In-situ coronary thrombosis without atherosclerosis in a young male: A case of multifactorial thrombophilia

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Abstract
We present the case of a 27-year-old male with an acute anterior Q-wave myocardial infarction due to in-situ thrombosis of the left anterior descending artery (LAD), with no angiographic signs of atherosclerosis. The clinical presentation revealed a multifactorial etiology involving immune activation (positive lupus anticoagulant, high SARS-CoV-2 IgG), genetic predisposition (heterozygous mutations in MTHFR, MTRR, PAI-1), and modifiable factors (smoking, stress). The case highlights diagnostic challenges in young patients without traditional risk factors, as well as the importance of adhering to validated APS testing protocols. Particular attention is drawn to the premature switch from warfarin to edoxaban, prompting reconsideration of anticoagulation strategy in the context of suspected APS. This report emphasizes the need for individualized evaluation and treatment planning in atypical arterial thrombosis, especially in the context of potential post-COVID immune dysregulation.

Keywords
myocardial infarction, in-situ thrombosis, antiphospholipid syndrome, thrombophilia, COVID-19, young adults, genetic risk

Introduction

Arterial thrombosis in young individuals without conventional cardiovascular risk factors remains a diagnostic challenge, often prompting extensive investigation into less typical etiologies. While the prothrombotic role of SARS-CoV-2 infection is well documented [1–3], emerging evidence suggests that even asymptomatic or subclinical exposure may lead to delayed immune-mediated vascular events [4,5]. This case adds to the expanding literature on post-COVID thrombosis by illustrating a complex interplay of immune activation, inherited thrombophilia, and metabolic factors—occurring in the absence of atherosclerosis or established autoimmune disease. It underscores the need for comprehensive evaluation, adherence to validated diagnostic protocols, and cautious therapeutic decision-making, particularly when antiphospholipid syndrome (APS) is suspected but not yet confirmed.

Case presentation

A 27-year-old male, active smoker (10 pack-years), with no metabolic syndrome or history of ischemic heart disease, presented on March 30, 2025, with acute chest pain unrelieved by nitroglycerin, fentanyl, or morphine.

- **ECG:** QS complex in V1, absence of R-wave progression in V2–V4, ST depression in leads II, III and aVF (Figure 1).
- **Biomarkers (10 hours post-symptom onset):** Troponin I > 50x ULN; CK-MB > 10x ULN. Leukocytosis: 14.0 G/L, ALT: 60.5 U/L (~1.5× ULN), AST: 374.0 U/L (~9.3× ULN).
- **TT Echocardiography:** Hypokinesia of the anteroseptal segment; LVEF 42%.
- **SARS-CoV-2 serology:** IgG = 2124.1 AU/ml (~301.6 BAU/ml), indicating previous likely asymptomatic infection.
- **Genetic thrombophilia testing:** Heterozygous mutations: SERPIN1 (675 5G/4G), MTHFR A1298C, MTRR A66G. Homocysteine: 16.6 µmol/L (normal <15 µmol/L). A comprehensive thrombophilia screening panel was conducted, including testing for factor V Leiden and the prothrombin G20210A mutation, and protein S levels—all of which returned within normal limits.
- **Protein C activity:** 157% (normal 70–140%).
- **LA screen (04.04.2025 against the background of enoxaparin):** 48 seconds (normal ≤ 44 sec); anticardiolipin and β2-GPI antibodies within normal limits.
- **Screening for thrombocytopenia and systemic signs of autoimmune disease:** Yielded negative results
- No family history of cardiovascular or autoimmune disorders was reported

Coronary angiography (12 hours post-symptom onset) revealed a mural thrombus in the proximal LAD with TIMI III flow and no signs of atherosclerosis, dissection, or vasospasm. Thrombolysis and thrombectomy were not performed (Figures 2 and 3).

- **Discharge ECG:** Persistent QS complexes in V1–V2, minimal R-wave in V3 (1 mm), no positive dynamics in V4, confirming completed transmural Q-wave MI (Figure 4).
- **Global longitudinal strain (GLS) on speckle-tracking echocardiography:** GLS significantly reduced to −13.6%. Significant impairment in segmental strains of the anterior, anterior septal, apical and apical segments of the left ventricle. LVEF 52%.

