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Original Research

Role of thrombotic thrombocytopenic purpura in myocardial infarction for elevation of ST segment

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ABSTRACT:
Treating myocardial infarction in the setting of immune thrombocytopenic purpura (ITP) is always a challenge especially if the platelet count is labile. Cardiologists dealing with such patients should keep a delicate balance between thrombotic and bleeding complications. Renal and neurological involvements are frequently seen in thrombotic thrombocytopenic purpura (TTP). Cardiac involvement, however, has been rarely reported. In this article, we present 2 cases of myocardial infarction in patients with TTP. The first patient developed ST-segment elevation myocardial infarction early in the course of the disease and died before plasmapheresis could be initiated. In the second case, a young women presented with non–ST-segment elevation myocardial infarction that resolved promptly with plasmapheresis. Hence, a high degree of suspicion with prompt diagnosis and treatment is needed to prevent mortality associated with cardiac involvement in TTP. Conclusion: MI, thought to be due to microthrombi from platelet aggregation, rarely is a presenting or early feature of TTP.
Keywords: thrombotic thrombocytopenic purpura, myocardial infarction, cardiac involvement

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INTRODUCTION

Platelets play a pivotal role in the pathogenesis of Acute Coronary Syndromes (ACS) and thrombocytosis has been demonstrated to be an important risk factor for Acute Myocardial Infarction (AMI); indeed, in patients with essential thrombocythemia the incidence of AMI is about 9.4%.[1] Nevertheless, AMI has been reported also in patients who suffer from thrombocytopenia that could be associated with several conditions.[2,3]

Thrombocytopenia is defined as a platelet count of <150 x 10^9/L and it is classified as mild (100-150 x 10^9/L), moderate (50-100 x 10^9/L) or severe (<50 x 10^9/L). Thrombocytopenia is generally expected in 13% of patients, whereas this condition is present in 5% of ACS patients suffering from thrombocytopenia. It is more frequent in several conditions such as older patients, diabetes, renal insufficiency, heart failure and sometimes is considered as a risk factor of AMI, for example in patients with Kawasaki disease.[4-6]

As reported in autoptic samples, the pathogenesis of an occlusive thrombus in these patients share similarities with classic atherosclerotic plaque rupture, shedding light on hidden aspects that go beyond platelet count.[7] Indeed, likewise of rodent models, patients with thrombocytopenia may be predisposed to coronary thrombosis because their platelets are larger and more adhesive to the vascular surface.[8,9] Furthermore a higher platelet microparticles activation has been shown in ACS patients with idiopathic thrombocytopenic purpura and middle-aged patients than in control groups.[10,11]

The American Heart Association (AHA) and the European Society of Cardiology (ESC) strongly recommend in ACS the Dual Antiplatelet Therapy (DAPT) consisting of aspirin and a P2Y12 receptor antagonist.[12,13] Although DAPT reduces the incidence of stent thrombosis an increased bleeding risk is present. Hence, the management of antiplatelet therapy in ACS patients with thrombocytopenia turn out to be challenging both for the concomitant higher risk of bleeding and ischaemic events in this group.[14,15] In ACS, actual scores such as the PRECISE-DAPT score, might evaluate the usefulness

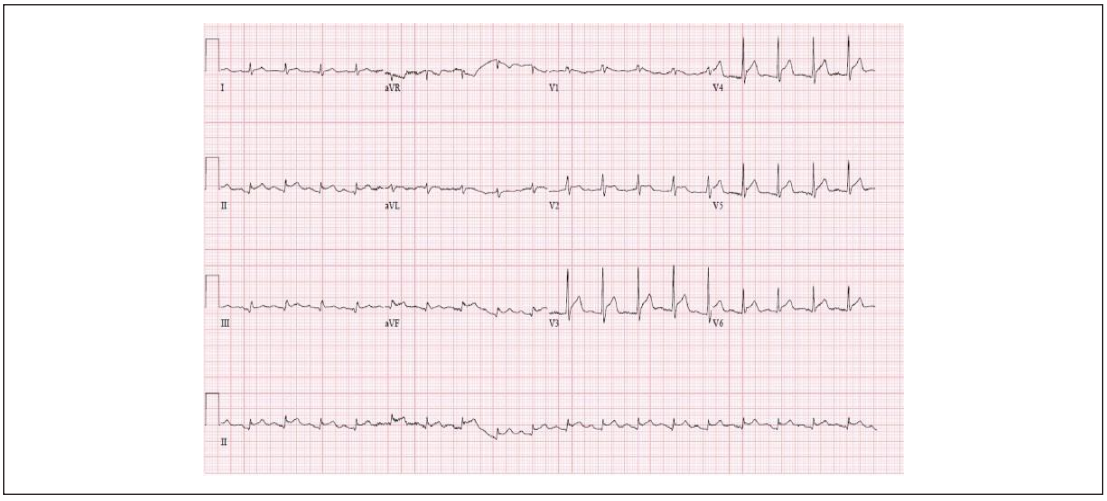
of DAPT duration balancing the ischemic protection and minimizing bleeding risks in the individual patient on the basis of hemoglobin value, white blood cells count, age of the patient, creatinine clearance and a general history of prior bleeding without specific indications (type of bleeding, platelet count, platelet function, secondary predisposing hemorrhagic conditions).[16]

In this report, we present a rare case where myocardial infarction was seen as a presenting feature of an underlying hematologic disease, thrombotic thrombocytopenic purpura (TTP). This case highlights the importance of a thorough, yet efficient, clinical evaluation in which the history, physical exam, ECG and laboratory data were needed to make the appropriate triage decision and not miss an unusual diagnosis.

