



ST-Segment-Elevation Myocardial Infarction Unmasking Underlying Systemic Lupus Erythematosus or Representing Thrombotic Thrombocytopenic Purpura? Report of a Challenging Case

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Abstract

Thrombotic thrombocytopenic purpura (TTP) is a multisystem disorder that frequently manifests itself with renal and neurological involvements. Cardiac involvement, however, has been rarely reported. In this report, we present a rare case of acquired TTP with acute myocardial infarction (AMI) as the initial manifestation. Although AMI was successfully managed by percutaneous coronary intervention, the patient developed hemolytic anemia, fever, marked thrombocytopenia, oliguria, and renal dysfunction, requiring treatment with plasma exchange and corticosteroids. TTP, albeit extremely rare, should be considered in cases with unexpected thrombocytopenia during acute-phase treatment for AMI as it can be highly lethal if not treated immediately.

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Introduction

Thrombotic thrombocytopenic purpura (TTP) is an uncommon syndrome characterized by the concomitant occurrence of severe thrombocytopenia, microangiopathic hemolytic anemia (MAHA), fever, renal dysfunction, and fluctuating neurological signs.¹ However, patients with TTP rarely exhibit the full clinical picture (the pentad). Idiopathic

TTP is caused by an acquired reduction in the activity of the von Willebrand factor cleaving protease (ADAMTS-13) due to an immunoglobulin G (IgG) autoantibody, resulting in the formation of large von Willebrand factor multimers. These oversized particles, in turn, trigger the formation of large platelet plugs and diffuse microemboli, leading to life-threatening, multi-organ ischemic injuries.^{1, 2} Cardiac involvement is not frequently seen as the initial thrombotic

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event of TTP, even though the heart continues to be one of the most frequently involved organs at autopsies.³⁻⁵ TTP-like cases of MAHA that occur simultaneously with connective tissue disease (CTD) are rare but clinically relevant manifestations.⁶

In this report, we describe a rare case of systemic lupus erythematosus (SLE)-associated TTP that presented as acute myocardial infarction (AMI) with no clinically apparent damage to other relevant organs. Furthermore, there were no abnormal laboratory findings to suggest that TTP was the underlying thrombotic disease at the initial presentation.

Case Report

A 29-year-old man without known coronary risk factors was admitted to our emergency department owing to a constellation of prolonged squeezing retrosternal chest pains accompanied by dyspnea, malaise, low-grade fever, and night sweats. On admission, his blood pressure was 135/80 mmHg and his pulse rate was 94 beats per minute. An electrocardiogram showed an ST-segment elevation, predominantly observed in leads I, aVL, and V₁-V₆ (Figure 1). The laboratory data on admission revealed an elevated level of cardiac troponin T (1617 ng/mL). The white blood cell count, the hemoglobin level, the platelet count, and the serum creatinine level were within the normal range (9700/mm², 13.8 g/dL, 203000/L, and 0.9 mg/dL, respectively).

The patient was diagnosed with anterior ST-segment-elevation myocardial infarction (STEMI), for which he was administered a loading dose of aspirin (300 mg), clopidogrel (600 mg), and atorvastatin (80 mg). The patient underwent an emergency cardiac catheterization. The coronary

angiography showed a thrombotic lesion primarily narrowing the proximal-to-mid portion of the anterior descending coronary artery with the total occlusion of the distal segment (Figure 2). A subsequent percutaneous coronary intervention (PCI) was performed by balloon angioplasty, followed by the implantation of a drug-eluting stent. Following the PCI, metoprolol succinate (23.75 mg/d), enalapril (2.5 mg/BD), atorvastatin (80 mg daily), aspirin (80 mg/d), and clopidogrel (75 mg/d) were administered. A transthoracic echocardiographic examination revealed hypokinesia in the apical segments of the left ventricle and reduced left ventricular ejection fraction (45%). There was no visible shunt flow in the computational fluid dynamic study, nor was there bubble passage after the injection of agitated saline at rest and after the Valsalva maneuver. The patient showed clinical improvements, and he was discharged after 2 days.