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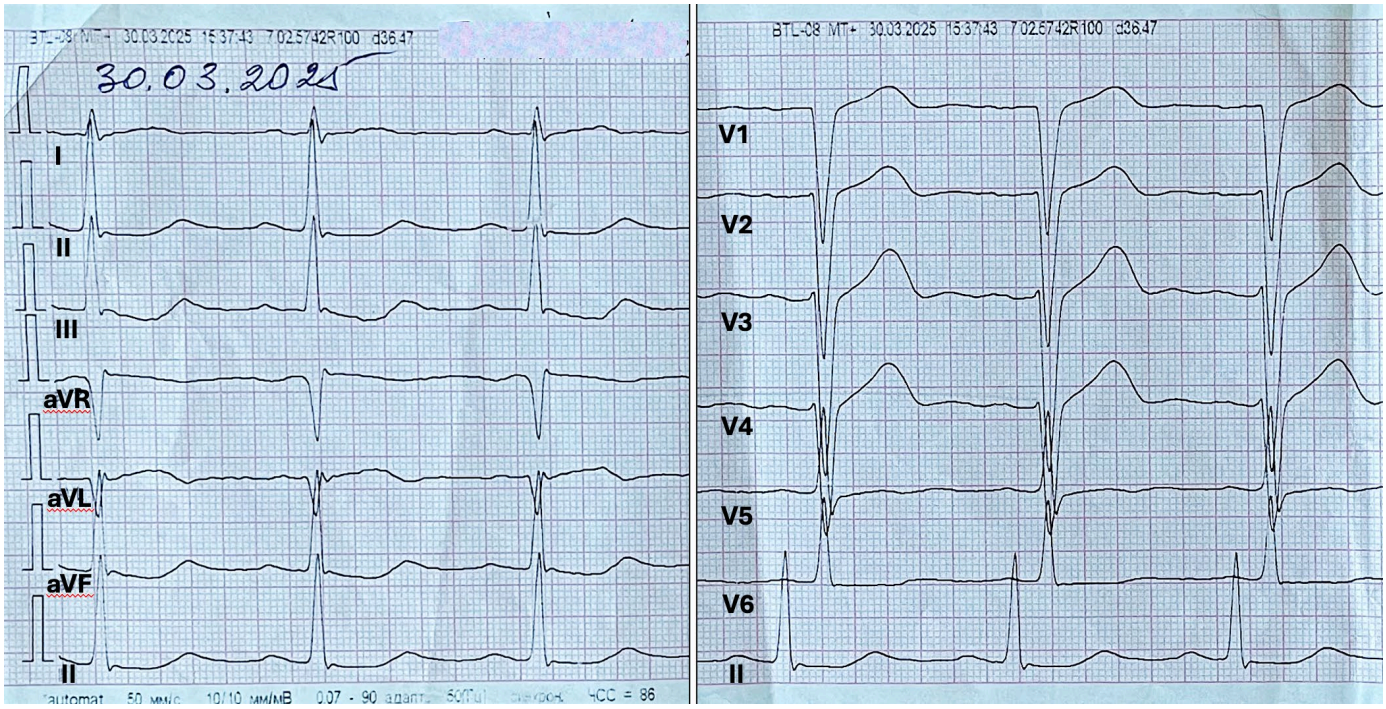

Figure 1 - Electrocardiogram. QS complex in V1, absence of R-wave progression in V2–V4, ST depression in leads II, III, and aVF.

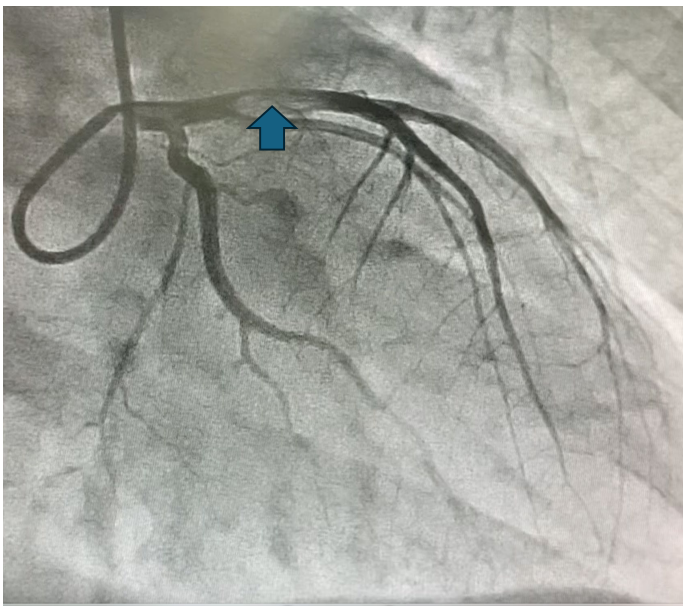

Figure 2 - Angiogram of the left coronary artery. Coronary angiography (12 hours post-symptom onset) revealed a mural thrombus in the proximal left anterior descending artery (LAD) with TIMI III flow and no signs of atherosclerosis, dissection, or vasospasm.

