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Case Report

# MINOCA: A Rare Case Report and Brief Review of Literature

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**Abstract**

Myocardial infarction with non-obstructive coronary arteries (MINOCA) is a syndrome showing clinical evidence of myocardial infarction with normal or near-normal coronary arteries on angiography. The management of this syndrome is strongly dependent on the underlying pathophysiological mechanism. We report the case of a 63-year-old man who presented with posterior ST-segment elevation myocardial infarction (STEMI) with non-obstructed coronaries as an atypical presentation of a giant pheochromocytoma. This pathology is a rare endocrine neoplasia, resulting in several cardiovascular manifestations, including type-2 myocardial infarction and transient cardiomyopathy. Although the Scientific Statement From the American Heart Association and the European Society of Cardiology guidelines do not report pheochromocytoma as a potential cause of MINOCA, our case reiterates the importance of considering this diagnosis, especially in patients with concomitant transient cardiomyopathy and hypertensive crisis. A correct and prompt diagnosis in this context may avoid life-threatening complications.

**Keywords:** MINOCA; Pheochromocytoma; STEMI

## Abbreviations

ACH-test: Acetylcholine Provocation Testing; AMI: Acute Myocardial Infarction; CK: Creatine Kinase; CMR: Cardiac Magnetic Resonance Imaging; CT: Computed Tomography; ECG: Electrocardiogram; ESC: European Society of Cardiology; GTN: Glyceryl Trinitrate; IVUS: Intravascular Ultrasound; MI: Myocardial Infarction; MIBG-SPECT: 123I-Metaiodobenzylguanidine-Single Photon Emission Computed Tomography; MINOCA: Myocardial Infarction with Non-Obstructive Coronary Arteries; STEMI: ST-Segment Elevation Myocardial Infarction; UFH: Unfractionated Heparin; TTE: Transthoracic Echocardiogram

## Introduction

Myocardial infarction with non-obstructive coronary arteries (MINOCA) is a syndrome with different causes, characterized by clinical evidence of myocardial infarction with normal or near-normal coronary arteries on angiography. Its prevalence ranges between 5% and 25% of all myocardial infarction. The prognosis is extremely variable, depending on the cause of MINOCA. The key principle in the management of this syndrome is to clarify the underlying mechanisms to achieve patient-specific treatments. Clinical history, electrocardiogram (ECG), cardiac enzymes, echocardiography, coronary angiography and left ventricular angiography represent the first level diagnostic investigations to identify the causes of MINOCA [1]. Cardiac magnetic resonance imaging is one of the key diagnostic tools for the differential diagnosis of MINOCA. The Acute Myocardial Infarction (AMI) clinical criteria for MINOCA consist of the well-established 'Fourth Universal Definition of Myocardial Infarction' [2]. This contemporary definition is focused upon a positive cardiac biomarker and corroborative clinical evidence of an AMI. The angiographic criteria for 'non-obstructive coronary arteries' detailed in the MINOCA definition utilizes the conventional cut-off of <50% stenosis, which is consistent with contemporary angiographic guidelines [3]. The most common causes of MINOCA are represented by coronary plaque disease, coronary dissection, coronary artery spasm, coronary microvascular spasm, Takotsubo cardiomyopathy, myocarditis, coronary thromboembolism, other forms of type 2 myocardial infarction and MINOCA of uncertain aetiology [4,5]. Currently the Scientific Statement from the American Heart Association and the European Society of Cardiology (ESC) guidelines do not report pheochromocytoma as a potential cause of MINOCA. We present a rare case of MINOCA as the initial presentation of a giant pheochromocytoma.

