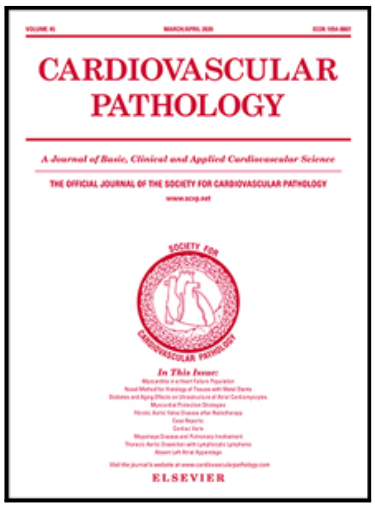

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Highlights

- Including the hypothesis of a rare condition can be crucial for the diagnostic work-up and treatment of myocardial infarction with non-obstructive coronary arteries (MINOCA).
- An integrated imaging assessment including trans-esophageal echocardiogram (TEE) and cardiac nuclear magnetic resonance (CMR) is of paramount importance for the management of MINOCA.
- According to the available evidence surgical excision represents an effective treatment for cardiac papillary fibroelastoma (CPF).

Aortic valve fibroelastoma presenting with myocardial infarction with non-obstructive coronary arteries (MINOCA): a case report and review of the literature

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Abstract:

Cardiac papillary fibroelastomas (CPFs) are rare benign cardiac tumors more often involving the left-sided valves and related with threatening embolic complications. We report the case of a 35-year-old woman presenting with relapsing-remitting chest pain and elevated cardiac troponins. After a negative coronary angiography, an integrated imaging assessment based on echocardiography and cardiac magnetic resonance showed a pedunculated mass on the aortic valve causing an intermittent obstructive engagement of the right coronary ostium. A tailored surgical treatment was performed and the histopathological examination of the specimen revealed mesenchymal tissue with the characteristics of CPF.

Keywords:

MINOCA; aortic valve; cardiac papillary fibroelastoma; cardiac tumors; Myocardial Infarction; Cardiac imaging.

1. Introduction

Myocardial infarction with non-obstructive coronary arteries (MINOCA) defines a group of heterogeneous clinical settings which satisfy the criteria for acute myocardial infarction (AMI) diagnosis in the absence of angiographic evidence of ≥50% diameter stenosis in any major epicardial vessel [1]. Plaque disruption, coronary thromboembolism, coronary artery spasm, coronary microvascular dysfunction, and spontaneous coronary artery dissection are mentioned among the most common causes of MINOCA; nevertheless, in up to 25% of patients the etiology remains unknown [2]. Because of the heterogeneous etiology and pathogenesis, there is no standard treatment protocol for the management of MINOCA. A case by case comprehensive analysis of the potential causes, even the rarest, is thus of paramount relevance for both prognostic and therapeutic purposes. Cardiac papillary fibroelastomas (CPFs) are rare benign primary cardiac tumors (PCTs) which in most cases involve the aortic valve. CPFs can be asymptomatic and, as a consequence, the diagnosis can be incidental. Nevertheless, harmful embolic complications of CPFs have been described [3]. We report the case of a young patient presenting with MINOCA very likely caused by a CPF of the aortic valve.

2. Case Report

A 35-year-old woman with known mitral valve prolapse and history of migraine accessed the Emergency Department because of several episodes in the previous three days of chest pain arising at rest and followed by spontaneous relief within few minutes. The admission ECG showed sinus rhythm, isolated premature ventricular contractions (PVCs), and incomplete right bundle branch block (RBBB). Admission high sensitivity cardiac troponin I (hs-cTnI) was 5853 pg/ml. Cell blood count (CBC), serum creatinine (SCr), and C-reactive protein (CRP) were within the normal range. The first cardiac point of care ultrasound (POCUS) showed preserved ejection fraction and the absence of both segmental wall motion abnormalities and pericardial effusion. The patient was diagnosed with non-ST elevation acute coronary syndrome (NSTE-ACS) and addressed to the Cardiology Division. After an urgent coronary angiography which showed non obstructive coronary artery disease, the patient was referred to intensive care unit (ICU) with a working diagnosis of myocardial infarction with non-obstructive coronary artery (MINOCA) for a close monitoring and comprehensive imaging assessment. Single antiplatelet therapy (SAPT) with low dose aspirin (100 mg q.d.) and betablocker therapy (carvedilol 6.25 mg b.i.d.) were started.

