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Acute ST-elevation myocardial infarction in a young patient with antiphospholipid syndrome

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Abstract

Acute coronary syndrome rarely occurs in young individuals and is seldomly associated with antiphospholipid syndrome. We report the case of a 26-year-old Hispanic man who presented with acute ST-elevation myocardial infarction and was treated with urgent percutaneous transluminal coronary angioplasty. He experienced stent thrombosis within 48 h of intervention and subsequently developed a left apical thrombus. Hypercoagulable state studies were obtained at admission and 12 weeks after the event establishing the diagnosis of antiphospholipid syndrome.

Keywords

Antiphospholipid syndrome, anti-cardiolipin, antiphospholipid anticoagulant, lupus antibody, stent thrombosis, ST elevation, ST-elevation myocardial infarction

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Introduction

Antiphospholipid syndrome (APS) is an immune-mediated, acquired hypercoagulable state that can cause arterial and venous thrombosis. Its incidence is estimated around 5 per 100,000 per year, with a median age of diagnosis of 34 years.[1] In rare occasions, acute coronary syndrome (ACS) can occur in patients with APS.

Case report

A 26-year-old man presented with severe mid-sternal chest pain of 3-h evolution. Associated symptoms included diaphoresis, shortness of breath, and dizziness. He denied previous similar symptoms. He had no history of diabetes mellitus, cigarette smoking, hypertension, hyperlipidemia, family history of early coronary artery disease, or sudden cardiac death. He denied illicit drug or anabolic steroid use. He did have a remote history of a pulmonary embolism (PE) at 7 years of age. At that time, work-up for hypercoagulable state was negative, as per history.

Physical examination revealed tachycardia of 110 bpm and blood pressure of 130/70 mmHg. Cardiac auscultation revealed regular rhythm with normal S1 and S2; there were no murmurs. Lungs were clear to auscultation. A 12-lead electrocardiogram (ECG) showed 3–4 mm ST-segment elevations in leads I, aVL, and V2 through V6, consistent with acute ST-elevation myocardial infarction (STEMI).

The patient was treated as per standard management of STEMI, including low-molecular-weight heparin (LMWH), nitrates, enalapril, metoprolol succinate, aspirin, and clopidogrel. He also underwent coronary angiography within 30 min of arrival to the emergency room (ER), which demonstrated total occlusion of the proximal left anterior descending (LAD) coronary artery (Figure 1). A bare metal stent, Vascular

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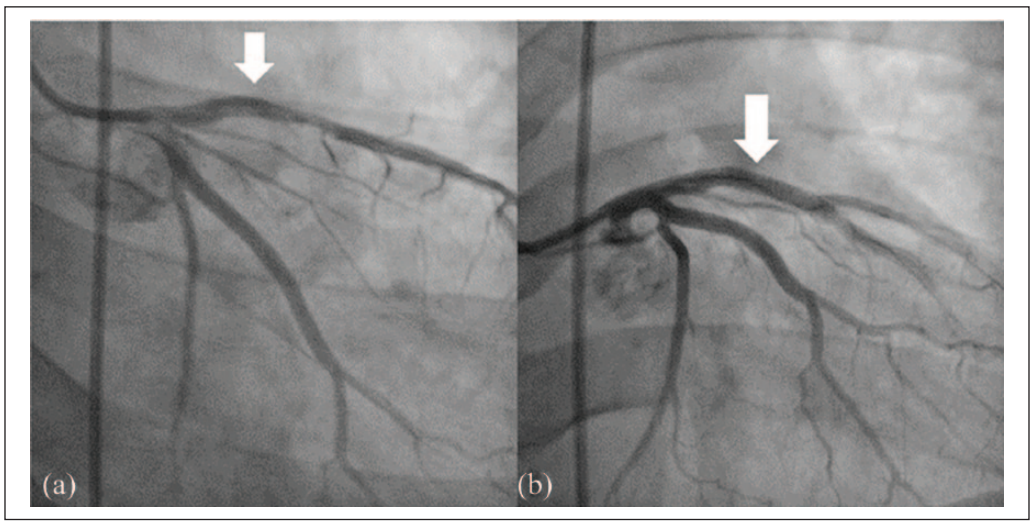

Figure 1. (a) Left coronary angiogram showing thrombus at the proximal left anterior descending (LAD) coronary artery (arrow). (b) Successful deployment of a bare metal stent at the proximal LAD (arrow). Vascular Multi-Link Vision 3.5 mm × 18 mm (Abbott Santa Clara, CA).

