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BEGINNER

CASE REPORT: CLINICAL CASE SERIES

Scared to Death

Emotional Stress Causing Fatal Myocardial Infarction With Nonobstructed Coronary Arteries in Women

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ABSTRACT

Myocardial infarction with nonobstructed coronary arteries (MINOCA) can be triggered by intense emotions. We report 5 cases of emotional stress–related death where forensic examination attributed myocardial infarction to a coronary spasm, with the ultimate cause of death being arrhythmias in 4 cases and cardiac rupture in the fifth. (**Level of Difficulty: Beginner.**) (J Am Coll Cardiol Case Rep 2020;2:2400–3) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

The acronym MINOCA (myocardial infarction with nonobstructed coronary arteries) defines a condition in which clinical evidence of myocardial infarction (MI) is associated with angiographically normal or nearly normal coronary arteries (stenosis <50%) (1). MINOCA is 3 times more frequent among women and accounts for approximately 6% of cases of MI, with a prognosis similar to that of "obstructive" (type 1) MI (2). Patients may die during the acute phase of MINOCA, and although we are not aware of any specific analysis of the causes of death in this setting, it is reasonable to assume that death may result from ventricular arrhythmias or mechanical complications of transmural MI (in patients with longer survival after symptom onset), as in type 1 MI. An intense emotion may cause a MINOCA, possibly through an intense catecholamine release in the myocardium, which may trigger a coronary artery spasm or directly induce cardiomyocyte necrosis with a typical histological appearance of contraction band necrosis (3). Here we report 5 cases of fatal MI that were classifiable as MINOCA and that occurred after an intense emotion. These cases were identified from a systematic search of all forensic examinations performed over a 10-year time span at a single university hospital (University Hospital of Pisa).

LEARNING OBJECTIVES

- To learn that sudden cardiac death can occur shortly after an intense emotion.
- To understand the plausible mechanisms underlying this phenomenon.
- To learn the findings on forensic examination.

CASE DESCRIPTIONS

CASE 1. A 46-year-old woman was found dead in her bed by her husband the morning after a violent

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altercation between them. At autopsy, a large area of contraction band necrosis was present within the left ventricular (LV) free wall, although the epicardial coronary arteries did not display any significant stenosis.

CASE 2. A 71-year-old woman was tied up during a home invasion robbery and was found dead shortly afterward. At autopsy, the only pathological finding was extensive contraction band necrosis in the subendocardial region of the LV free wall.

CASE 3. An 85-year-old woman was the victim of a robbery. She called her neighbors for help, but a few minutes later she reported chest pain and lost consciousness. On first medical contact, the patient was in cardiac arrest, and resuscitation maneuvers were unsuccessful. Forensic examination demonstrated an extensive area of transmural contraction band necrosis in the LV free wall, with a few coronary artery stenoses <50% in the left anterior descending and circumflex arteries.

CASE 4. An 82-year old woman was tied to a chair during a home invasion robbery and was found dead in that position. Forensic examination showed subendocardial contraction band necrosis in the anterolateral region of the left ventricle, with coronary artery stenoses <50% in the circumflex and right coronary arteries.

CASE 5. An 86-year-old woman was robbed in the castle where she lived alone. She was dragged on the floor by her hair and forced to reveal the location of the safe. Approximately 1 h later, while reporting the theft, she reported intense retrosternal chest pain and was brought to the emergency department. The electrocardiogram showed marked ST-segment elevation in leads V_2 to V_6, and high-sensitivity troponin T (hs-TnT) levels were increased (106 ng/l [reference value <14 ng/l]). A transthoracic echocardiogram demonstrated an akinetic area in the midcavity and apical portion of the anterior LV wall, together with hypokinesia of the remaining distal segments. Coronary angiography was performed approximately 2 h after symptom onset and showed only 2 nonsignificant stenoses (both <30%) in the right coronary artery (**Figure 1A**). The patient remained stable and asymptomatic over the next 2 days, with modestly raised hs-TnT (660 ng/l on the first day and 380 ng/l on the second day). Follow-up echocardiograms showed hypokinetic LV distal segments. On the third day, the patient died suddenly of cardiac arrest refractory to resuscitation maneuvers. Post-mortem examination revealed a full-thickness rupture in the distal portion of the anterior LV wall that caused pericardial tamponade (**Figures 1B and 1C**). Around the rupture, histological examination demonstrated an area of transmural myocardial necrosis, in full accordance with an MI occurring a few days earlier (**Figure 1D**). The absence of significant coronary artery stenoses was confirmed.

