Acute Myocardial Infarction Caused by Thrombotic Microangiopathy Complicated With Myelodysplastic Syndrome

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Summary

Thrombotic microangiopathy (TMA) is a rare but lethal multisystem disease characterized by peripheral thrombocytopenia, microangiopathic hemolytic anemia, fever, and various stages of renal and neurological dysfunctions.

The causes of TMA are mainly thrombotic thrombocytopenic purpura (TTP) or hemolytic-uremic syndrome (HUS), and cases of TMA related to myelodysplastic syndrome (MDS) are quite rare. Herein, we report a case of acute myocardial infarction (AMI) caused by TMA which is strongly suspected to have a relationship to MDS, and discuss the treatment of our patient who needed antplatelet or anticoagulant therapy after AMI, while on the other hand, had pancytopenia and a bleeding event due to MDS.

Key words: Acute coronary syndrome, Thrombosis, Thrombocytopenia

A MI still causes death at a high rate, although the mortality rate is decreasing because of the improvement of devices and medication treatments. Atherosclerosis, plaque rupture, and thrombosis are the main causes of AMI; however, AMI can sometimes occur only with thrombi and without any atherosclerotic changes.

TMA is characterized by multi-organ dysfunction due to systemic thrombosis and the causes are mainly TTP and HUS, and there are few reports of acute coronary syndrome due to TMA. Herein, we report a rare case of AMI related to TMA, and as the cause of TMA, TTP and HUS were ruled out and MDS was strongly suspected.

Case Report

A 79-year-old man presented to our hospital complaining of a 1-day history of chest and abdominal compression. He did not take any medication or have any cardiovascular risks. He was admitted to another hospital the day before, and blood tests and an electrocardiogram (ECG) did not reveal anything wrong other than mild thrombocytopenia (platelets 89,000/μL). An analgesic was prescribed, but his compression continued so he was admitted to our hospital. Vital signs at arrival were stable and he was conscious. Initial laboratory findings revealed severe progressive thrombocytopenia (platelets 33,000/μL) accompanied by mild anemia. Hemolytic anemia was reflected by an undetectable level of haptoglobin, and high levels of indirect bilirubin (14.0 mg/dL) and fractured red cells. The myocardial enzymes were elevated with mild elevation of brain natriuretic peptide, and severe proteinuria, hematuria, and a high level of beta2-microglobulin in urine (7,600 μg/L) represented renal function failure. The ECG showed sinus rhythm and ST-segment elevation in leads V3-5 and echocardiography revealed asynergy of the anterior segment, so emergent coronary angiography (CAG) was performed under suspicion of anterior AMI. It revealed a filling-defect of the left anterior descending artery (LAD) and thrombosis was strongly suspected. Percutaneous coronary intervention (PCI) was performed immediately following the diagnostic procedure. LAD was successfully recanalized with thrombus aspiration, and the last intravascular ultrasound (IVUS) showed little progression of the atherosclerosis at the lesion, so neither balloononing nor stenting was performed.

For evaluating the thrombosis of other organs, head and neck magnetic resonance imaging was performed, which unexpectedly revealed a left posterior cerebral artery embolism. Abdominal vessel microthrombosis was also suspected to have caused the abdominal pain and acute renal function failure, though an enhanced CT did not show obvious thromboembolism. There was the possibility of an intracardiac source, but transesophageal echocardiography revealed no obvious intracardiac thrombus and shunt, and left atrial appendage flow velocity was not low. The dimension of the left atrium was within the normal range (38 mm) with left ventricular mild diastolic dysfunction (E/A 0.63), and ECG monitoring during the hospitalization did not show continuous atrial fibrillation, so the involvement of atrial fibrillation was not strongly suspected. Systemic microthrombosis, including in a coronary artery was strongly suspected, so anticoagulation was started. Systemic
atherosclerotic disease was not obvious and the platelet count was low, therefore, antiplatelet therapy was not undertaken because of the increased risk of bleeding events.