The trans-thoracic echocardiogram (TTE) revealed, in the parasternal long axis (PLAX) view, a round-shaped hyperechoic floating mass attached to the aortic valve **(Figure 1)**. The trans-esophageal echocardiogram (TEE) performed the following day confirmed the presence of a 10 x 8 x 8 mm mass on the right coronary cusp. In the following three days the patient kept complaining of anginal symptoms coupled with an oscillating trend of the hs-cTnI levels **(Figure 2).** The 5th day a cardiac nuclear magnetic resonance (CMR) was performed and revealed preserved systolic function, no late gadolinium enhancement (LGE) pathologic patterns, and no signs of oedema. CMR allowed to rule out an acute myocarditis and demonstrated on the T1-weightened imaging an isointense mass on the right cusp of the aortic valve which turned hyperintense during the assessment of LGE in phase-sensitive inversion recovery (PSIR) **(Figure 3)**. After excluding the above mentioned most common causes of MINOCA, the hypothesis of repetitive episodes of myocardial ischemia due to the transient obstruction of the right coronary ostium determined by the pedunculated mass was formulated. The case was discussed in Heart Team and the surgical intervention was performed 2 days later. After median sternotomy, extracorporeal circulation, and aortotomy, the excision of the mass from the right coronary cusp of the aortic valve was successfully accomplished. The histopathological examination of the specimen revealed a small tumor consisting of papillary fronds covered by a single endocardial layer and a avascular fibro-elastic stroma leading to diagnosis of cardiac papillary fibroelastoma (CPF)**(Figure 4)**. The patient was discharged 1 week after surgery and addressed to a cardiovascular rehabilitation program. At 2 months from surgery a mild aortic regurgitation was detected and the patient did not report any recurrence of chest pain. During the second follow-up visit at 6 months, the clinical status and the echocardiographic findings were stable and an annual follow-up program for the following 3 years was planned.

3. Discussion

PCTs are rare autopsy findings, described in 0.02% of cases. CPFs are ranked as the third most common PCTs after myxomas and lipomas representing the 11.5% of all PCTs [4]. However, a recent large registry showed as the incidence of CPF is probably higher than any other PCT with one case every 1100 TTE performed in a referral base population [5]. CPFs are avascular, pedunculated and composed of collagen and elastic fibers with endothelial covering. These tumors typically localize on the left ventricular side of the mitral valve and on the aortic side of the aortic valve, conversely, right sided valves involvement is rare. The pathophysiology is not fully understood; one major hypothesis considers this tumor acquired

and developing from chronic organization of microthrombi induced by minor endothelial damage [6]. Several histopathological similarities with Lambl's excrescences (LE) have been described and, in some instances, these lesions may appear virtually identical microscopically [7]. Even though some authors reported the distinction between the two entities to be only artificial, some paramount macroscopic differences exist, since LEs are usually filamentous, smaller than CPFs, and involve the valve surfaces exposed to high shear stress [7,8]. Immunohistochemical investigations of the covering cells of CPFs and cardiac myxomas revealed the positivity for vimentin, factor VIII-related antigen, and CD34, suggesting a possible vascular endothelial origin; however, whether CPF is a hamartomatous, neoplastic, or reparative process has not been definitely clarified [9].

Because mostly asymptomatic, CPFs are often incidental autopsy or echocardiographic findings; for this reason, as mentioned above, the real incidence as well as the quote of the symptomatic ones seem difficult to reliably define [10]. The largest case analysis comprehensive of 725 cases [11] reported a wide range of clinical presentations related to size, location, and growth rate. Embolism represents the most frequent complication of the CPF leading to a detectable clinical scenario such as stroke and peripheral ischemia; valvular dysfunction is conversely uncommon. An involvement of coronary arteries has also been occasionally described in terms of acute coronary syndromes and sudden cardiac death [12-18]. The pathogenesis of these phenomena is still unclear; embolization of tumor fragments or of superimposed thrombi have been hypothesized. Furthermore, the onset of acute coronary syndromes has been rarely related to the ability of floating CPFs to prolapse into a contiguous coronary ostium [16-18].

In our case we reported a relapsing-remitting course of chest pain and myocardial damage that differs from the sharp clinical manifestations of coronary arteries embolism. Thus, in view of the high mobility of the pedunculated mass, it is possible to assume that this singular progression could have been the result of a transient coronary ostium occlusion. Cardiac imaging is crucial in the diagnosis of CPF. TEE demonstrated higher sensitivity in identifying CPF than TTE and the mass usually appears as hyperechoic and with shimmering borders [3,19]. No consensus exists on the recommended treatment for this tumor; however, a retrospective analysis of 511 patients with echocardiographic evidence of CPF demonstrated a lower risk of stroke and mortality in the group that underwent surgical removal compared with the group medically treated [5]. A subsequent analysis of the medical therapy group demonstrated no significative differences in 5-years rates of cerebrovascular accidents

according to the treatment with aspirin, warfarin or clopidogrel. Shave excision with valve sparing is the most common approach, while surgical valve replacement is described as the treatment of choice in only 1-10% of cases [5,11,20]. The first technique demonstrated low rates of tumor recurrence after surgery ranging from 0 to 1.6% in a follow-up period of 3-11 years [5,11,20].

