Open Journal of
Clinical & Medical
Case Reports

Volume 4 (2018)
Issue 10

ISSN 2379-1039

A case of devastating coronary spasm syndrome: Autopsy-proven acute anterolateral myocardial infarction leading to sudden cardiac arrest following unremarkable coronary angiography

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Abstract

A 51-year-old woman presented with general fatigue and was diagnosed with severe iron deficiency anemia due to chronic gastrointestinal bleeding. On her third hospital day, she suddenly went into cardiac arrest shortly after complaining of chest tightness and was sent to our heart center. An urgent coronary angiography showed no significant abnormality in the three main coronary arteries. Despite an intensive course of treatment, she died due to multiple organ dysfunctions on the fifth day from her original admission. Autopsy subsequently revealed an acute anterolateral infarction, possibly triggered by a severe coronary spasm of the left main coronary artery. This report describes this unusual form of severe coronary spasm as a new entity.

Keywords

coronary spasm; left main coronary artery; myocardial infarction; ventricular fibrillation

Introduction

Variant angina, first described by Prinzmetal et al. in 1959, is caused by transient and recurrent coronary spasm, leading to repetitive episodes of transmural myocardial ischemia [1]. Coronary spasm plays an important role in the pathogenesis of ischemic heart disease, including stable angina, unstable angina, myocardial infarction, and sudden death [2]. Transmural myocardial ischemia caused by occlusive coronary artery spasm can be complicated by malignant ventricular arrhythmias and can result in sudden death or, if prolonged, acute myocardial infarction [3]. Spasm of the Left Main Coronary Artery (LMCA) is a rarely reported cause of variant angina [4].

Herein we report a rare case of sudden cardiac arrest due to ventricular fibrillation, most likely induced by a spontaneous LMCA spasm, and acute, extensive myocardial infarction in a patient without a history of heart disease.

Case Report

A 51-year-old woman presented at a local hospital with general fatigue and dizziness and had no remarkable past medical history, or family history that included heart disease or sudden death. She had never shown any documented episode of chest pain, abdominal pain nor melena before this admission. She smoked 1 package of cigarettes a day for 30 years and drank alcohol in moderation several times a month. Previous annual health checkups, including Electrocardiograms (ECGs) and chest X-rays, were unremarkable.

Her vital signs were reported as follows; blood pressure 122 / 60 mm Hg; heart rate 72 bpm; and respiratory rate 14 min^{-1} and oxygen saturation 98% on room air. Her physical examinations were unremarkable except for her pale conjunctiva and a positive fecal occult blood test. Her ECGs and chest X-ray were within normal range at admission. Her blood test revealed a reduced hemoglobin level of 6.5 mg/dl with a low mean corpuscular volume of 67.9 fL, and a low serum ferritin level of 3 ng/ml. This resulted in a diagnosis of iron deficiency anemia, and Gastroendoscopy was performed the following day where a single Dieulafoy's lesion was detected in her stomach. Endoscopic clipping was successfully performed to control active gastrointestinal bleeding followed by four units of red blood cell transfusion and the commencement of an oral iron supplement. On the third hospital day, she abruptly complained of chest tightness and several minutes later, she had a witnessed cardiac arrest. The bedside heart monitor initially showed ST-segment elevations, with subsequent Ventricular Fibrillation (VF) (Figure. 1A). Electrical defibrillation was attempted several times, but VF persisted. Thus, she was transferred from the local hospital to our cardiovascular center while undergoing cardiopulmonary resuscitation.

On arrival at our emergency room, her heart monitor initially showed VF, which converted to sinus rhythm following electric shocks 45 minutes after her initial collapse. She remained hemodynamically unstable in the catheterization room; her blood pressure was 61 / 40 mmHg, and her pulse was 105 / min. Her initial ECG at our institution demonstrated ST-segment elevations in leads V2-V5 with wide QRS morphology (Figure 1B). An intra-aortic balloon pump and a percutaneous cardiopulmonary support device were inserted for hemodynamic support with therapeutic hypothermia. Emergent coronary angiography was then performed but revealed no obstructive lesions in the three main coronary arteries (Figure 2). Spasm provocation testing was not performed due to her hemodynamic instability while subsequent whole-body computed tomography and repeat gastroendoscopy added no further contributory information. Creatine Kinase (CK) levels were elevated the following day and peaked at 14,566 mg/dl (CK-MB, 742 IU/L). Transesophageal Echocardiography (TTE) under mechanical circulatory supports showed severe hypokinesis of the entire left ventricular wall with a marked dilation of the left ventricle. Nevertheless, we could not delineate the extent of myocardial damage within the territory of the affected coronary arteries. Despite invasive management, she died on the fifth hospital day following her original admission due mostly to multiple organ failures.