CASE 1

A 55-year-old female presented with 1 episode of blood mixed stool and 4 days of dark colored urine. She, however, denied any abdominal pain, nausea, vomiting, change in bowel habit, polyuria, pain, or burning on micturition. Her past medical history was significant for right knee replacement and lumbar disc herniation. She had no similar episode in the past, and no family history of any bleeding disorder or malignancy. She had no known allergies and took no medications. Her vitals were stable at presentation. Physical examination was significant for the presence of mild icterus and absence of any pallor, petechial rash, lymphadenopathy, or hepatosplenomegaly. Laboratory investigations at presentation showed hemoglobin of 13.5 g/dL, hematocrit of 37.7%, platelet count of 8500/µL, serum blood urea nitrogen of 58 mg/dL, serum creatinine of 2.75 mg/dL, and total bilirubin of 4.0 mg/dL with unconjugated bilirubin of 2.7 mg/dL. Her initial EKG showed nonspecific findings. Subsequent tests showed an elevated LDH (2288 IU/L) and a low haptoglobin (less than 10 mg/dL) with many peripsheral schistocytes. So with a probable diagnosis of TTP, she was planned for plasmapsheresis. Meanwhile, ADAMTS-13 workups were sent, which was later reported as an ADAMTS-13 activity of less than 10% with an elevated ADAMTS-13 antibody titer of 20 U/mL. However, she suddenly developed severe shortness of breath before the planned plasmapsheresis. There were widespread ST-segment elevations on his EKG with a serum troponin of 4.15 ng/mL and left ventricular wall hypokinesia on bedside echocardiography (Figure 1). Her condition worsened rapidly over the next few minutes, and she developed cardiac arrest and expired.

Figure 1. Electrocardiogram of case 2 showing ST-segment elevation



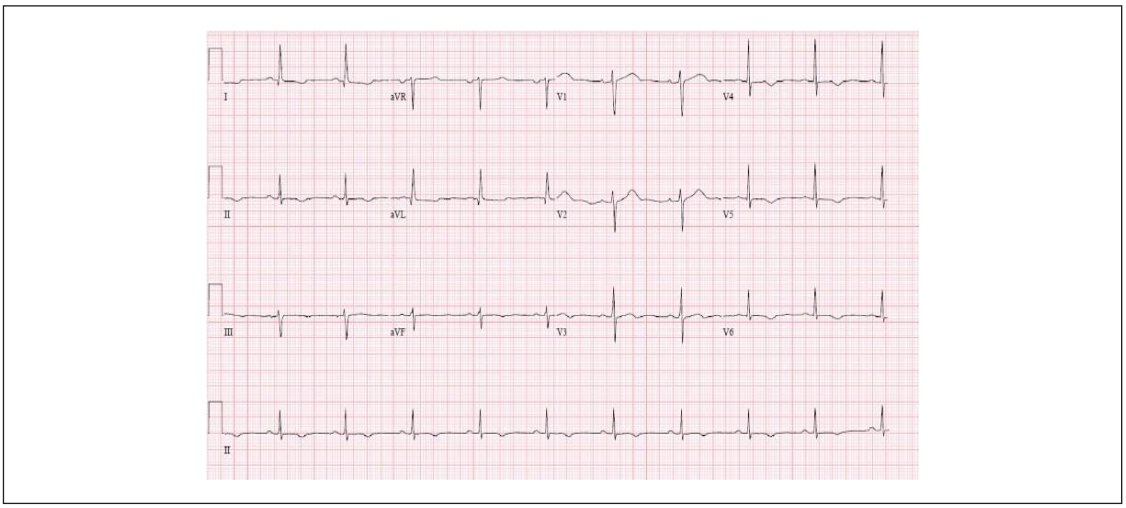
Our first patient had TTP complicated by STEMI early in the course of the disease with subsequent cardiac arrest and death.

CASE 2

A 42-year-old female presented to our emergency department with left-sided chest discomfort associated with blood-smeared sputum and blood in urine for 2 day. Physical examination was significant for icterus and absence of any petechial rash, lymphadenopathy, or hepatosplenomegaly. Laboratory tests were significant for leukocyte of 16 000/µL (normal = 4500-11 000/µL), hemoglobin of 10.2 g/dL (normal = 13.5-17.5 g/dL), hematocrit of 33% (normal = 41% to 53%), platelet of 14 000/µL (normal = 130 000-400 000/µL), blood urea nitrogen of 42 mg/dL (normal = 8-20 mg/dL), serum creati nine of 1.8 mg/dL (normal = 0.4-1.3 mg/dL), and total bilirubin of 3.3 mg/dL (normal = 0.3-1.2 mg/dL) with unconjugated bilirubin of 2.8 mg/dL (normal = 0.2-1.1 mg/dL). Serum troponin was elevated at 1.05 ng/dL (normal <0.05 ng/dL), which subse- quently trended up to 1.12 ng/dL and 1.81 ng/dL, while the initial electrocardiography (EKG) showed T-wave inversion in lateral leads (V5-V6) with echocardiogram showing lateral wall hypokinesia (Figure 2). A diagnosis of NSTEMI was made, but owing to severe thrombocytopenia, no antiplatelet therapy or other

