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Non-ST-segment elevation myocardial infarction with non-obstructive coronary arteries due to a type-A thymoma: A case report

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ABSTRACT

Introduction: Myocardial infarction with non-obstructive coronary arteries (MINOCA) has become an increasingly recognized subgroup in patients with acute myocardial infarction, with a recent cohort study reporting a prevalence of 8.8%. This report describes a patient who presented with non-ST-segment elevation myocardial infarction (NSTEMI) due to an incidental anterior mediastinal mass.

Case presentation: An 80-year-old woman presented to our emergency department with a chief complaint of progressive shortness of breath associated with retrosternal chest pain for one day duration. Computed tomography (CT) angiogram of the chest was conducted, which revealed an anterior mediastinal mass. Upon admission, the patient developed an acute episode of recurrent severe chest pain, which was diagnosed as an NSTEMI. Emergent cardiac catheterization was performed because of unstable vital signs; however, the results showed no evidence of atherosclerotic changes in the major coronary arteries, compatible with the diagnosis of MINOCA. The mediastinal mass was later confirmed to be a type A thymoma on CT-guided biopsy.

Conclusion: Myocardial infarction in patent coronary arteries due to an anterior mediastinal mass is rare. Further studies are needed to standardize the diagnosis and management protocols for the potential etiologies of MINOCA.

1. Introduction

Myocardial infarction with non-obstructive coronary arteries (MINOCA) is a collective concept characterized by evidence of myocardial infarction (MI) in the absence of obstructive coronary artery disease (CAD), with no coronary artery stenosis ≥50% and no other alternative cause for presentation, according to the Fourth Universal Definition of MI [1]. The rationale for defining such a subgroup in patients with acute myocardial infarction (AMI) is due to the differing prognoses and subsequent treatment plans with

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their AMI counterparts with obstructive CAD. However, accurate diagnosis of MINOCA remains a challenge due to the heterogeneity of underlying causes [2]. Herein, we present the clinical course of our patient, who was initially admitted with a preliminary diagnosis anterior mediastinal mass, which was an incidental finding. Development of NSTEMI was noted, which revealed patent coronary arteries on coronary angiography. The study aimed to review the diverse clinical presentations of thymomas, assess the contemporary consensus on the diagnosis and management of MINOCA, and discuss the plausible underlying mechanisms contributing to MINOCA.

2. Case presentation

An 80-year-old woman, previously diagnosed with hypertension and hyperlipidemia, presented to our emergency department (ED) with a chief complaint of progressive shortness of breath for the duration of 1 day, which was accompanied with chest tightness and non-radiating retrosternal chest pain. The patient denied previous episodes of chest pain, and no other relevant associated symptoms were previously noticed.

Upon arrival at the ED, the patient demonstrated hypertensive urgency with a blood pressure of 191/99 mmHg, heart rate of 114 beats per min, respiratory rate of 18 breaths per min, and oxygen desaturation of 68% under ambient air. The patient was slightly drowsy but was still conversant and oriented to person, place, and time. The breathing sounds were bilaterally coarse upon auscultation, and normal heart sounds without obvious murmurs or pericardial rubs were recorded. The remainder of the systemic physical examination results were unremarkable. Hypertensive urgency and hypoxemia were managed by initiating anti-hypertensives and non-invasive ventilation, respectively.

Chest radiography (Fig. 1) demonstrated bilateral fine reticular opacities, widened mediastinum, cardiomegaly, and bilateral blunted costophrenic angles. An electrocardiogram (EKG) (Fig. 2A) showed sinus tachycardia with mildly elevated ST-segments at the inferior leads, and no dynamic changes were seen on follow-up EKG studies (Fig. 2B). The laboratory test results upon arrival at the ED and follow-up values of cardiac enzymes are shown in Table 1. In addition, echocardiography showed normal left atrial and ventricular sizes, good left ventricular contractility, and no pericardial effusion or regional wall motion abnormalities. A cardiologist at the ED diagnosed as possible recent NSTEMI or secondary hypoxemia related acute coronary syndrome. Dual antiplatelet therapy (DAPT) with loading Aspirin 300 mg plus Ticagrelor 180 mg was prescribed within 2 hours of ED admission. Six hours later, her clinical presentation suggested that a large myocardial infarction was unlikely because of echocardiography revealed very good left ventricular ejection fraction without regional wall motional abnormality, cardiac enzyme (creatine kinase and creatine kinase-myocardia band) decreasing, Troponin-T elevation, and no observed pulmonary edema. The hypoxemic and hypercapnic respiratory distress and hypotension were unlikely caused by acute coronary syndrome. Emergent cardiac catheterization was not introduced immediately.