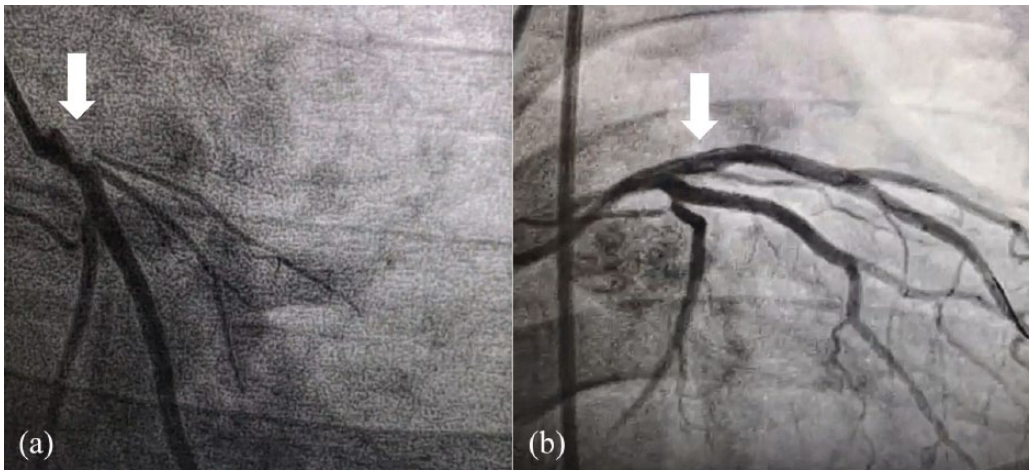

Figure 2. (a) Left coronary angiogram showing thrombosed stent at the proximal left anterior descending coronary artery (arrow). (b) Angiography after successful thrombus aspiration and ballooning of the distal left anterior descending (LAD) and first diagonal coronary arteries (arrow).

Multi-Link Vision 3.5 mm × 18 mm (Abbott Santa Clara, CA), was selected based on the probability of a hypercoagulable state and possible need for prolonged anticoagulation.

Following thromboaspiration of the LAD, pre-stent ballooning was performed with application of 6 ATM, for 30 s. After baseline angioplasty, the balloon was removed. After that, the stent was inspected for normal catheter centering. Distal LAD and D1 arteries were ballooned with 2.0 cm catheter at 6 ATM for 30 s and then repeating the process four times each, achieving a post-stent measurement of minimal luminal diameter (MLD) of 3.5 mm.

After the procedure, he was started on intravenous eptifibatide for 24 h, as well as LMWH and dual antiplatelet therapy. Two days later, the patient developed severe chest pain, similar to initial presentation. ECG showed new ST-segment elevations in leads I, aVL, and V2 through V6. A repeat coronary angiography demonstrated stent thrombosis; thrombus aspiration and ballooning of the LAD and first diagonal coronaries were successful (Figure 2).

A follow-up echocardiogram showed severe global hypokinesia and an ejection fraction of <30%. Contrast echocardiogram confirmed the presence of a left ventricular apical thrombus. Partial thromboplastin time mixing studies for lupus anticoagulant (PTT-LA) was prolonged at 53 s, dilute Russell viper venom test (dRVVT-LA) was prolonged at 47 s, and hexagonal phase phospholipid test (HPPL) was positive. Antibodies for beta glycoprotein (β_2-GPI) and all anti-cardiolipin (aCL) isotypes were absent. ANA and

Table 1. Laboratory results.

Hypercoagulable state work-up studies at admission			
Troponin-I (1st)	0.55 ng/dL	PTT-LA	53 s
Troponin-I (2nd)	15.0 ng/dL	dRVTT-LA	47 s
NT-Pro-BNP	371 pg/mL	HPPL	Positive
PT	13.1 s	Anti-β2GP1	<9 SGU
PTT	26.4 s	Anti-cardiolipin	Negative
INR	0.9	Homocysteine	7.6 µmol/L
ANA	Negative	Protein C & S	77%/71%
Anti-Sm	Negative	Antithrombin III	84%
Anti-RNP	Negative	CRP	284 mg/L
Anti-SS-A/Rho	Negative	Factor VIII	79%
Anti-SS-B/La	Negative	Fibrinogen	422 mg/dL
Anti-dsDNA	11 IU/mL	Amphetamine	Negative
C3 and C4	Normal	Cocaine	Negative
ANCA antibodies	Negative	Opioids	Negative
Hypercoagulable state work-up 12 weeks after initial set			
PT	12.2 s	Homocysteine	9.3 µmol/L
PTT	29.2 s	Protein C & S	82%/93%
INR	3.3	Antithrombin III	92%
PTT-LA	57 s	CRP	40 mg/L
dRVTT-LA	44 s	Factor VIII	79%
Hexagonal-LA	Positive	Factor V Leiden	Not sent
Anti-β2GP1	<9 SGU	Fibrinogen	239 mg/dL
Anti-cardiolipin	Negative	Prothrombin 20210	No mutation
		MTHFR gene	No mutation