## Case Presentation

A 63-year-old man was admitted to the emergency unit of our hospital for the sudden onset of chest pain, sweating, nausea and headache. He suffered from type II Diabetes Mellitus in diet therapy and was under corticosteroids treatment for a recent lumbar disk disease. Pulmonary congestion was found at thoracic auscultation and blood pressure was 200/100 mmHg. At the current admission, the initial ECG showed ST depression >1mm in leads V1-V4 and ST-segment elevation (>0.5mm) in additional posterior chest wall leads V7-V9 and isolated posterior myocardial infarction5 was diagnosed (Figure 1A and 1B). Bedside echocardiography was also performed, showing moderate left ventricular dysfunction with posterolateral and lateral wall akinesia. The laboratory results showed significantly increased values for high-sensitivity Troponin T (7528ng/L, reference range: 0.0-34 ng/L) and creatine kinase (CK) (560 U/L, reference range: 30-200 U/L). After treatment with loop diuretics and labetalol intravenous (i.v.), the patient showed an adequate clinical improvement. He was, then, admitted to the Coronary Intensive Care Unit, where treatment with loading dose of 250mg acetylsalicylic




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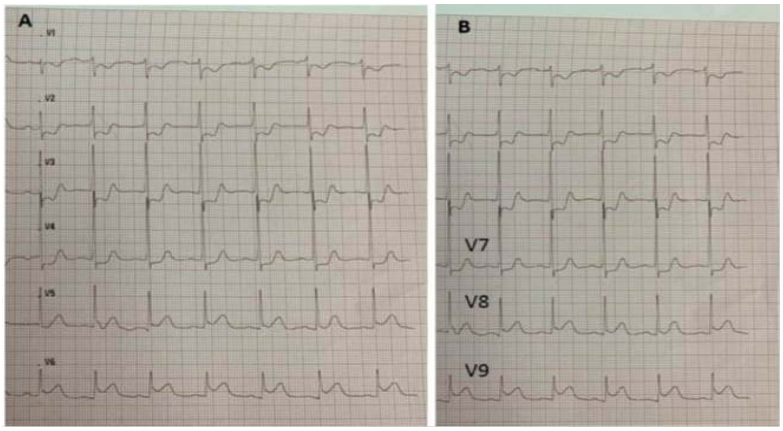


**Figure 1:** ECG showing ST depression >1mm in leads V1-V4 (A) and ST-segment elevation (>0.5mm) in additional posterior chest wall leads V7-V9 (B).

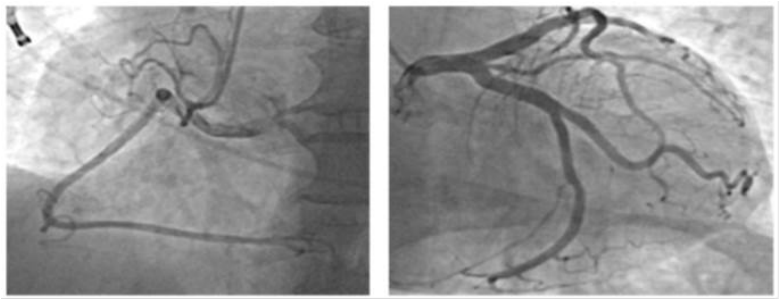

**Figure 2:** Coronary angiogram showing non-obstructed coronaries.

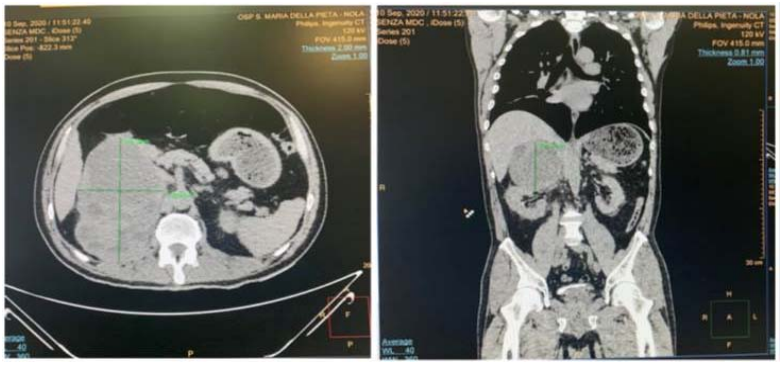

**Figure 3:** Computed tomography scan of the chest, abdomen, and pelvis showing a giant mass of 15x10x10 cm occupying the right adrenal situs.