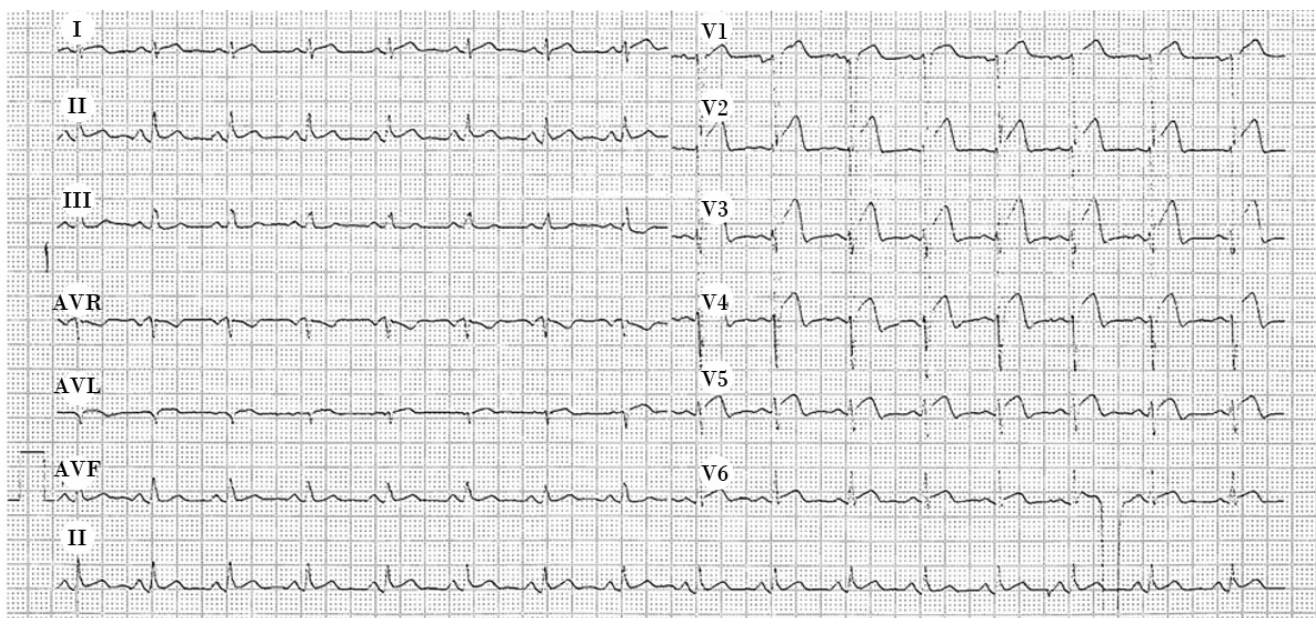
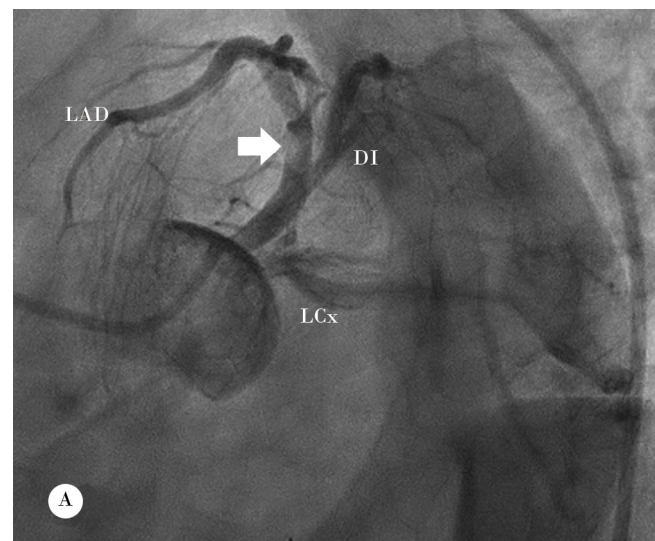


Figure 1. The electrocardiogram at the first presentation reveals a normal sinus rhythm with abnormal ST-wave elevations in leads I, aVL, and V₁-V₆.