cardiac intervention was done. He was, however, started on amioda- rone as he had multiple episodes of nonsustained ventricular tachycardia. Subsequent tests showed an elevated serum lactate dehydrogenase (LDH) level of 1550 IU/L (normal = 98-192 IU/L) and a low haptoglobin level of less than 10 mg/dL (normal
= 34-200 mg/dL) with many schistocytes on peripheral smear. ADAMTS-13 activity of less than 10% (normal >66%) with elevated ADAMTS-13 antibody titer of greater than 140 U/mL (normal <12 U/mL) confirmed the diagnosis of severe acquired TTP, and the patient was started on plasmapheresis. Over the subsequent days, his symptoms resolved and there was significant improvement in his platelet count, LDH, serum creatinine, and bilirubin, and his troponin level began trending down. Her hospital course was, however, complicated by a rapid drop in platelet count after skipping a session of plasmapheresis. So a diagnosis of refractory TTP was made, and the patient was put back on daily plasmapheresis schedule and started on weekly rituximab at a dose of 375 mg/m^2 body surface area. He responded well to rituximab, and the frequency of plasmapheresis was slowly tapered off after 3 doses of rituximab with plans for 3 more doses as an outpatient. He continued to remain asymptomatic while her hematological parameters stabilized with a platelet count of 256 000/µL at discharge.

Figure 2. Electrocardiogram of case 1 showing T-wave inversion



Our second patient had TTP complicated by NSTEMI at presentation, as evidenced by his left-sided chest discomfort, elevated troponin, EKG changes, and focal ventricular hypokinesia on echocardiogram. Absence of other risk factors for coronary artery disease and the prompt resolution of the episode with plasmapheresis supports TTP as the cause of his NSTEMI. her clinical course was further complicated by episodes of nonsustained ventricular tachycardia

DISCUSSION

TTP is defined as a severe, thrombotic microangiopathy that is characterized primarily by systemic platelet-von Willebrand factor aggregation, organ ischemia, profound thrombocytopenia and fragmentation of erythrocytes.[17] Intravascular coagulation is not considered a prominent feature of the disorder. Clinically, widespread organ dysfunction is usually present. Pathologically, focal areas of necrosis and hemorrhage may be seen in the pancreas, adrenals, heart, brain and kidneys.[18] Although myocardial injury and necrosis are observed in a large number of patients with TTP, it is infrequently the initial presentation and most likely thought to be due to microthrombi from massive platelet aggregation than plaque rupture–thrombosis cascade.[19] Various studies have determined the incidence of myocardial infarction in TTP to range from 15–41%. However, the heart is one of the most frequently involved organs at autopsy examination of patients with TTP. Mortality is considerably higher in patients with TTP who have positive cardiac biomarkers, necessitating closer monitoring in this subgroup.[20]

MI in TTP is thought to be likely due to micro-thrombi from massive platelet aggregation.[21] Widespread myocardial involvement at autopsy with microthrombosis of the small vessels supplying the myocardium has been reported in up to 77% of the patients dying from TTP. However, MI as a presenting or early feature of TTP is rarely seen, with a reported incidence for any cardiac involvement in TTP being 10% to 40% in a few limited clinical cohorts.[22,23] This discrep- ancy between clinical and autopsy findings may account for sudden death resulting from unrecognized cardiac events.

Prompt diagnosis and treatment is necessary as mortality is significantly higher in patients with TTP who have cardiac involvement.[21] A study by Benhamou et al showed that a car- diac troponin I level greater than 0.25 µg/L in patients with TTP was associated with more refractory disease and 3-fold increase in the risk of death.[24] There is, however, a

lack of established guidelines for the management of these cases. The management of TTP-induced MI is challenging as severe thrombocytopenia and accompanying acute renal failure usu- ally precludes any invasive therapy in the form of cardiac catheterization and percutaneous intervention or any medical management in the form of antiplatelet and anticoagulant therapy.[25] Early initiation of plasmapheresis, which involves removing large volume of the patient's plasma containing any ADAMTS-13 antibody and replacing it with donor plasma with normal ADAMTS-13 activity, is essential to prevent fur- ther myocardial damage and associated mortality.[26]

CONCLUSION

MI, thought to be due to microthrombi from platelet aggregation, rarely is a presenting or early feature of TTP. As illustrated by our cases, however, it can be an early complication of TTP. A high degree of suspicion and prompt diag nosis is necessary, because mortality is significantly higher in patients with TTP who have positive cardiac biomarkers. Early initiation of plasmapheresis is essential to reduce mortality.

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