At autopsy, 6 hours post mortem, the heart was placed in a 10% neutral buffered formalin solution and then in paraffin. The heart weight was slightly raised at 350g and concentric hypertrophy of the left ventricle was noted with both ventricles significantly dilated. Serial ventricular sections showed transmural hemorrhagic myocardial necrosis from the anterior wall through the septum up to the

posterolateral wall that included anterior and posterior papillary muscles. As a result, extensive myocardial infarction was observed, leaving parts of the posterior wall intact (Figure 3A). Histopathological findings of the affected myocardium revealed that there were massive red blood cells interspersed between cardiomyocytes throughout the entire myocardial wall, suggesting a transmural hemorrhagic myocardial infarction (Figure 3B). In addition, high-power field image of the affected area confirmed that a majority of cardiomyocytes were fully coagulated, with a loss of nuclear morphology and muscle striation with typical contraction band necrosis documented (Figure 3C). Increased infiltration of neutrophils to interstitium was also visible.

The entire left coronary artery was sliced every 2 mm for close macroscopic observation (Figure 4A) where a mild formation of a fibrous plaque was seen partially in the Left Anterior Descending artery (LAD) and Left Circumflex Coronary artery (LCX). However, no finding of typical plaque ruptures was noted in either of the coronaries with only minimal arteriosclerotic changes with fibrous plaque in the LAD, LCX as well as the right coronary arteries. Serial sections of the LMCA showed minimal but diffuse intimal thickening, with no thrombi, erosions, or plaque rupture at the proximal and distal sites respectively (Figure 4B & 4D). A high-power image of aproximal LMCA site showed a relatively normal endothelialized surface that was confirmed by immunostaining for an endothelial marker: CD 34 (Figure 4C). However, segmental disruption of internal elastic lamina was partially observed in the distal LMCA (Figure 4D) where localized fibromuscular plaques were formed with medial smooth muscle cells proliferated (neointimal hyperplasia) (Figure 4E & 4F). There was no remarkable change in the other main coronary arteries, and other major organs showed no distinctive abnormalities that could account for her death.

Discussion

We reported a case of sudden cardiac arrest after hospitalization for the treatment of chronic anemia in a 51-year-old woman with no known past medical history. When first hospitalized at another institution, she was suspected of suffering from Acute Coronary Artery Syndrome (ACS), but emergent angiography revealed near-normal coronary arteries. Post mortem, the autopsied heart showed extensive transmural myocardial infarction, and histological findings added key information to clarify the potential mechanism of the myocardial infarction. The infarct area covered almost the entire myocardium, except for areas supplied by the Right Coronary Artery (RCA), which implied that an occlusion of the LMCA, whether functional or mechanical, was the probable cause. Moreover, the autopsy findings showed minimal atherosclerotic changes without any evidence of erosions or plaque rupture in the LMCA, indicating that a spasm was the cause of the extensive myocardial infarction. We could not rule out the simultaneous occlusion of the proximal LAD and LCX, but this seldom happens. Although some rare cases of simultaneous multivessel coronary spasm leading to cardiopulmonary arrest or collapse have been reported [5], emergent coronary angiography failed to show any findings to indicate these mechanisms were present in this case. Additionally, the histological findings support our hypothesis that an LMCA spasm-induced myocardial infarction was the most likely cause of the patient's death. The localized breakdown of a blood vessel wall at the LMCA site that includes the segmental disappearance of internal elastic lamina and neointimal hyperplasia may have been caused by previous coronary spasm events (could be a silent attack in most cases) and consequently thrombus formations. Suzuki et al [6] reported that neointimal hyperplasia was one of the most characteristic histological findings of plaque in

patients with variant angina.

Other possibilities that could be suggested in this setting include Takotsubo Cardiomyopathy (TCM), which often mimics ACS in the absence of angiographically significant coronary artery stenosis. However, in the present case, the TTE showed a diffuse left ventricular hypokinesis, not a typical reversible left ventricular apical ballooning although we did not perform a left ventriculography during cardiac catheterization. Of course, we cannot completely rule out TCM because several theories regarding the exact etiology of TCM have been proposed and are being investigated including multi vessel coronary artery spasm. Nevertheless, the pathological findings of the patient's myocardium were not typical of patients with TCM which usually affects the left and right ventricles without any relation to the territory of an individual coronary artery [7]. Similarly, myocarditis can often be an unrecognized cause of rapidly progressive heart failure and fatal arrhythmia. In our case, however, microscopic examination did not reveal any interstitial lymphocytes infiltrating the affected myocardium, which is a noteworthy characteristic for myocarditis [8]. Thus, the presence of this condition was less probable in our patient.