PTT-LA: partial thromboplastin time for lupus anticoagulant antibody; dRVVT-LA: dilute Russell viper venom; NT-pro-BNP: N-terminal pro b-type natriuretic peptide; HPPL: hexagonal phase phospholipid; PT: prothrombin time; PTT: partial thromboplastin time; INR: international normalized ratio; ANA: antinuclear antibody; Anti-Sm: Anti Smith; Anti-RNP: anti-ribonucleoprotein; CRP: C-reactive protein; anti-dsDNA: anti-double-stranded DNA; ANCA: antineutrophil cytoplasmic antibodies; Anti-β2GP1: anti-beta glycoprotein antibody; MTHFR: methylenetetrahydrofolate reductase.

anti-ds-DNA were negative, homocysteine levels were low at 7.6 µmol/L, and other studies for hypercoagulability were unremarkable (Table 1).

The patient was started on warfarin to target international normalization ratio (INR) 3.0–4.0 as he presented arterial thrombosis. Hydroxychloroquine, high-dose statin, aspirin, clopidogrel, carvedilol, and enalapril were also prescribed. He was discharged home with a wearable defibrillator.

Three months later, repeat PTT-LA was 57 s, dRVTT-LA 44 s, and HPPL was positive. These results established diagnosis of APS as per the modified Sapporo criteria (Table 2). A follow-up echocardiogram revealed a left ventricular ejection fraction of 25%, for which patient underwent implantation of a cardioverter-defibrillator for primary prevention of sudden cardiac death. Clopidogrel was discontinued 6 months after myocardial infarction in order to decrease bleeding risk. The patient has experienced no further thrombotic events after 1 year of follow-up.

Discussion

The modified Sapporo criteria require clinical evidence of at least one thrombotic event in the presence of a positive laboratory test for a known antiphospholipid antibody and a confirmatory test 12 weeks after the initial positive test.[3] Our patient met these criteria as he had a history of PE and presented an acute myocardial infarction (AMI) with positive serologic tests for APS on different occasions.

The mechanism by which APS induces a hypercoagulable state has not yet been fully elucidated. It is speculated that it entails inappropriate activation of endothelial cells, tissue factors, c5a anaphylatoxins, and complement pathways, which ultimately deregulate the coagulation cascade.[4,5]

APS usually presents with deep venous thrombosis, transient ischemic attacks, and ischemic strokes, but rarely ever myocardial infarction. Even though AMI is uncommon in patients with APS, Cerveras et al.[6] established AMI as the second most common cause of death in APS patients. Cardiac manifestations of APS include accelerated coronary atherosclerosis, valvular abnormalities, early bypass graft failure, pulmonary hypertension, intracardiac thrombi, myocardial microthrombi formation, and non-inflammatory microvasculopathies.[7] Circulating antiphospholipid antibody (aPL) are thought to bind to cardiac tissue, including the valvular endothelium, leading to superficial damage.

Table 2. International criteria for the classification of antiphospholipid syndrome.[2]

Clinical Criteria

1. Vascular thrombosis:
   (a) One or more clinical episodes of arterial, venous, or small vessel thrombosis confirmed by appropriate imaging study or histopathological analysis.
2. Pregnancy morbidity
   (a) One or more unexplained death of a morphologically normal fetus at or beyond the 10th week of gestation.
   (b) One or more premature births of a morphologically normal neonate at or before the 34th week of gestation due to preeclampsia, eclampsia, or placental insufficiency.
   (c) Three or more unexplained consecutive spontaneous abortions before the 10th week of gestation, excluding hormonal, anatomical, and progenitor genetical abnormalities.

Laboratory Criteria

1. LA detection criteria as established by ISTH Scientific and Standardization Subcommittee for the Standardization of Lupus Anticoagulant
   (a) Prolongation of screening tests that are phospholipid-dependent (Hexagonal (II), KCT, dilute prothrombin time, aPTT or dRVVT)
   (b) Mixing study demonstrate the presence of inhibitors in platelet-free normal plasma
   (c) Correction of the prolonged clotting time by adding excess phospholipids
   (d) Exclusion of other coagulopathies (heparin or factor VIII inhibitor)
2. Anticardiolipin antibody
   (a) Medium or high IgG and/or IgM isotype titers in the blood (defined as >99th percentile; >40 GPL or MPL)
3. Anti-B2-glycoprotein I antibody
   (a) High IgG and/or IgM isotype titers in blood (defined as >99th percentile; >40 GPL or MPL).