Persistent respiratory distress and progression to sudden hypotension were observed. Computed tomography (CT) angiography of the chest (Fig. 3A–C) was performed, which showed no definite aortic dissection, intramural hematoma, or obvious pulmonary

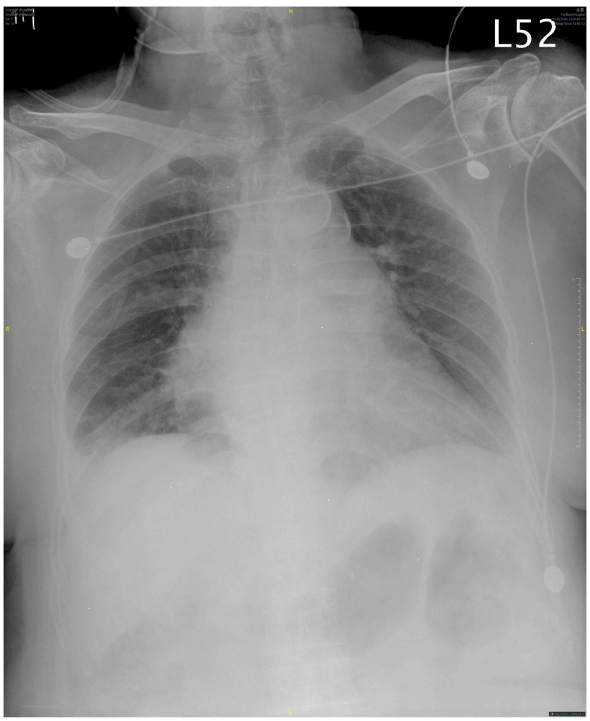

Fig. 1. Anterior-posterior chest radiograph upon arrival revealed a widened mediastinum, cardiomegaly and enlarged cardiac silhouette at right heart border.