In general, patients who present with coronary spasm more commonly complain of typical chest pain and exhibit luminal narrowing on coronary angiography. In many cases, these patients have frequent attacks in response to potential stimulants, such as smoking, and often take medication for coronary spasm symptoms. With this in mind, the present case may suggest a new form of coronary spasm which should be identified as Devastating Coronary Spasm Syndrome (DCSS) and can be defined as"a sudden onset coronary spasm leading to fatal arrhythmia or extensive myocardial infarction with high mortality, without any proceeding symptoms or documentation of angina attack". As a result, catastrophic changes were observed in the wide range of suddenly damaged myocardium where typical pathological changes following an acute myocardial infarction, such as myocardial necrosis and neutrophilic infiltrate, were on process with some delay that is worth noting. In the present case, macrophage, neutrophil infiltration and fibrovascular response, which were common findings at 3-7days following acute myocardial infarction [9], were not prominent on histopathological examinations of the damaged myocardium. Of course, there was a possibility that the massive myocardial necrosis arose as a result of perfusion disturbance during her hemodynamic instability before death, not due to acute myocardial infarction. The entire damaged myocardium area, however, was restricted to regions supplied by the left coronary artery. We could speculate that these repairing mechanisms were delayed because this cardiac event was caused by a sudden-onset form of widespread and hemorrhagic infarction.

Devastating Coronary Spasm Syndrome may be a compelling explanation for the cause of some sudden cardiac deaths as 2 to 8% of patients with aborted sudden death have no apparent heart disease and up to 70% within that group have spontaneous or inducible coronary artery spasm [10]. DCSS may therefore account for some cases of sudden death related to coronary spasm, although a definitive diagnosis is challenging because of the nature of its presentation. Another property of this entity may be the difficulty in making a diagnosis in order to prevent a life-threatening attack in advance – indeed, the possible diagnosis of spasm-induced myocardial infarction in this case was not identified until post mortem. Of note, the histopathological findings in the LMCA suggest that coronary spasm, whether silent or symptomatic, might have previously affected the patient. Further research on this special form of coronary spasm is required starting with thorough interviews and investigations at annual health checks

to identify patients who are likely to develop DCSS.

In summary, we have described a rare case of sudden cardiac arrest with no significant medical history except for smoking cigarettes, whose cause was proven to be acute myocardial infarction at autopsy. To our best knowledge, no other case report has described a devastating clinical course potentially complicated by LMCA spasm-induced myocardial infarction, in which the cause of death was provenat autopsy.