MINOCA is a group of heterogeneous conditions and its optimal management crucially depends on the understanding of the underlying cause. Nevertheless, since it has been reported that the diagnosis remains unsolved in 8-25% of cases [2], considering also uncommon clinical scenarios could be of great relevance. An integrated imaging assessment including TEE and CMR can provide important anatomic details and allow to detect rare clinical conditions and thus an effective tailored treatment.

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FIGURES

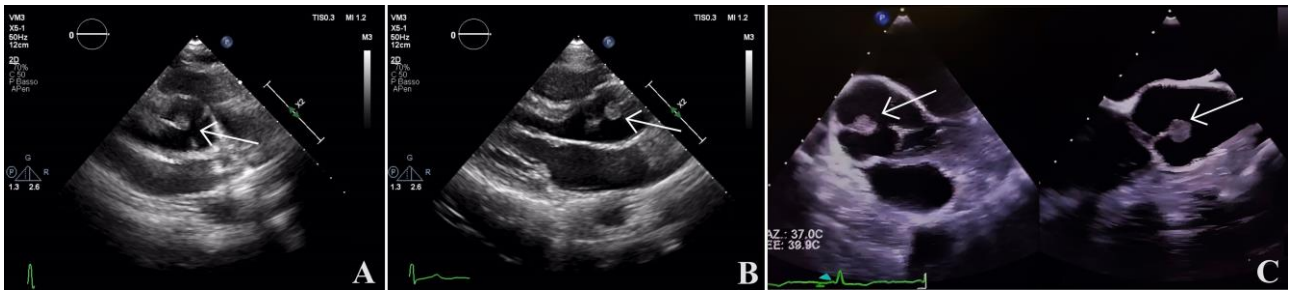

Figure 1. Trans-thoracic echocardiogram (TTE) revealed a floating round-shaped hyperechoic mass with shimmering borders on the aortic valve (arrows) in **(A)** parasternal long axis (PLAX) and **(B)** parasternal short axis (PSAX) views. These findings were then confirmed by trans-esophageal echocardiogram (TEE) **(C)**.

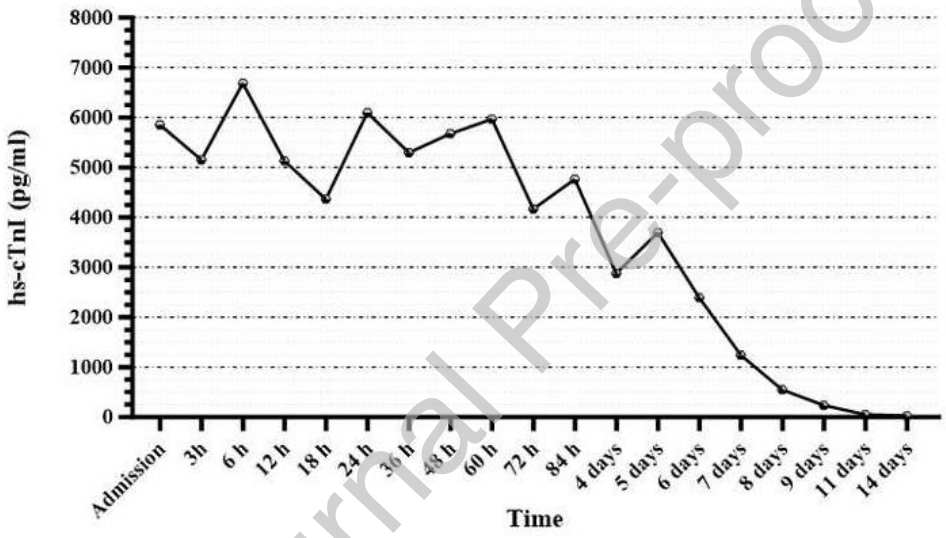

Figure 2. High sensitivity cardiac troponin I (hs-cTnI) levels presented an oscillating trend

suggesting a transient coronary ostium occlusion by the tumor.