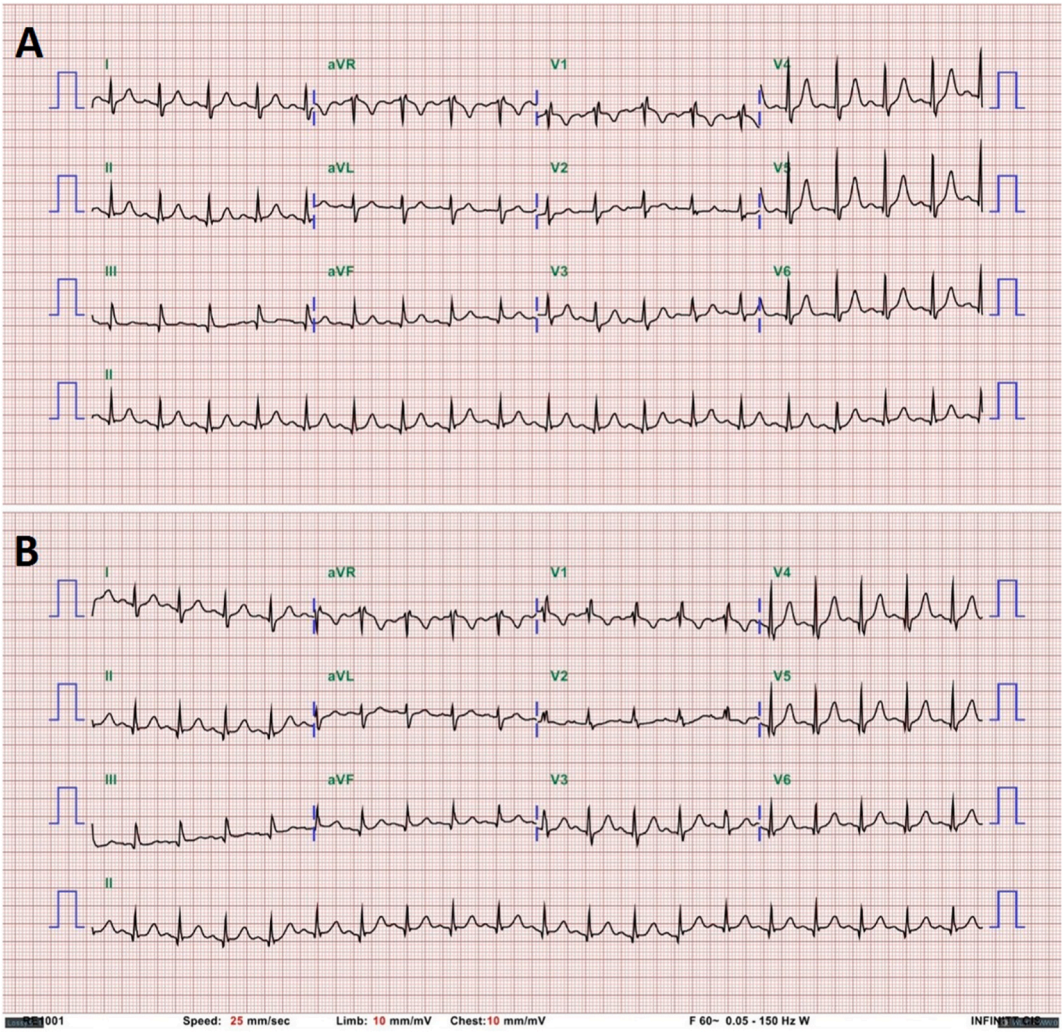

Fig. 2. Electrocardiogram upon (A) arrival showed sinus tachycardia with mildly elevated ST-segments noted at the inferior leads. (B) No dynamic changes were seen upon subsequent EKG taken 12 hours later.

thromboembolism in the main vessels; a right anterior mediastinal mass, well demarcated with minimal contact with the surrounding great vessels and no adjoining abnormal lymph nodes, favoring thymoma; and subpleural alveolar infiltrates in the basal right middle and lower lung fields, favoring possible aspiration pneumonia. The patient was stabilized with noninvasive positive-pressure ventilation and inotropic agents. The admitting diagnosis was right anterior mediastinal mass, favoring thymoma, and was managed as a possible acute coronary syndrome with dual antiplatelet therapy.

On the 4th day after ED admission, recurrence of severe typical cardiac chest pain with radiation to the neck and left shoulder was observed, with subsequent elevation of high-sensitivity Troponin-T (Table 1); however, no acute ST-segment changes were detected compared to previous EKG studies (Fig. 4). The Troponin-T values in the blood of this patient increased slowly after second day of ED admission and reached 1101 ng/L on day 4 (Table 2). An acute NSTEMI episode was suspected, and emergent coronary catheterization was indicated because of unstable vital signs at the time. Coronary angiography (Fig. 5A–F) showed diffusely slow coronary flow with patency in all three coronary arteries. We shifted to high-flow nasal cannula oxygen therapy immediately after coronary catheterization, which the patient could tolerate without further complaints. Pain relief was provided, although no other immediate intervention was performed, and chest pain gradually improved, with subsequent resolution of cardiac enzyme elevation on serial blood examinations.

No other acute cardiac events were noted over the remainder of the hospital course, and CT-guided biopsy was performed. Tissue biopsy confirmed an epithelial malignancy of thymic origin, compatible with type A thymoma (Fig. 6A–F). Serial Troponin T levels showed maintained at high values for 3 days post-catheterization and slowly decreased after one week (Table 2). We gradually weaned off the high-flow nasal cannula oxygen therapy. The patient was discharged after biopsy, and was administered focal radiotherapy instead of tumor resection as preferred by the patient, considering the risk of surgery owing to old age. There was noted tumor regression and the condition improved for 1 year after radiotherapy. There was no cardiac event during radiotherapy and follow-up

Table 1
Laboratory data upon arrival at the emergency department, on ward admission and pre-cardiac catheterization.