Figures

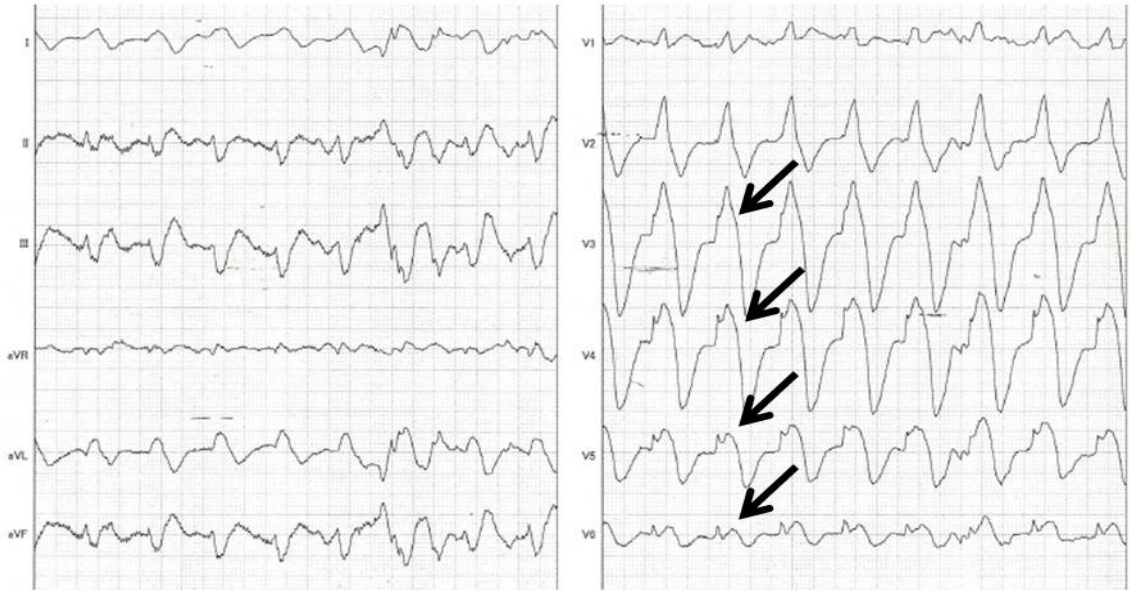

Figure 1: Heart monitor recordings during the first Ventricular Fibrillation (VF) episode and electrocardiography after successful Cardiopulmonary Resuscitation (CPR). A): Bedside electrocardiographic recording, showing ST-segment elevation (arrow) before progression to VF, which was not controlled with prompt electrical defibrillation. B): The 12-lead electrocardiogram following CPR on admission to our cardiovascular center, showing significant ST segment elevation in leads V2-V6 (arrow).

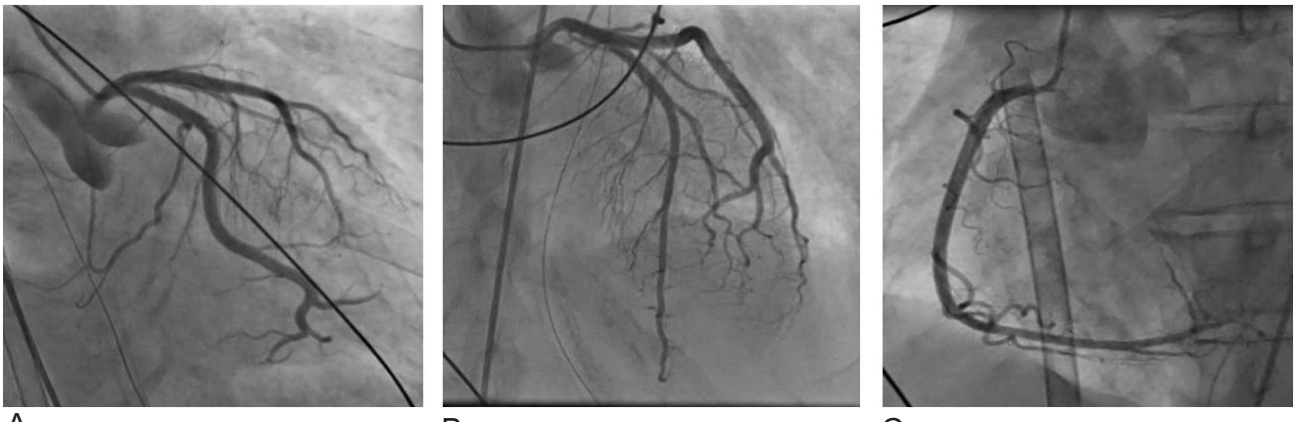

Figure 2: Coronary Angiography (CAG). Fluoroscopic left CAG in caudal (A) and cranial views (B), and the right coronary artery in left anterior oblique view (C). CAG did not show any significant stenosis.

