patient in whom a pheochromocytoma manifested with myocarditis and multi-organ failure.

Clinical Case Presentation

A 54-year-old man was transported to the emergency room of a hospital in Messina due to the onset of dyspnoea and tachycardia. In clinical history we report a previous lobectomy after spontaneous pneumothorax due to rupture of apical pulmonary bullae, recent intake of non-steroidal anti-inflammatory drugs (NSAIDs) and steroids for discopathy. After a few minutes the situation, his clinical conditions worsened rapidly, with the appearance of reduced oxyhaemoglobin saturation and loss of consciousness. The patient was then subjected to invasive mechanical ventilation. A chest x-ray was performed showing subtle bilateral pulmonary consolidations (Figure 1 Panel A); the electrocardiogram documented sinus tachycardia with a frequency of 140 beats per minute; haematochemical tests revealed an increase in mycardionecrosis indices, inflammation indices and liver and kidney function indices. An echocardiogram was performed which highlighted akinesia of the mid-basal segments of the inferior wall of the inferior interventricular septum (SIV), diffuse hypokinesia of the remaining segments with global pump function which was severely reduced (EF around 20%). The patient was then sent for emergency coronary angiography, which was found to be free of hemodynamically significant stenoses; therefore he was transferred to the intensive care unit of another hospital in Messina. Here invasive ventilatory assistance and continuous monitoring of vital parameters continued. At this point the suspicion of myocarditis increased and was considered among the first diagnostic hypotheses, so much so that infectious disease consultancy was requested, which indicated the execution of various culture and virological tests recommending starting empirical antibiotic therapy. An abdominal computerised axial tomography (CT) scan with contrast medium was also performed which documented the presence in the left adrenal lodge of a rounded, richly vascularised solid foam of approximately 3x3 cm (Figure 2). Due to suspicion of pheochromocytoma, urinary and serum catecholamines were ordered. Throughout the entire process there was a slow and progressive improvement in clinical, laboratory and instrumental parameters. 3 days after the acute event he was extubated and subjected to non-invasive mechanical ventilation alternating with high-flow oxygen therapy; a second control echocardiogram was repeated which showed an EF: equal to 35% (parameters increasing compared to the first echocardiogram). Culture tests and virological tests were carried out, which were negative and the antibiotic therapy was suspended, also due to the improvement in the inflammation indices. Seven days after the acute event, the patient was weaned from non-invasive mechanical ventilation and treated with oxygen therapy alone; the chest x-ray showed a reduction in lung thickening (Figure 1 panel B) and the third echocardiogram documented a further increase in cardiac functional parameters, with EF:

47%. Once stabilised, he was transferred to the NICU; where he performed a cardiac magnetic resonance which showed in the PSIR-TFE sequences for the study of "Late Gadolinium Enhancement" an increase in the medium-myocardial signal of the middle-basal segments of the infero-lateral and inferior wall of the left ventricle, of this last examination we only have the result and not the images. In the meantime, the results of the urinary metabolites arrived (Table 1) which showed a significant increase in noradrenaline and adrenaline: the diagnosis of myocarditis due to pheochromocytoma was therefore confirmed. The patient was discharged with an indication for adrenal medullary scintigraphy and surgical examination.

Case Discussion

Pheochromocytoma is a great disease simulator. The classic triad of headache, palpitations and paroxysmal hypertension is not always present. Recognition requires a high index of suspicion as it can present atypically with dilated cardiomyopathy, sudden death, severe sepsis, acute myocardial infarction or, as in this case, myocarditis and multi-organ failure. This may at least partly explain because it is still a relatively rare diagnosis, despite being present in up to 1:2,000 autopsies, as shown by a retrospective study of 38,596 autopsies from Australia by McNeil *et al* [4]. Catecholamines exert a direct effect on myocardial receptors. Long-term elevation of catecholamine levels leads to downregulation of beta-adrenergic receptors, thus inducing suboptimal myofiber functioning and reduced numbers of contraction units [5]. Furthermore, catecholamines can increase the permeability of the sarcolemmal membrane, leading to calcium influx giving rise to profound changes in intracellular calcium mechanisms. This can consequently lead to acute myocarditis, with diffuse interstitial inflammatory infiltrates and myocardial necrosis [6], as well as a decrease in global pump function as we saw in our patient. Pulmonary oedema can have many causes, among which cardiac factors are frequent [7]. A contributing physiological mechanism may be sympathetic crashing acute pulmonary oedema (SCAPE) - also called "flash" oedema, characterised by high endogenous catecholamine levels leading to elevated pulmonary pressure, increased capillary permeability and local release of inflammatory cytokines [8]. The patient's pheochromocytoma presented with acute onset tachycardia with pulmonary oedema and acute catecholamine-induced heart failure, which rapidly worsened to multiorgan failure (central nervous system, kidney, liver, lungs, heart). Pulmonary oedema as the first presentation of pheochromocytoma is uncommon and usually fatal [9]. In most pheochromocytoma patients pulmonary oedema is cardiac in origin; nonetheless, noncardiogenic pulmonary oedema is also seen [10]. It is thought to occur as a result of catecholamine-induced transient increase in pulmonary capillary pressure due to pulmonary venoconstriction and altered capillary permeability [11]. Sukoh *et al.* reported a case with noncardiogenic pulmonary oedema associated with pheochromocytoma and found neutrophil accumulation in the lung in this case [12]. Although there are some previous reports of noncardiogenic pulmonary oedema associated with pheochromocytoma, findings of bronchoalveolar lavage fluid had not been reported. Acute respiratory distress (ARDS) is known to involve neutrophil accumulation in lung, and these neutrophils have a pivotal role for respiratory dysfunction; this suggests that the neutrophil accumulation in