acid i.v., bolus 70-100U/kg of unfractionated heparin (UFH) and P2Y12 inhibitor loading dose (ticagrelor 180mg p.o.) was initiated. A coronary angiography was carried out within 60min from ST-segment elevation myocardial infarction (STEMI) diagnosis, showing no significant coronary abnormalities (Figure 2). Intracoronary imaging, at the time of cardiac catheterization, with intravascular ultrasound (IVUS) and intracoronary acetylcholine provocation testing (ACH-test) were also performed excluding atherosclerotic plaque rupture or erosion and microvascular spasm respectively. The day after, a cardiac magnetic resonance imaging (CMR) excluded the diagnosis of myocarditis. Surprisingly, CMR showed subendocardial late gadolinium enhancement in the posterolateral and lateral wall, corroborating diagnosis of ischemic injury. In the next days, the patient experienced several episodes of hypertensive crisis followed, after pharmacological treatment with i.v. labetalol or Glyceryl trinitrate (GTN) intravenous infusion, by sudden drops in blood pressure. In one case, severe hypotension required fluids and vasoactive amines administration for hemodynamic stabilization. Suspecting the etiological possibility of an adrenergic crisis, a computed tomography (CT) scan of the chest, abdomen, and pelvis was performed, which demonstrated a giant mass of 15x10x10 cm occupying the right adrenal situs, suspicious of a pheochromocytoma (Figure 3). After a proper wash-out from potentially interfering medications, very high levels of urinary epinephrine 16403nmol/24h (normal values 3-109

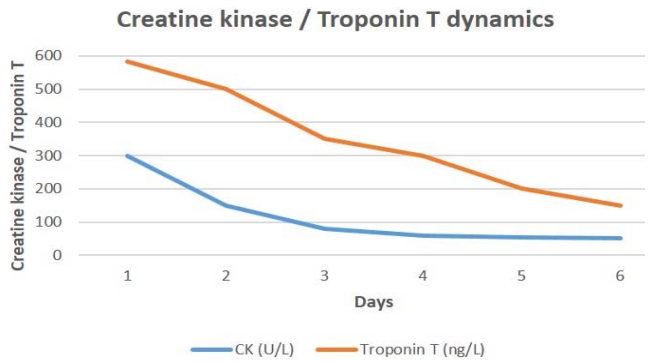


**Figure 4:** Trend of Troponin T and CK values.

**Table 1:** Pre-operative values of urine catecholamines biochemically confirmed pheochromocytoma.

| Cathecolamines | Pre-operative Sample | Reference range |
|---|---|---|
| Urine Epinephrine | ↑ 16403,0 nmol/24h | 3-109 |
| Urine Norepinephrine | ↑ 33759,0 nmol/24h | 89-473 |
| Urine Dopamine | ↑ 3169,0 nmol/24h | 424-2612 |

nmol/24h), norepinephrine 33759nmol/24h (normal values 89-473 nmol/24h) and dopamine 3169nmol/24h (normal values 424-2612 nmol/24h) confirmed the diagnosis of pheochromocytoma (Table 1). A treatment with a selective competitive α1-adrenergic receptor inhibitor (doxazosin) and a β-blocker (metoprolol) were initiated, which markedly reduced the recurrence of hypertensive crises. With the titration of the dosages of both drugs (α and β-blocker) an adequate control of the blood pressure values was obtained. At discharge, an echocardiography revealed the complete recovery of the left ventricular ejection fraction and there was improvement of the signs of myocardial ischemia at ECG. Meanwhile, troponin T and CK values decreased (Figure 4). After seven days from the beginning of symptoms, the patient was transferred to the department of general surgery of another hospital, where he underwent a 123I-metaiodobenzylguanidine-single photon emission computed tomography (MIBG-SPECT), showing increased uptake in the right adrenal gland in line with a diagnosis of pheochromocytoma. Subsequently, the patient underwent excision of right adrenal gland by standard laparotomy instead laparoscopic resection for the large size of mass and its safe and complete removal. Histological exam confirmed the presence of pheochromocytoma without signs of malignancy. Furthermore, three months after surgery, a transthoracic echocardiogram (TTE) control confirmed a normal cardiac function while there were no more signs of myocardial ischaemia at ECG.