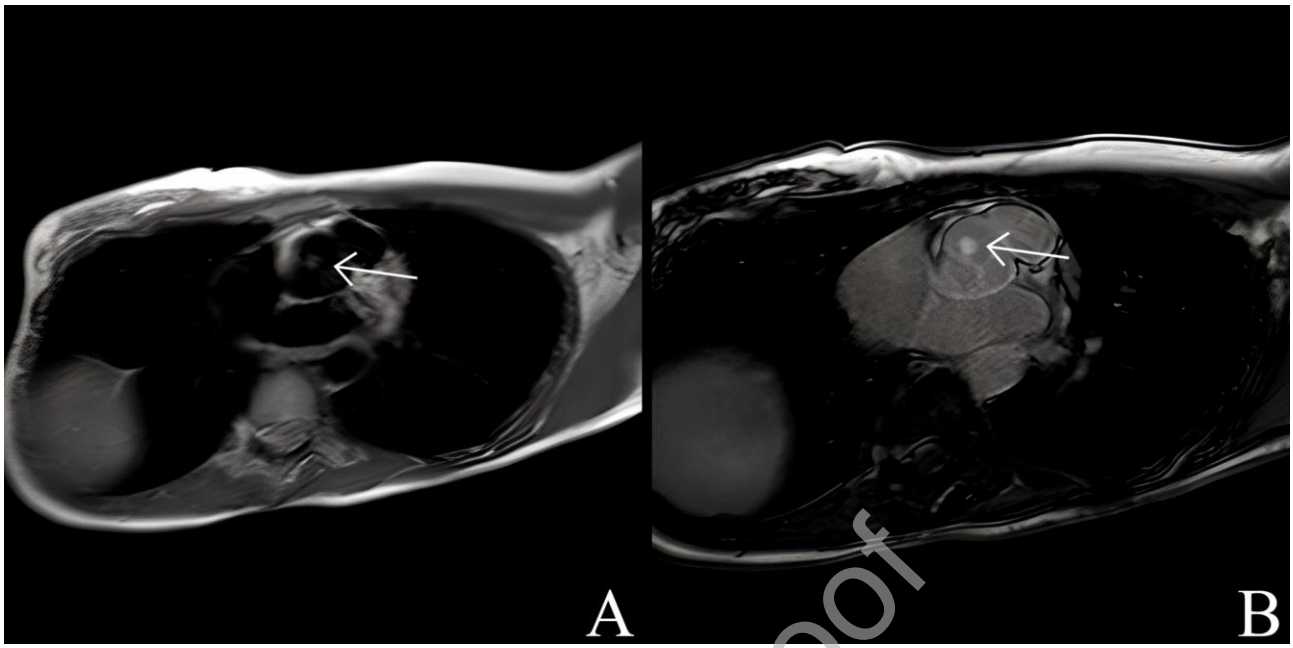

Figure 3. (A) On Cardiac magnetic resonance (CMR), T1-weightened imaging showed an isointense mass on the right cusp of the aortic valve (arrow). **(B)** The study of late gadolinium enhancement (LGE) in phase-sensitive inversion recovery (PSIR) demonstrated higher signal of the mass (arrow) compared with the myocardium.

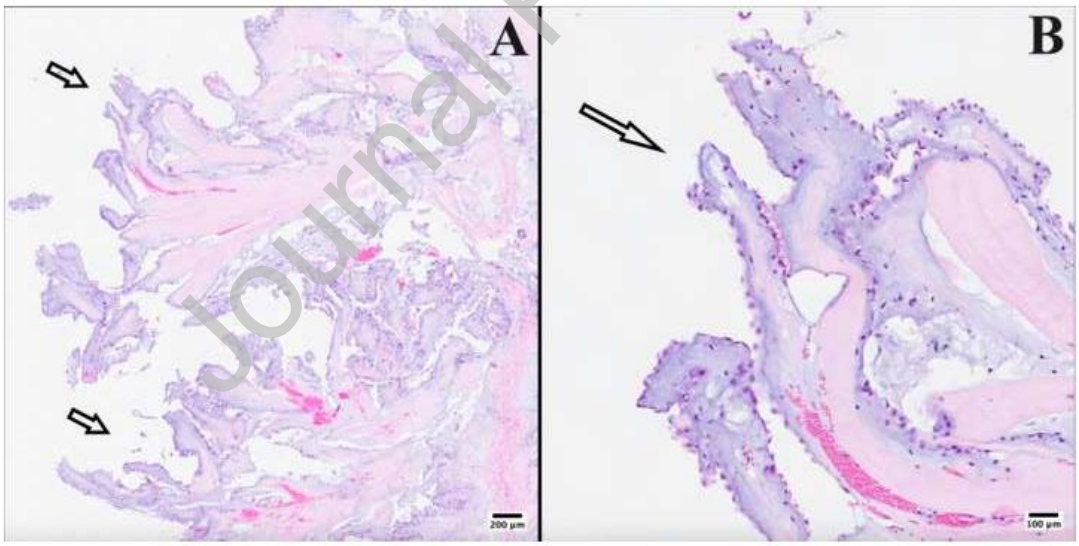

Figure 4. The lesion consisted of small narrowed and elongated papillary fronds (arrows) **(A)** covered by a single layer of endothelial cells (arrow) **(B)**; the stroma was formed by mucopolysaccharides and elastic fibers. Hematoxylin and eosin.

DECLARATION OF INTEREST STATEMENT

All authors do **not** have any financial or personal relationships with people or organizations that could inappropriately influence their work. No funding has been allocated to this project.