LA: lupus anticoagulant antibody; ISTH: International Society on Thrombosis and Haemostasis; KCT: kaolin clotting time; aPTT: activated partial thromboplastin time; dRVVT: dilute Russell viper venom time; GPL: IgG phospholipid units; MPL: IgM phospholipid units; APS: antiphospholipid syndrome.
For APS to be confirmed, positive aPL laboratory tests should be positive on at least two occasions, and 12 weeks apart.

Lupus anticoagulant antibody (LAA) is the most common antiphospholipid in APS, and it is considered a risk factor for both venous and arterial thrombosis. A positive LAA, as in our patient, increases the risk of AMI by 5.5%, and the risk for angina pectoris by 2.7%.[8,9] Similarly, the IgG isotype of anticardiolipin (aCL) is strongly atherogenic and associated with worse cardiovascular outcomes, although this antibody was not present in our patient. In the end, all individual aPLs increase the risk for thrombosis and atherosclerosis. However, the more aPLs present in an individual, the worse the outcomes and the higher the risk of thrombosis in APS patients, irrespective of their anticoagulation status and known conventional risk factors.[10,11]

It is rare for young individuals to suffer AMI as their vascular endothelium is not yet significantly affected by atherosclerosis. Nevertheless, AMI in APS is likely due to thrombus formation rather than of premature atherosclerosis. This case illustrates that ACS is possible in a patient with primary APS without traditional risk factors for atherosclerosis or preexisting structural heart disease. Thus, a hypercoagulable state should be suspected in young individuals who present ACS.

Primary PCI and thromboaspiration, if needed, are the treatment of choice in young patients with STEMI and APS. Patients with APS still have significant morbidity and mortality despite PCI and anticoagulation treatment. Optimal management is still debatable, as patients have worse long-term clinical outcome due to higher rates of need for target lesion revascularization. Our patient presented with stent thrombosis, which has an incidence of 0.8% in the general population.[12] However, due to the rarity of APS and stent thrombosis, there is not enough data to establish a direct link between the two. There are some documented cases of recurrent stent thrombosis that make a case for APS as a risk for stent thrombosis.[13] Interestingly, recurrent stent thrombosis has occurred in APS patients on optimal anticoagulation therapy, suggesting the presence of unforeseen variables at play.

The combination of a hypercoagulable state in APS patients, along with increased blood stasis due to ventricular wall akinesia, and endothelial injury from the infarcted tissue increase the likelihood of apical thrombus. Risk factors for developing intracardiac thrombi are associated with significant size AMI, anterior wall location, ejection fraction of ⩽40%, severe apical akinesia, or a left ventricular aneurysm. All of these factors were present in our patient. Prashanth et al.[14] previously published a similar case of an APS patient developing intracardiac thrombi in the setting of an anterior wall MI. The incidence of intracardiac thrombi in APS is unknown.

Patients with definite APS and a first venous thrombosis event should be treated with anticoagulation with a vitamin K antagonist (VKA) to a target INR of 2.0–3.0 for at least 3–6 months. In patients who present with arterial thrombosis, the high-intensity VKA therapy with target INR of 3.0–4.0 is recommended. However, there is much controversy regarding this approach as clinical trials regarding high-intensity VKA therapy have yielded mixed results with an increased risk of bleeding.[15] Also, there are several reports of thrombotic recurrence in the presence of

high-intensity VKA.[16] Prospective cohort studies are needed to clarify the appropriate timing of and selection criteria for high-intensity VKA therapy. For primary thromboprophylaxis, a low-dose aspirin therapy has been shown to be effective in decreasing first thrombotic event among SLE patients and asymptomatic aPL patients. In subjects with single positive aPL test results, aspirin has been shown to be equally effective for preventing recurrence of thrombotic events.[17] Similarly, statin therapy has been shown to reduce prothrombotic biomarkers.[18]

Conclusion

APS should be suspected in young individuals with unexplained thrombotic events, including AMI. Proper immunological work-up should be performed promptly, as an early diagnosis can decrease disease burden. Careful history taking should be undertaken with emphasis on prior thrombotic events, such as PE or deep venous thrombosis. Percutaneous transluminal coronary angioplasty (PTCA) is the treatment of choice for APS patients who present with STEMI. This strategy has resulted in satisfactory long-term results with low complication rates. Once APS is confirmed, long-term anticoagulation should be continued and maintained at the appropriate INR range. Just as for patients without APS, secondary preventive measures for coronary artery disease should be provided in order to decrease morbidity and mortality in these patients.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or The National Heart, Lung, and Blood Institute.

Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

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Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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