## Discussion

Pheochromocytomas are infrequent endocrine tumors with an incidence of 1-2 cases per 1,000,000 adults [6]. They are chromaffin cell tumors derived from the neural crest and associated with catecholamine production, assessed by urine metanephrine and normetanephrine excretion [7,8]. The clinical presentation is highly variable; therefore, the differential diagnosis can become a real challenge. The most frequent manifestation is paroxysmal or maintained hypertension, described in more than the 60% of patients. Other symptoms include palpitations, hyperthermia, diaphoresis, headache and abdominal pain [9]. The elevated circulating catecholamines can lead to different cardiovascular manifestations, as type-2 myocardial infarction and transient cardiomyopathy. The pathophysiological mechanism responsible for these manifestations is not well known. Persistent high levels of catecholamines have been related with the dysregulation of beta-adrenergic receptors, myofibril dysfunction and reduction of the contractile units [10]. In addition, direct myocardial injury induced by catecholamines and their oxidation products is a possibility, given the induced increase in sarcolemma permeability, cytosolic calcium concentration and even direct myocardial necrosis. Moreover, the sustained adrenergic stimulation has been shown to generate an intense vasoconstriction and coronary spasm, which aggravates myocardial damage [11]. In fact, focal myocardial necrosis and inflammatory cells are present in 50% of patients who die with a pheochromocytoma, and these findings could be related to clinically significant ventricular dysfunction [12]. There are several case reports of pheochromocytomas in the literature, presenting with left ventricular dysfunction, such as transient cardiomyopathies or Takotsubo cardiomyopathy also in its variants [9,13,14]. However, there are few reported cases of MINOCA caused by pheochromocytomas. Recently, Melson E et al. reported the case of a 79-year-old Caucasian woman who presented with non-ST elevation myocardial infarction with non-obstructed coronaries as an atypical presentation of a pheochromocytoma [15]. Despite there is a clear diagnostic algorithm for MINOCA using a traffic-light approach [16], proposed by a Scientific Statement from the American Heart Association and subsequently provided by the European Society of Cardiology guidelines [17], investigation for pheochromocytoma is not included as one of the differential diagnoses. Although type-2 Myocardial Infarction which is the mechanism of ischemia in pheochromocytoma is included in the consensus document for MINOCA, Type-2 MI is an umbrella term. For this reason, pheochromocytoma could be added among the potential causes of this syndrome. The present case report demonstrates that pheochromocytoma may be a cause of MINOCA. The case we described showed ST-segment elevation myocardial infarction with non-obstructed coronaries with concomitant transient cardiomyopathy and hypertensive crisis. Further analysis revealed the presence of pheochromocytoma. A diagnostic process is needed to include pheochromocytoma as a differential diagnosis for MINOCA and create specific recommendations for the appropriate management of these patients. Early diagnosis of pheochromocytoma can avoid life-threatening complications, such as the cardiovascular and cerebrovascular complications. In conclusion, our case reiterates the importance of considering this diagnosis, especially in patient presenting hypertensive crisis.

## Declaration

**Author contribution:** Luigi Nunziata: Wrote the draft and collected data; Saverio Ambrosino and Mario Volpicelli: Provided expertise and feedback; Michele Capasso and Luigi Caliendo: Revised the manuscript and provided final approval.

**Consent:** The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with Committee on Publication Ethics (COPE) guidance.

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