Variable	Reference Range	Upon ED Arrival (Day 1)	On Ward Admission (Day 2)	Pre-Cath (Day 4)
Hemoglobin (g/dL)	12.0–16.0	13.2		
Hematocrit (%)	35.0–48.0	41.7		35.6
White-cell count (10^3/μL)	3.8–10.4	9.21		7.09
Differential count (%)				
Neutrophils	40.0–75.0	67.1		
Lymphocytes	20.0–50.0	24.8		
Monocytes	3.0–10.0	6.4		
Eosinophils	0.0–7.0	1.5		
Basophils	0.0–2.0	0.2		
Platelet count (10^3/μL)	140–400	152		
Sodium (mmol/L)	136–146	137		
Potassium (mmol/L)	3.5–5.1	3.7		
Blood urea nitrogen (mg/dL)	7–25	15		
Creatinine (mg/dL)	0.60–1.20	0.3		
Alanine aminotransferase (U/L)	<31	100		
Aspartate aminotransferase (U/L)	13–39	180		
N-terminal pro-B-type natriuretic peptide (ρg/ml)	<125	117		
Creatine Kinase (U/L)	20–170	2792	1637	784
Creatine Kinase-myocardia band (U/L)	0–24	223	97	91
Troponin-T (ng/L)	<14	586.7	377	1101
Lactate (mmol/L)	0.61–2.47	0.95		

Abbreviations: Pre-cath, Pre-cardiac catheterization; ED, emergency department.

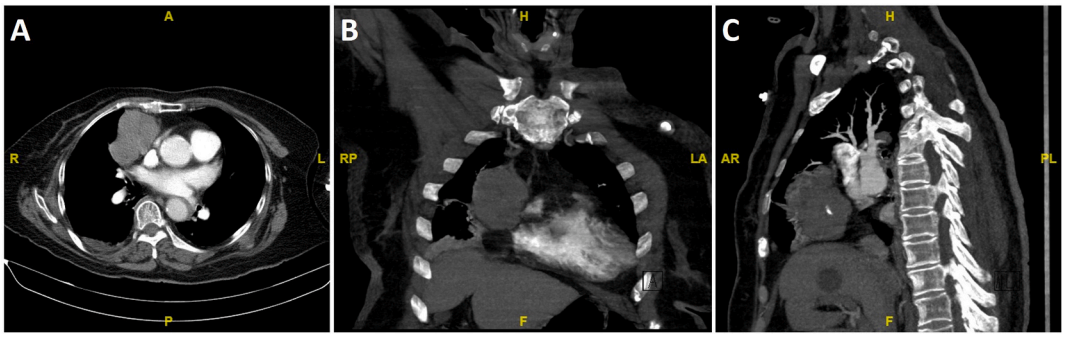

Fig. 3. (A) Transverse, (B) coronal, and (C) sagittal sections of the chest computed tomography angiogram demonstrating a 7 × 4.7 cm lobular homogenous hyperdense tumor with modest enhancement and oval calcification at right anterior mediastinum.