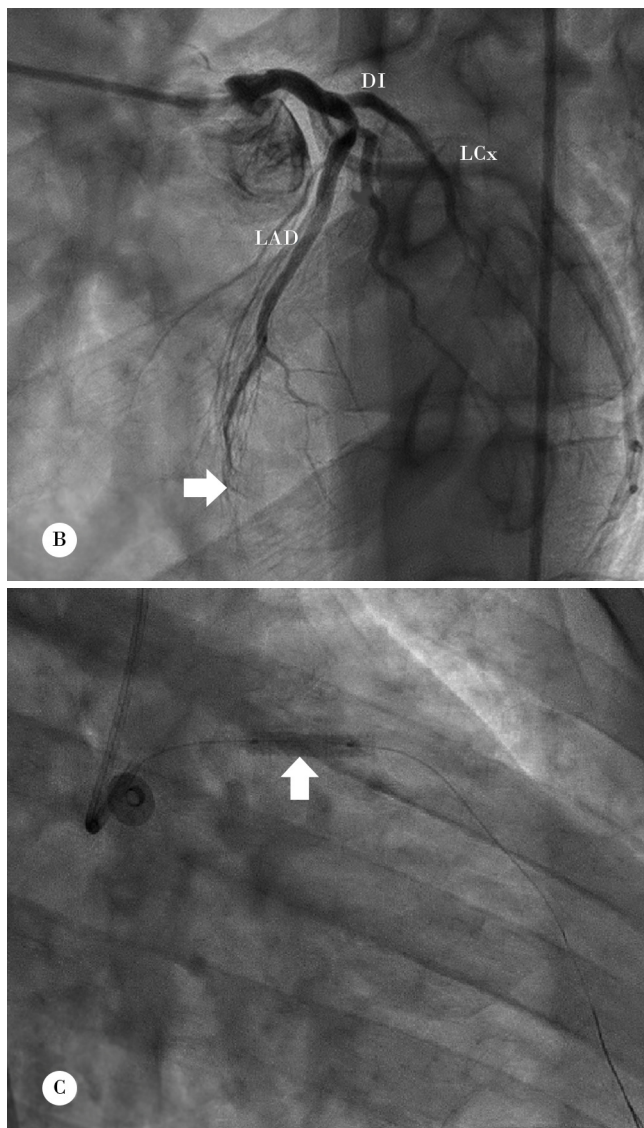


Figure 2. The emergent coronary angiography illustrates thrombotic lesions in the mid and distal parts of the LAD, which was successfully recanalized by percutaneous transluminal coronary angioplasty. The Spider view (A) visualizes a thrombotic lesion with a narrowing (arrow) at the proximal-to-mid portion of the LAD. The LAO cranial view (B) shows a cutoff edge due to a thrombus (arrow) at the distal portion of the LAD with direct stenting (C) for the proximal stenosis of the LAD (arrow).

LAO, Left anterior oblique; LAD, Left anterior descending artery; DI, Diagonal artery branch 1; LCx, Left circumflex artery

Nonetheless, the patient returned 7 days later with the signs and symptoms of a systemic illness. He complained of myalgia, fever, weakness, diffuse arthralgia, and mild vague abdominal discomfort associated with oliguria. On admission, the patient had a blood pressure of 87/53 mmHg, a pulse rate of 102 beats per minute, and an oral temperature of 38 °C, and he appeared ill and drowsy. Additionally, his mental status and neurologic orientation aspects exhibited slight disturbances. An electrocardiogram

showed ST-segment resolution (Figure 3), and a computed tomography scan of the brain was unremarkable. Laboratory studies demonstrated significant depletion in the platelet count (17,400/L) and the hemoglobin level (9.4 g/dL), but the serum creatinine level was elevated (2.4 mg/dL). The measured values of the WBC count, the prothrombin time, the international normalized ratio, and the partial thromboplastin time were within normal limits, and his urine tested positive for protein. The level of cardiac troponin T was decreased compared with that in the first admission (817 ng/mL).