ABBREVIATIONS AND ACRONYMS

hs-TnT = high-sensitivity troponin T

LV = left ventricular

MI = myocardial infarction

MINOCA = myocardial infarction with nonobstructed coronary arteries

DISCUSSION

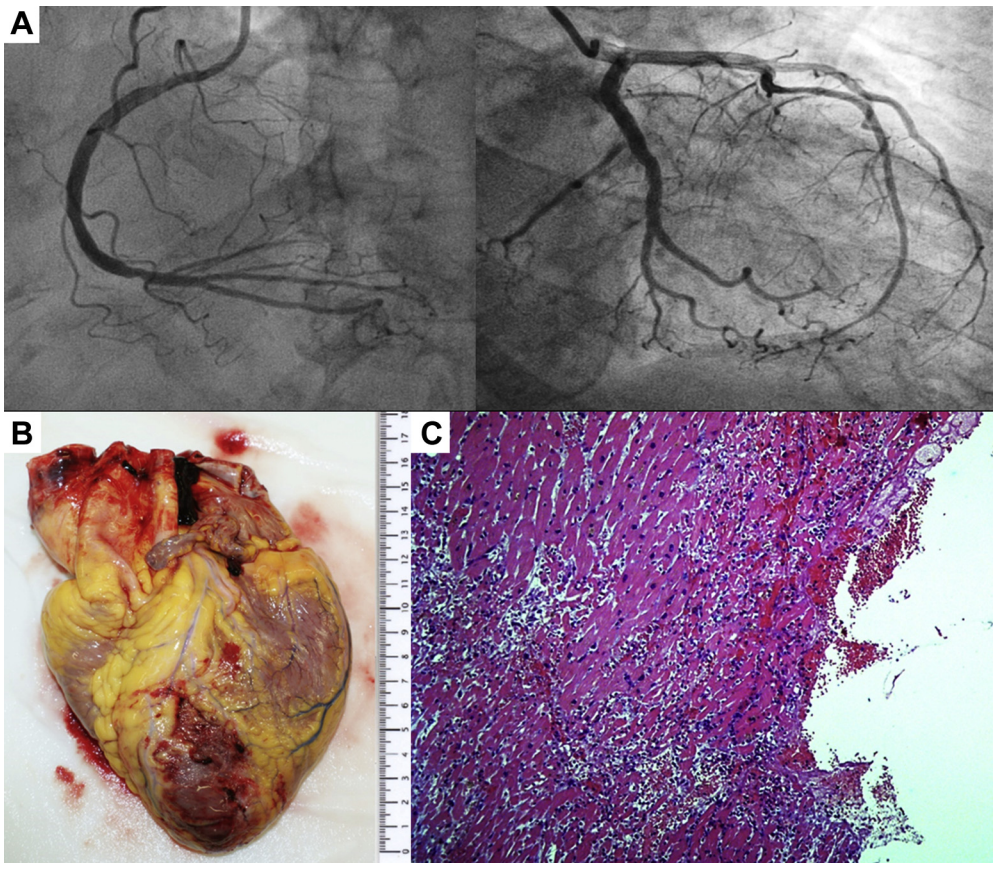
In the first 4 cases, the diagnosis of MI was made during autopsy, and the only significant pathological finding on forensic examination was an area of myocardial necrosis, either subendocardial or transmural. In these cases, a malignant ventricular arrhythmia elicited by myocardial ischemia or necrosis could be assumed to be the direct cause of death. In contrast, the fifth patient died 3 days after a clinical diagnosis of MINOCA because of cardiac rupture related to extensive, transmural necrosis, with echocardiographic evidence of diffuse hypokinesis of distal segments, compatible with an initial form of takotsubo cardiomyopathy (**Table 1**). In all cases, a working diagnosis of MINOCA was made according to the diagnostic criteria proposed by the European Society of Cardiology (1), whereas the American Heart Association considers takotsubo syndrome to be a separate entity from MINOCA (4).

Patients either had no coronary artery stenoses (Cases 1 and 2) or <50% stenoses (Cases 3, 4, and 5). Given that no evident cause of oxygen supply-demand imbalance (e.g., plaque rupture or erosion, thromboembolism, coronary dissection) emerged, the MI events could be most likely attributed to an emotional stress-induced epicardial or microvascular spasm. Notably, an embolic cause of the MI could not be completely ruled out in these cases, but it seemed very unlikely because no evidence of embolic material was found in the coronary arteries.