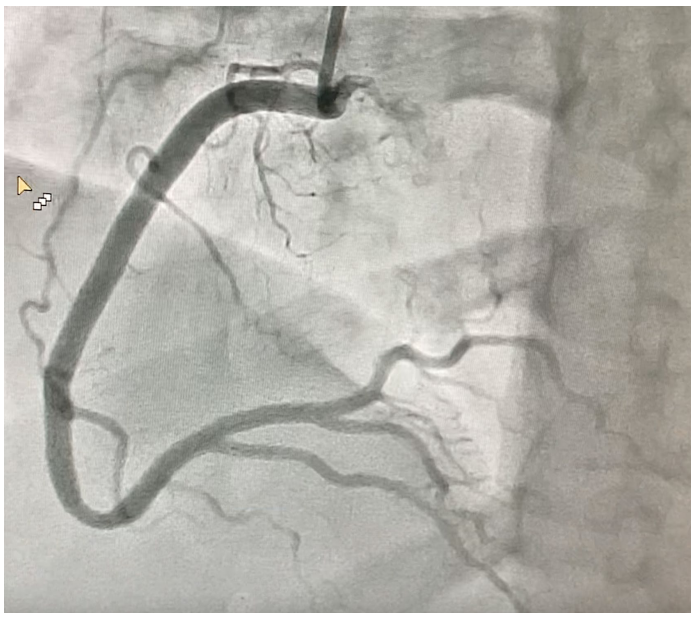

Figure 3 - Angiogram of the right coronary artery. The right coronary artery is normal.

Treatment course

1. **Acute phase:** Enoxaparin + warfarin + clopidogrel.
2. **After 4 weeks:** Unjustified switch to edoxaban + clopidogrel.
3. **After 2 months:** An episode of recurrent unstable angina; patient was restarted on enoxaparin, then warfarin (INR 2–3) + clopidogrel.

Final diagnosis

Acute anterior Q-wave myocardial infarction (type 2 ESC 2018), dated March 30, 2025, without atherosclerosis (angiography showed mural thrombus in proximal LAD, TIMI III). Killip class I. Background conditions: multifactorial thrombophilia:

– **Genetic:** heterozygous for SERPIN1 (675 5G/4G), MTHFR A1298C, MTRR A66G

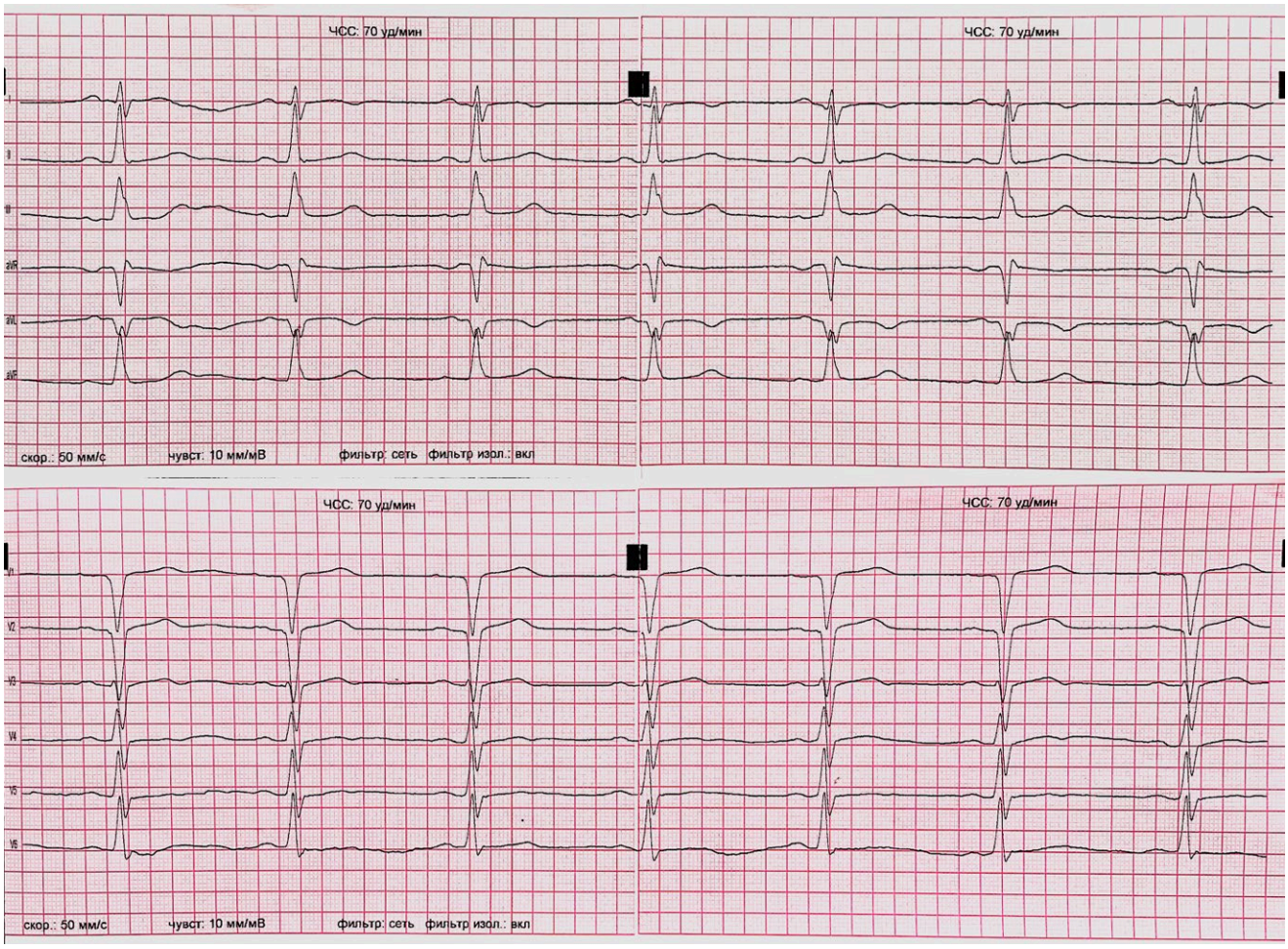

Figure 4 - Electrocardiogram (discharge). Persistent QS complex in V1–V2, minimal R-wave in V3 (1 mm), no positive dynamics in V4, confirming completed transmural Q-wave MI.

- **Serologic:** prolonged LA screen, elevated IgG to SARS-CoV-2 (2124.1 AU/ml)
- **Metabolic:** hyperhomocysteinemia (16.6 μmol/L). Additional risk factors: active smoking, chronic stress.

Discussion

This case illustrates the multifactorial and complex nature of in-situ coronary thrombosis in a young patient without a family history of cardiovascular disease, APS, or systemic connective tissue disorders. Given the patient's age and the absence of coronary artery atherosclerosis, hypertension, diabetes mellitus, or dyslipidemia, smoking and significant psychoemotional stress related to military service were the only modifiable risk factors for the cardiovascular event. This prompted an investigation into potential thrombotic predictors, including immunological and genetic factors [6,7].

During the acute phase of transmural myocardial infarction, laboratory testing revealed a positive lupus anticoagulant (anticardiolipin and β2-glycoprotein I antibodies were within normal limits), heterozygous carriage of prothrombotic (MTHFR, MTRR) and antifibrinolytic (PAI-1) mutations, mild hyperhomocysteinemia, and elevated IgG levels against SARS-CoV-2. This constellation of abnormalities was regarded as potentially thrombogenic but insufficient to establish a definitive diagnosis of APS or another specific nosological entity. Active smoking and severe psychoemotional stress associated with military service may have contributed to a synergistic effect among the prothrombotic factors.

Although APS with initial manifestation as in-situ coronary thrombosis cannot be excluded, a modest increase in lupus anticoagulant levels in the absence of anticardiolipin or β2-glycoprotein I antibodies—detected only once during acute myocardial infarction—does not meet diagnostic criteria for APS. Repeat serological testing is recommended after 12 weeks, in accordance with BSH and EULAR guidelines [8-10]. Notably, initial screening was performed during enoxaparin therapy, with blood samples drawn more than 12 hours after injection, thereby minimizing the risk of false-positive results.