All the antiplatelet medications of the patient were discontinued, but his condition started to deteriorate on the third day of the current presentation with worsening neurological status, oliguria, and hematemesis, necessitating intensive care unit admission. The platelet count decreased to 8000/L, the creatinine level increased to 4.4 mg/dL, and the lactate dehydrogenase level was 3164 IU/L. The corrected reticulocyte count was 3.2%, while a peripheral blood smear revealed an increased number of fragmented red blood cells called “schistocytes” with a frequency of at least 3% (Figure 4).

A provisional diagnosis of TTP was made, and the ADAMTS-13 level assay was requested. Once-daily plasma exchange with fresh frozen plasma was initiated. Further workup revealed low levels of complement components (C3: 56 mg/dL, C4: 9 mg/dL, and CH50: 36 mg/dL). The antinuclear antibody (ANA) titer was greater than 1/320, and the nuclear staining pattern was speckled. Anti-cardiolipin, lupus anticoagulant, and β 2-glycoprotein-I (all with IgM and IgG) antibodies were absent. Other laboratory tests, including anti-double-stranded DNA, anti-SSA, anti-SSB, anti-Smith antibodies, RF, P-ANCA, and C-ANCA, were within the normal range. The markers of viral serology for hepatitis A, B, and C, as well as HIV antibodies, were negative. The ADAMTS-13 activity was 0.1%, and the ADAMTS-13 inhibitor was 0.9 Bus/mL (<0.5). The presence of microangiopathic anemia, a reduced ADAMTS-13 activity, a high titer of ANA, and low levels of complement components suggested a diagnosis of SLE-associated TTP. The once-daily plasma exchange was continued, and prednisolone (1 mg/kg/d) was initiated. After 10 days of plasma exchange and 7 days of corticosteroid therapy, the patient showed improvement: the platelet count increased to 253 000/L, the hemoglobin level stabilized at 10.7 g/dL, the creatinine level decreased to 1.07 mg/dL, the lactate dehydrogenase level dropped to 396 U/L, and the corrected reticulocyte count was less than 1%. Antiplatelet agents (ASA 80 mg/d and Plavix 75 mg/d) were initiated, and the patient was discharged thereafter on prednisolone (50 mg/d) and hydroxychloroquine (200 mg/d). He was in disease remission after 14 months, with a normal platelet count and renal function, maintained with low-dose prednisolone.