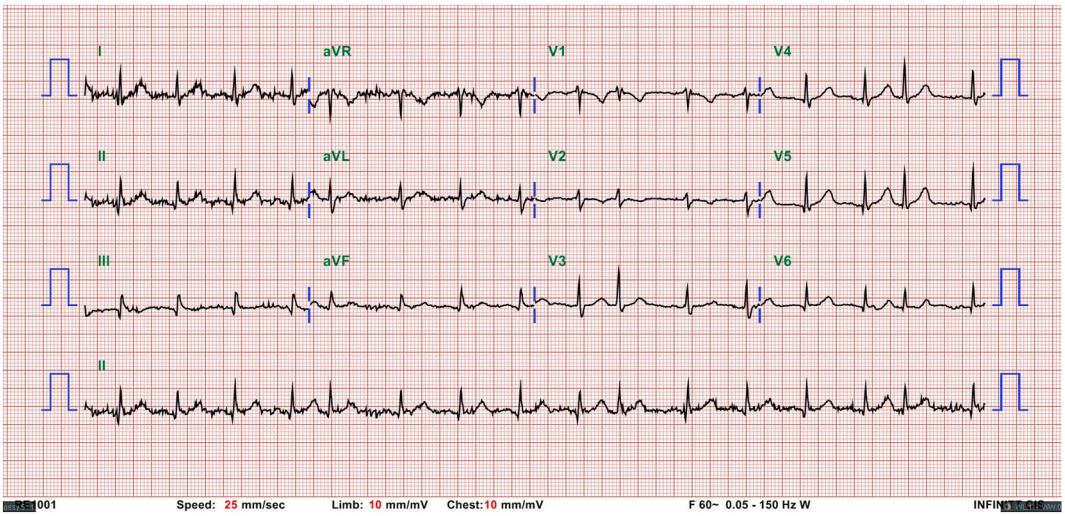

Fig. 4. Pre-cardiac catheterization electrocardiogram showed no acute ST-segment changes compared with previous EKG.

Table 2
Serial Troponin-T values upon arrival at the emergency department, on ward admission, pre-cardiac catheterization and post-cardiac catheterization, and follow-up.

Day and time/event	TROPONIN-T (ng/L)
Day 1 17:00/ED admission	
Day 1 18:21	586.7
Day 1 19:36	596.4
Day 1 23:03	802.1
Day 2 05:48	377
Day 2 12:26	**356.9**
Day 4 02:35	997.4
Day 4 08:52/pre-catheterization	1101
Day 4 17:28/post-catheterization	1194
Day 4 23:27	1141
Day 5 04:38	1087
Day 5 11:47	1143
Day 5 17:19	1134
Day 6 04:27	866.2
Day 6 05:34	840.7
Day 10 06:15	614.9
Day 28 06:26	372.2
After 3 months	150
After 12 months	80.5

Abbreviations: ED, emergency department.

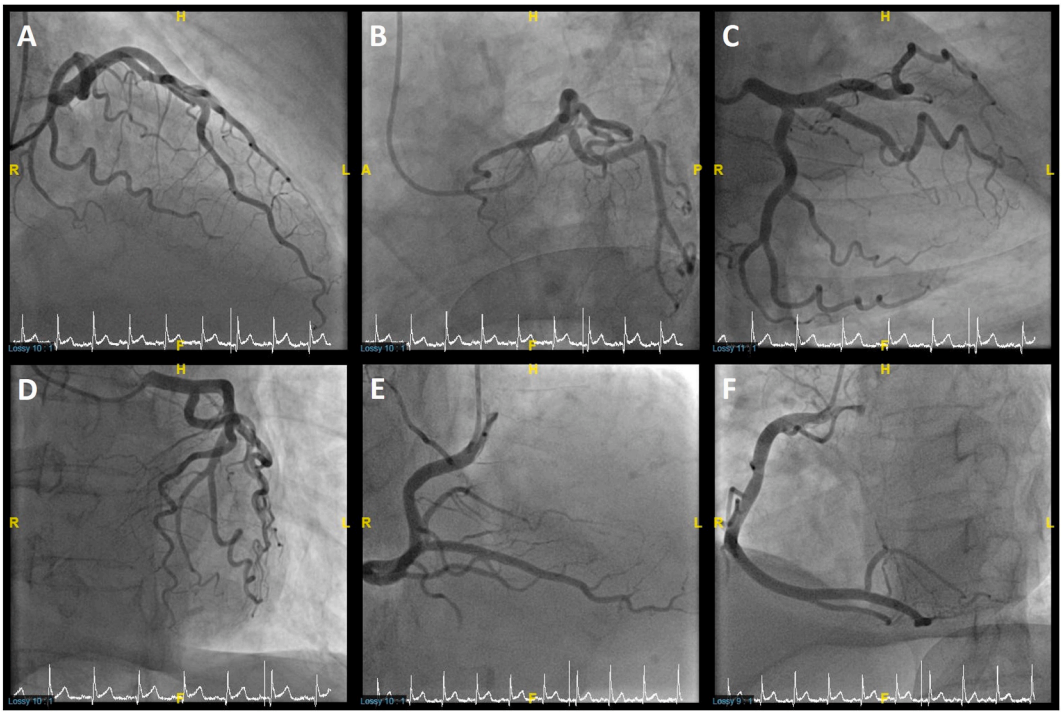

Fig. 5. Coronary angiography depicting patent coronary arteries. (A–D) Different views of left anterior descending artery and left circumflex artery. (E–F) Different views of right coronary artery.

visits, and her Troponin T levels were further reduced.