An intense emotion may trigger a MINOCA, as suggested by a study where 76% of patients with MINOCA reported an emotional stress, compared with only 32% of patients with MI secondary to coronary obstruction (5). In this study, when cases of takotsubo syndrome were excluded, 17% of patients with MINOCA reported an acute emotional distress versus 6% of patients with “obstructive” MI (5).

Spasm of the epicardial coronary arteries and/or intramural arterioles is a common pathogenic

FIGURE 1 Fatal Transmural Myocardial Infarction Without Significant Coronary Artery Stenoses



Case 1. **(A)** Coronary angiography showing no significant stenoses in the right coronary artery **(left)** or the left anterior descending and circumflex arteries **(right). (B and C)** Full-thickness rupture in the distal portion of the left ventricular anterior wall. **(D)** Cardiomyocyte necrosis with red blood cell and neutrophil infiltrates (hematoxylin and eosin stain, original magnification ×20).

mechanism in MINOCA and has been found on provocative testing in 27% of these patients (6). Coronary artery spasm is defined as total or subtotal (>90%) coronary artery occlusion, with ischemic electrocardiographic changes occurring either spontaneously or in response to a provocative stimulus (7). Coronary artery spasm is generally transient, causing Prinzmetal angina, but occasionally it may be sufficiently prolonged to induce an MI (8). Endothelial dysfunction, abnormal regulation of myofibril contraction, and reduced parasympathetic tone are all possible causes of vascular hyperreactivity. On this substrate, macrovascular or microvascular spasm may be elicited by sudden surges of sympathetic activity, as in the case of intense emotions (4) or exogenous substances (e.g., methamphetamines or cocaine). Emotional triggers could also promote cardiac electrical instability and increase the risk of ventricular arrhythmias, and possibly cardiac arrest, following myocardial ischemia and necrosis. The possibility of a stress-related trigger of MINOCA is also corroborated by the circadian and circaseptan variations in its onset, with an increased risk in the early morning and on Mondays (9).

Another possible mechanism of cardiomyocyte necrosis, not mutually exclusive with epicardial or microvascular spasm, is a local increase in catecholamines, following a sudden increase in sympathetic outflow to the heart (4). The same mechanisms could explain the development of the specific form of MINOCA known as takotsubo syndrome, which is also elicited by intense emotions and typically develops in middle-aged or older women (10). A disease continuum can be postulated, ranging from local cardiomyocyte necrosis triggering fatal arrhythmias to more extensive damage leading to the alterations of

TABLE 1 Timeline

Event	Case 1	Case 2	Case 3	Case 4	Case 5
Event type	Altercation	Robbery	Robbery	Robbery	Robbery
Time of day of the event	Evening	Evening	Evening	Evening	Evening
Death	?	?	~1 h after the robbery	?	3 days after coronary angiography
Body found	Day after (morning)	Around 3 h after the robbery	–	Day after (morning)	–
Likely cause of death	Ventricular arrhythmia	Ventricular arrhythmia	Ventricular arrhythmia	Ventricular arrhythmia	Left ventricular wall rupture

LV geometry and function characteristic of takotsubo syndrome. Cardiac rupture in the setting of takotsubo syndrome is an extremely rare phenomenon, and only approximately 20 cases showing this association have been reported (11). When the first clinical manifestation is not sudden cardiac death, an effort should be made to elucidate the pathophysiology of MINOCA to provide therapies targeting disease mechanisms, for example, antispastic agents such as calcium channel blockers or nitrate when epicardial coronary vasospasm is believed to be the underlying cause (4). Furthermore, modulation of the neurohormonal response to stress holds some promise, and an ongoing trial is evaluating the potential benefit of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in MINOCA (Randomized Evaluation of Beta Blocker and Angiotensin Converting Enzyme Inhibitor /Angiotensin Receptor Blocker Treatment in MINOCA Patients; NCT03686696).

CONCLUSIONS

Fatal MINOCA may occur shortly after an intense emotion. We report 5 cases where forensic examination established a diagnosis of MI and attributed it to a coronary macrovascular or microvascular spasm, with the ultimate cause of death being arrhythmias in 4 cases and LV free wall rupture in the fifth.

AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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