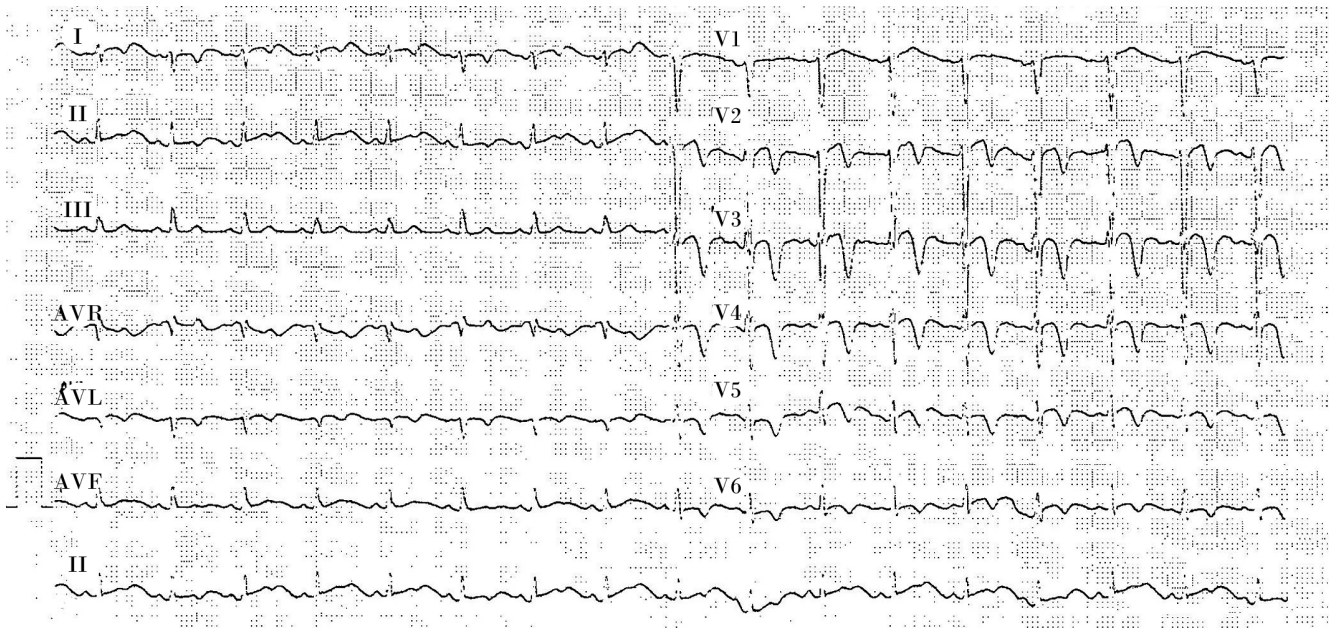


Figure 3. The electrocardiogram in the second admission shows a normal sinus rhythm with ST-segment resolution in leads I, aVL, and V1–V6.

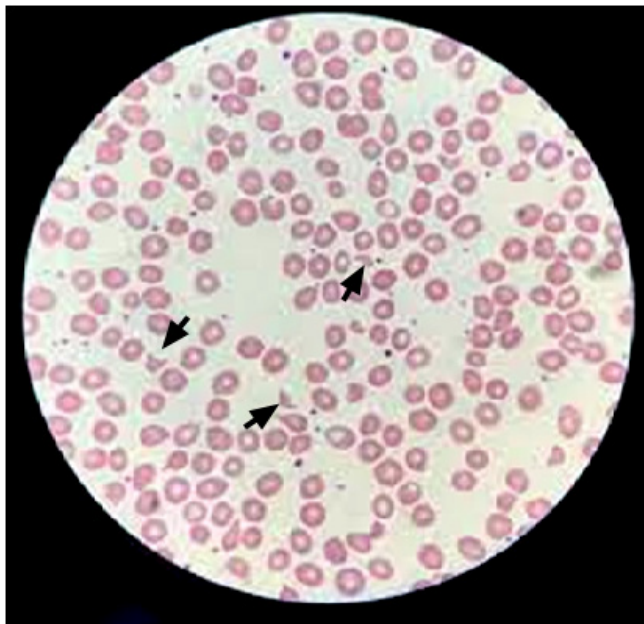


Figure 4. Peripheral blood smear (H&E staining with 40X magnification) illustrates an increased number of schistocytes (black arrows).

Discussion

In this report, we presented a case with the typical acute coronary syndrome (ACS) features including left-sided chest pain; ST-segment elevations in leads I, aVL, and V₁–V₆; and elevated cardiac troponin T. Nevertheless, the patient was a young adult and had no risk factors for atherosclerosis. Furthermore, coronary angiography showed

only a thrombotic lesion, with subsequent evaluations for paradoxical emboli revealing no additional data.