3. Discussion

Mediastinal tumors are rare, in which thymic cancers account for approximately 20% of all cases and up to 50% of all anterior mediastinal tumors [3]. Thymic cancers can be further classified into thymomas, thymic carcinomas, thymic neuroendocrine tumors, and other types based on the 4th edition of the World Health Organization (WHO) classification of tumors of the thymus [4]. The

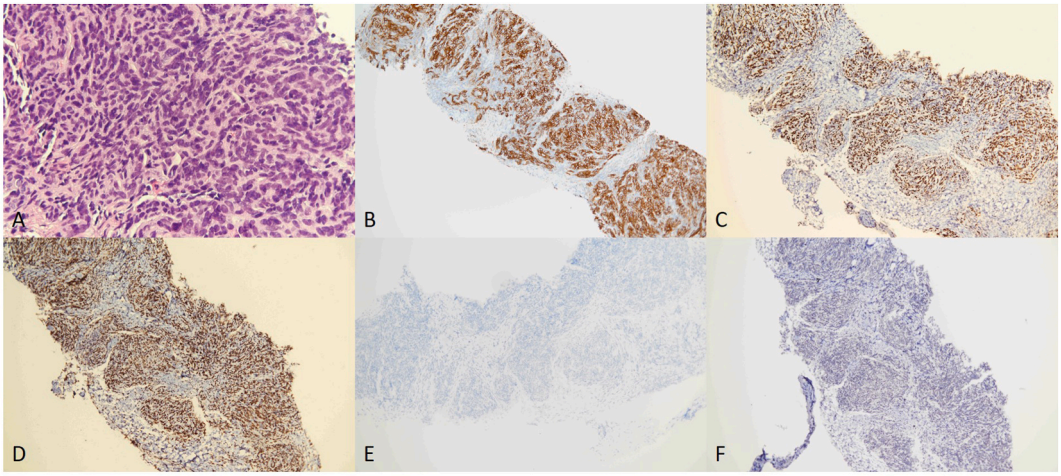

Fig. 6. Pathology and immunohistochemistry results depicting an epithelial malignancy positive for CK, p63, and TTF-1 stains, but negative for synaptophysin and CD117 stains. (A) Hematoxylin and eosin (H&E) 400×, ovoid-to spindle neoplastic cells with nuclear atypia and mitosis. Immunohistochemistry showing (B) CK positive, 200×, (C) p63 positive, 200×, (D) TTF-1 positive, 200×, (E) synaptophysin negative, 200×, (F) CD117 negative, 200×.

reported incidence rate of thymomas is 1.5 per million persons in the United States [5] and 6.3 per million persons in Taiwan [6].

Most thymoma cases are asymptomatic; hence, incidental diagnosis is common. Those who present with symptoms are widely variable, and most patients present with compressive symptoms due to local mass effect (e.g., cough, shortness of breath, chest discomfort, phrenic nerve palsy), constitutional symptoms (weight loss, fever, night sweats), or paraneoplastic syndromes, with myasthenia gravis being the most commonly associated [7,8]. Thymomas personating as acute coronary events are uncommon, and most reports in the literature are due to tumor invasion of adjacent cardiac structures [9–11]. Only a few reports have described a thymoma resulting in myocardial infarction without physical infiltration to the heart or pericardium [12], as in our case. Moreover, upon coronary angiography, no evidence of obstructive coronary artery disease was observed in our patient; therefore, the diagnosis of MINOCA was made.