A case described by Pervez et al. [11] involved in-situ coronary thrombosis in a young female with confirmed APS, occurring in the pre-COVID era in the context of a subtherapeutic INR. In contrast, our patient experienced a myocardial infarction in 2025. Between

2019 and 2022, and thereafter, he had no clinical signs of infection and was unvaccinated, yet showed high SARS-CoV-2 IgG titers, suggesting the possibility of a delayed immune response. The mechanisms underlying such responses remain poorly understood and warrant further investigation.

According to AHA guidelines (2019), in-situ thrombosis may be considered a potential mechanism of MINOCA. However, updated ESC guidelines (2020) define MINOCA as a working diagnosis that requires the exclusion of other known causes of myocardial ischemia, including congenital or autoimmune thrombophilia [12-15]. In this case, a mural thrombus in the proximal LAD was angiographically confirmed, with no signs of atherosclerosis, and immunogenetic markers of thrombophilia were identified. Thus, the ischemic mechanism is clearly established, excluding classification as MINOCA.

Recurrent ischemic symptoms occurred two months after the infarction while the patient was receiving edoxaban for five weeks. Although a direct causal relationship could not be confirmed, this episode underscores the complexity of anticoagulant management in suspected APS with concurrent thrombophilic factors. Current guidelines favor vitamin K antagonists for arterial thrombosis in APS, whereas direct oral anticoagulants (DOACs) are considered less effective in such scenarios [9,10]. Therefore, anticoagulant therapy should be individualized based on thrombotic risk and clinical context.

Repeat emergency coronary angiography was deferred due to symptom resolution and the absence of biomarker elevation indicative of myocardial necrosis. Nonetheless, this decision highlights the limitations of noninvasive monitoring in the assessment of recurrent ischemia in atypical thrombosis. Finally, due to the absence of cardiovascular or autoimmune conditions in the patient's immediate family, genetic counseling was postponed until APS status could be definitively determined.

Follow-up plan

Considering multifactorial thrombophilia, the absence of a confirmed diagnosis of APS, and a possible immune post-COVID component, the patient is recommended to undergo dynamic observation and the following examinations:

- Repeat serological testing for APS after 12 weeks: determination of the level of anticardiolipin antibodies (IgG/IgM), β2-glycoprotein I antibodies, and lupus anticoagulant in accordance with the BSH and EULAR recommendations.
- Cardiac magnetic resonance imaging (MRI) with contrast to assess residual myocardial changes and fibrosis and to exclude myocarditis as a possible concomitant condition.
- Consultation with a rheumatologist to exclude systemic autoimmune diseases and to assess the possible onset of systemic pathology.
- Hematologist consultation for a comprehensive reassessment of the thrombophilic profile and discussion of long-term anticoagulant therapy. Although testing for factor V Leiden and the prothrombin G20210A mutation has already been performed and yielded negative results, additional genetic evaluation may be considered if indicated. Genetic counseling is advised in case of persistent laboratory signs of thrombophilia, particularly in the context of future family planning.

Conclusion

The etiology of myocardial infarction in this case was multifactorial, involving synergistic effects of immune activation (elevated SARS-CoV-2 IgG, positive lupus anticoagulant), genetic predisposition (heterozygous mutations in MTHFR, MTRR, PAI-1), and modifiable risk factors (smoking, stress).

Although APS could not be confirmed, its diagnosis remains possible; repeat serologic testing after 12 weeks is essential.

In patients with arterial thrombosis and suspected APS, vitamin K antagonists are preferred over direct oral anticoagulants, particularly in the absence of complete serologic confirmation.

Clinical decisions should be individualized, integrating laboratory, genetic, and imaging findings to guide diagnosis and secondary prevention strategies.

Clinical significance

This case highlights the importance of a comprehensive diagnostic workup in young patients with myocardial infarction and no angiographic evidence of atherosclerosis. It demonstrates the potential interaction between post-COVID immune changes and inherited thrombophilia in triggering in situ coronary thrombosis. The case emphasizes the need to follow validated laboratory protocols (e.g., timing of LA testing), consider delayed immune responses in seronegative individuals, and exercise caution when modifying anticoagulation in patients with unclear thrombotic risk profiles.

Conflicts of interest

The authors declare no conflicts of interest.

Informed Consent Statement

Written informed consent to publish this paper was obtained from the patient.

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