the lung was caused by catecholamine drive [13]. Further examination, such as bronchoalveolar lavage fluid from pheochromocytoma patients without pulmonary oedema will be necessary to clarify this point. Another cause of acute manifestation of pheochromocytoma is linked to the intake of certain drugs, including steroids: Rosas AL, *et al.* described 4 cases in which the exogenous intake of steroids triggered a multisystem crisis from pheochromocytoma [14].

Our patient took high doses of NSAIDs and steroids due to discopathy. As regards the prognosis, the data are not univocal: according to the review by Batisse-Lignier M. *et al.*, in patients who presented a reduction in global pump function <30% at the time of acute illness, only 50% recovered normal left ventricular function with medical therapy, while 82.2% achieved recovery after surgery to remove the pheochromocytoma [15].

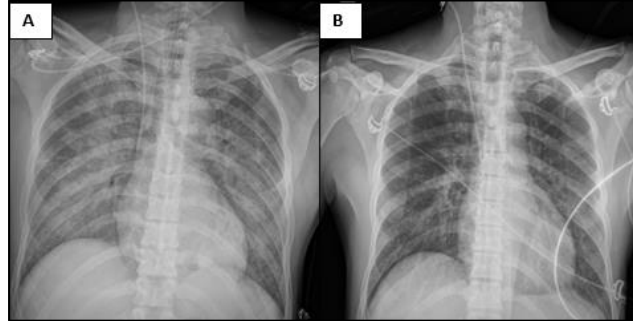


Fig 1: (Panel A-B): Chest x-ray at time 0 (Panel A) and subsequent check-up after 7 days (Panel B), where there is a clear reduction in the subtle and widespread pulmonary consolidations is documented



Fig 2: The arterial phase of the abdominal CT scan shows hyperenhancement of an expansion of approximately 3 cm in the adrenal lodge suggestive of pheochromocytoma.

Table 1: Urinary and serum dosage of catecholamines

Catecholamines	Laboratory results	Normal values range
Noradrenaline	121,6 picograms/24h	23-105 picograms/24h
Adrenaline	118,7 picograms/24h	4-20 picograms/24h
Dopamine	316,4 picograms/24h	62-446 picograms/24h
Vanillylmandelic acid (VMA)	9,4 milligrams/24h	1.6-7.3 milligrams/24h
Homovanillic acid (HVA)	5,4 milligrams/24h	1.82-6.92 milligrams/24h
5-Hydroxyindoleacetic acid(5-HI-AA)	4,5 milligrams/24h	2-8 milligrams/24h

Conclusion

The presented clinical case highlights the complexity and variability of the clinical presentation of pheochromocytomas, emphasising their nature as a "great mimic" capable of simulating many other conditions. In our 54-year-old patient, the pheochromocytoma manifested with a picture of myocarditis and multi-organ failure, representing an unusual and rare presentation of this pathology. The atypical presentation of our case, with clinical manifestations of dyspnoea, tachycardia, acute heart failure, and pulmonary oedema, initially suggested a possible cardiac origin of the syndrome. However, confirmation of a myocardial event was obtained through cardiac magnetic

resonance, with subsequent identification of the pheochromocytoma through biochemical tests and additional imaging. The case highlights the importance of considering pheochromocytoma as a possible cause in patients with multi-organ failure unexplained by other conditions, especially in the presence of cardiac symptoms and ventricular function abnormalities. Early diagnosis is crucial to initiate appropriate treatment, thereby improving recovery prospects.

Furthermore, our experience underscores the need for a high index of suspicion in complex clinical situations, especially considering that pheochromocytoma can present atypically, as in our case where it was associated with the use of

medications such as non-steroidal anti-inflammatory drugs and steroids. Lastly, a multidisciplinary approach is essential for managing patients with pheochromocytoma, involving specialists in cardiology, endocrinology, nephrology, and intensive care. Timely identification and cooperative management of complications can significantly improve clinical outcomes. In conclusion, our case contributes to the medical literature by highlighting the diversity of pheochromocytoma presentation and reiterating the importance of considering this pathology in diagnostic evaluations of patients with multi-organ failure of unknown origin.

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