TTP can rarely present with ACS due to microthrombus formation in the coronary vessels. The exact incidence of TTP-induced or TTP-associated ACS is unknown, probably due to underdiagnosis.⁷ Previous studies have identified ACS as a clinically significant manifestation of TTP, with an incidence ranging from 9.5% to 77.0% of all TTP cases, as secondary thrombotic events.^{3, 8–10} Still, TTP presenting with ACS as the initial presentation has been extremely rare.⁵ Despite therapeutic advances, thrombotic microangiopathy (TMA) is still associated with high mortality rates. Myocardial microthrombi in TMA, predominately in TTP, results in AMI and potentially contributes to the high mortality of these patients.^{3, 11, 12} Our case is different from those presented in previous studies because our patient's AMI preceded the clinical diagnosis of TTP.

Adverse events such as renal dysfunction, thrombotic and/or bleeding events, and thrombocytopenia can be common during the treatment of AMI due to the use of various types of drugs such as contrast agents, antiplatelet drugs, and heparin.¹³ These adverse events rendered TTP diagnosis in our case difficult, even though we observed a short gap between index manifestations and subsequent features. Notably, given the successful, uncomplicated primary PCI and short-term treatment with enoxaparin (24 h), we had a low clinical suspicion of heparin-induced thrombocytopenia. After nephrology and hematology consultations, we integrated the data considering all clinical and laboratory evidence. Cardinal manifestations including fever, disturbed mental status, oliguria, renal dysfunction, anemia, and thrombocytopenia confirmed the presumptive diagnosis of TTP. Whether it was a primary disorder or whether it arose

secondary to an external factor such as clopidogrel is unclear. More than 50 drugs can cause this syndrome, while drug-induced TTP/hemolytic uremic syndrome in the setting of clopidogrel is rare (frequency: <1 in 20 000). Although the typical expression is usually expected between 5 and 14 days after clopidogrel therapy,^{14, 15} it is not associated with the emergence of the ADAMTS-13 inhibitor.¹⁶ Accordingly, based on the marked decrease in the ADAMTS-13 activity and the presence of the ADAMTS-13 inhibitor, it is unlikely that TTP was caused by clopidogrel in our case. The first manifestation of the disease was a thrombotic event (anterior STEMI) in a young adult without a conventional coronary risk factor. Moreover, the discontinuation of clopidogrel after 3 days conferred no improvement. Hence, the natural course of the disease was not significantly altered.

TTP may occur secondary to systemic disorders such as CTD. Mannucci et al¹⁷ demonstrated that the mean plasma levels of ADAMTS-13 in patients with SLE were lower than those in controls, but the autoantibodies that inactivate ADAMTS-13 were not frequent in them. None of the patients in their study experienced any episodes of MAHA. Matsuyama et al¹⁸ showed that the ADAMTS-13 activity was significantly decreased in CTD-TMA. They also reported that severe deficiency in the ADAMTS-13 activity was predominantly detected in patients with rheumatoid arthritis- and SLE-TMA, which was closely associated with the presence of anti-ADAMTS-13 IgG antibodies. Because the manifestations of TTP are similar to those of SLE, it is sometimes difficult to make an accurate diagnosis of TTP in patients suffering from SLE. In our case, considering the low levels of complement components and the high ANA titer, it was conceivable that the TTP was associated with SLE. In light of the review cases of SLE-associated TTP, plasma exchange appears to improve outcomes rather than plasmapheresis without fresh frozen plasma infusion in SLE-associated TTP.^{6, 18} Even if a definite diagnosis of SLE cannot be established based on the well-known criteria, patients should be followed up to investigate more findings.

Conclusion

We report a rare case of SLE-associated TTP that presented with AMI as the first manifestation of the disease. Although extremely rare, the complications of TTP should be considered among the possible pathogenetic mechanisms in cases with unexpected thrombocytopenia during acute-phase treatment for AMI, as it can be highly lethal if not treated immediately.

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