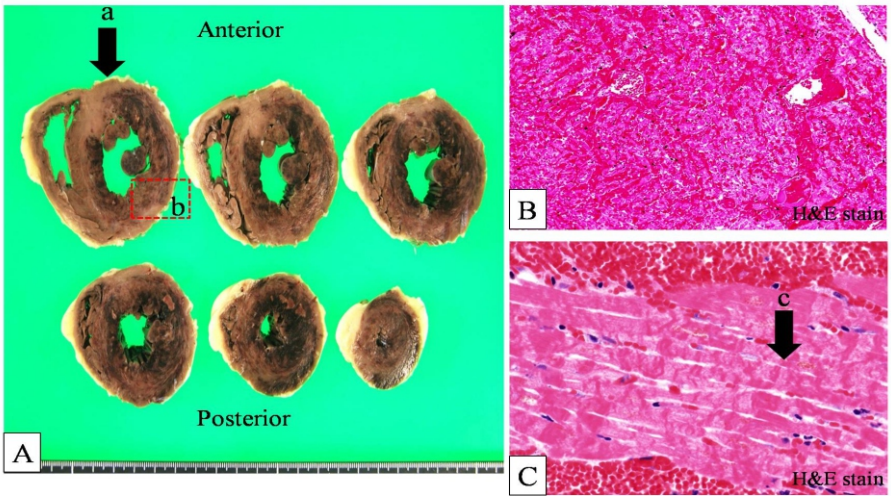

Figure 3: Photomicrographs of the autopsied heart. A: A whole heart fixed with Formalin. Serial ventricular myocardial sections of the heart showed an extensive transmural myocardial infarction with parts of the posterior wall intact (arrow (a)). B: Histological appearance of the infarct area indicated by arrow (b) in (A). There were massive red cells interspersed between cardiomyocytes, resembling "floating myocardial cells in a sea of blood". C: Higher power field image indicated by arrow (b) in (A). Loss of nuclei and striations in most myocytes was observed with contraction band necrosis (arrow (c)). Note that the breakdown of capillary vessel walls was also conspicuous, accompanied by large or small bleeding nests. Although the appearance of inflammatory cells was scarce, infiltration of neutrophils was seen mainly around vascular injury sites, partially within the interstitial tissue myocardium or myocardial tissue.

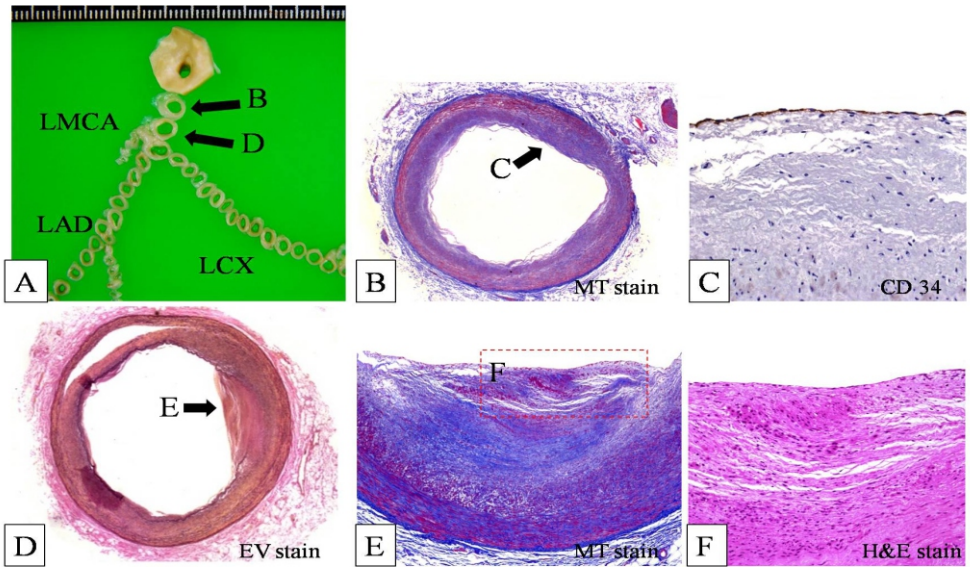

Figure 4: Photomicrographs of the autopsied left coronary artery.

A: Gross observation of the entire left coronary artery, focusing on the proximal (B) and distal (D) LMCA. The whole left coronary artery was sliced every 2 mm forclose observation disclosing that plaque rupture or thrombi formation were not found. B: The low-power image at the proximal LMCA (MT stain) indicated (B) in (A). A minimal, "diffuse intimal thickening" was uniformly apparent in the circumference. C: The high-power image indicated by arrow (C) in (B) (immunostaining for an endothelial cell marker, CD34) confirming that there were no erosions and plaque ruptures in the intima. D: A transverse section of the distal LMCA (EV stain). Segmental disruption of internal elastic lamina was partially observed (arrow E). E: In the high-power image indicated by arrow (E) in (D) (MT stain), localized fibromuscular plaques were formed with medial smooth muscle cells proliferated. F: Higher magnification view of the area (square (F) in (E)), displaying that a proliferation of characteristic spindle-shaped, smooth muscle cells (neointimal hyperplasia) was noted at the site. H&E, hematoxylin eosin; LMCA, left main coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery; MT, Masson trichrome; EV, Elastica van Gieson.

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Manuscript Information: Received: January 22, 2018; Accepted: May 17, 2018; Published: May 31, 2018

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Citation: Miura S, Inoue K, Amemiya K, Yamashita T, Ando K. A case of devastating coronary spasm syndrome: Autopsy-proven acute anterolateral myocardial infarction leading to sudden cardiac arrest following unremarkable coronary angiography. Open J Clin Med Case Rep. 2018; 1414.

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