The diagnosis of MINOCA is relatively straightforward and can be immediately made on coronary angiography in a patient presenting with features consistent with the universal AMI criteria, which concurrently demonstrates no coronary artery stenosis $\geq$50% in any potential infarct-related artery and without a clinically overt specific cause for the acute presentation [1]. However, because of the high sensitivity of myocardial cells to hypoxemia, which translates to angina, elevated cardiac enzymes, or even ST-elevations on the EKG exam [13,14], a plethora of non-obstructive causes can contribute to the diagnosis of MINOCA. Thus, clarifying the underlying pathogenic mechanism for each MINOCA patient remains challenging. Fortunately, in our case, for which we were provided with CT imaging beforehand, an underlying plausible cause was apparent once the diagnosis of MINOCA was made. The chest pain and elevated cardiac biomarkers were most likely due to the local mass effect of the thymoma, resulting in external compression of the coronary arteries. Similar phenomena have been reported in patients with myocardial bridging, neoplasms, and sinus of valsalva aneurysms [15]. Other possible etiologies of MINOCA may also have contributed to the presentation of our patient. These etiologies have often been broadly classified into epicardial (e.g., coronary plaque disease, coronary dissection, coronary artery spasms) and microvascular causes (e.g., coronary microvascular spasm, Takotsubo cardiomyopathy, myocarditis, coronary thromboembolism) [16]. Upon review, a possible coronary thromboembolic event due to the patient's underlying prothrombotic state or coronary vasospasms was also deemed a plausible mechanism for myocardial infarction in our case; however, no concrete evidence was obtained on coronary angiography. Slow coronary flow in all 3 coronary arteries was noticed on coronary angiography, which was compatible with microvascular dysfunction. Therefore, the episode of MINOCA was likely a result of diffuse vasoconstriction of coronary arterioles and capillaries.

Currently, there are no prospective randomized controlled trials for the treatment of MINOCA. Management plans should becausedirected and tailored for each individual. There are some general principles to be adhered to, however, according to the American Heart Association's statement for the diagnosis and management of MINOCA [17,18]. Modifiable CAD risk factors should be treated aggressively if atherosclerosis is suspected in patients with MINOCA. Cardioprotective medications such as antiplatelet agents, statins, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and β-blockers are not recommended for routine use because of possible contraindications; for example, β-blockers in patients with MINOCA cause coronary vasospasms. Current evidence supports the use of calcium channel blockers to alleviate symptoms in the presence of coronary vasospasms, although the benefits of long-acting nitrates are less clear. In our case of a supply demand mismatch caused by external compression from a thymic mass, removing the insult would be the most intuitive and acceptable approach. The role of a high-flow nasal cannula in patients with MINOCA has not yet been reported. Oxygen therapy for acute ischemic heart disease remains controversial [19]. A previous study suggested that routine application of high-oxygen therapy in patients with suspected myocardial infarction with normal room saturation of peripheral oxygen (SPO_2) is not recommended. In that study, the 1-year all-cause mortality was not reduced [20]. However, some studies have suggested

that, in cases of respiratory insufficiency in acute ischemic heart disease or post-cardiac surgery, high-flow oxygen therapy is a worthy option if conventional oxygen therapy is not sufficient [19]. In our case, the patient experienced hypoxemia before and after the coronary catheterization. We initiated high-flow oxygen therapy after patent coronary artery and cardiac function tests were performed. This treatment strategy might be considered as a reference for similar cases in future clinical practice.

4. Conclusions

This case illustrated a rare presentation of thymoma resulting in myocardial infarction with unobstructed coronary arteries. Mediastinal neoplasms may masquerade as acute coronary events, especially if the mass lesion closely abuts the relevant coronary structures. It is relevant to have an increased awareness of MINOCA, and additional studies are needed to address the potential etiologies and treatment in such cases.

Ethics approval and consent to participate

This study was approved by the FEMH Ethics Committee of Taiwan (FEMH-107139-F). Written informed consent for publication of this report was obtained from the patient.

Author contribution statement

All authors listed have significantly contributed to the investigation, development and writing of this article.

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Availability of data and materials

All data generated or analyzed in this study are included in this published article. The data are available upon reasonable request from the corresponding author.

Consent for publication

The patient provided written informed consent for inclusion of her clinical and imaging details in the manuscript for publication.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

AMI	acute myocardial infarction
CAD	coronary artery disease
CT	computed tomography
MINOCA	myocardial infarction with non-obstructive coronary arteries
NSTEMI	non-ST-segment elevation myocardial infarction

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