The patient did not experience a physically or psychologically stressful event or a previous infectious event including diarrhea, and vero toxin was not detected. Activated partial thromboplastin time, prothrombin time, and ADAMTS13 activity were within normal ranges, antinuclear antibody and the Coombs test were negative, and there was no evidence of HUS, TTP, antiphospholipid syndrome, paroxysmal nocturnal hemoglobinuria (PNH), or other autoimmune diseases. The disseminated intravascular coagulation (DIC) score was 3 due to thrombocytopenia, and the score was below the standard value of DIC. The pancytopenia worsened later, and he was ultimately diagnosed with MDS with deletions of the long arm of chromosome 20 [del (20q)] by bone marrow biopsy and peripheral blood smear. PNH is sometimes complicated with MDS and causes thrombosis, but it can be ruled out with flow cytometry.

Follow-up CAG did not show restenosis of the coronary arteries. Although anticoagulation with a vitamin K antagonist was controlled in the normal range, hemorrhoidal bleeding needing blood transfusion occurred so anticoagulation was stopped. Without anticoagulant or antiplatelet therapy, he did not have other cardiac and vascular events and was discharged from our hospital. The chemotherapy and hematopoietic stem cell transplantation were not appropriate and constant blood transfusion was not needed for the MDS so routine follow-up blood tests were planned. Without anticoagulant and antiplatelet therapy, his subsequent clinical course 6 months after leaving the hospital was favorable, and no clinically problematic event arose.

**DISCUSSION**

AMI caused by TMA complicated with MDS is quite rare, although myeloproliferative neoplasms such as polycythemia vera and essential thrombocythemia and PNH sometimes cause thrombotic embolism and AMI.4,8

There are few reports about thrombosis related to MDS, and few have reported thrombosis in abdominal vessels.5,6 MDS patients with trisomy 8 are reported to be likely to develop thrombosis, although no definite cause has been identified.7,8 MDS with del (20q) commonly presents with thrombocytopenia with or without mild anemia like our patient, and to the best of our knowledge, there is no report about thrombosis with MDS with del (20q).9

TMA is a rare but lethal multisystem disease characterized by peripheral thrombocytopenia, microangiopathic hemolytic anemia, fever, and various stages of renal and neurological dysfunctions.1 The major diagnoses associated with TMA are TTP and HUS, and the process of TMA begins with a pathological insult to endothelial cells, leading to the formation of fibrin and platelet rich thrombi in the microcirculation mainly due to the lack of ADAMTS13 activity and complement mutations.10 In our case, thrombocytopenia and hemolytic anemia were detected with the coincidence of thrombotic events including AMI at the early phase of MDS indicated by progressive pancytopenia, so the relationship between worsening MDS and TMA was suspected under the denial of other diseases causing the thrombosis. Our patient was diagnosed with AMI and systemic embolism caused by TMA complicated with MDS, although TMA complicated with TTP and HUS is well known, and the complication of MDS is uncommon.2 DIC is well known as the cause of thrombocytopenia and thrombosis but the coincidence of DIC and MDS is not known, and DIC was rejected in our case due to a DIC score lower than the standard value. Although anticoagulation for thrombosis should be stopped because of bleeding complications, no clinically problematic event occurred during 6 months of follow-up.
Atrial fibrillation is well known as the cause of thrombosis. In our case, although ECG monitoring during the hospital stay did not show continuous atrial fibrillation with the echocardiography findings of the normal dimension of the left atrium and no obvious intracardiac thrombus, we are confident the involvement of prehospital atrial fibrillation could not be completely ruled out.

Antiplatelet therapy is a mainstay for the management of AMI, and double antiplatelet therapy is strongly recommended if coronary stenting is performed. However, the management of patients with both AMI and thrombocytopenic diseases is challenging and there are no guidelines. In our case, CAG, IVUS, and head and neck magnetic resonance angiography did not show atherosclerotic changes, and stent implantation was not performed, so antiplatelet therapy was not performed because of the higher risk of bleeding complications due to thrombocytopenia and platelet dysfunction. Cardiac and systemic thrombosis was strongly suspected, and anticoagulant therapy was induced, but it had to be stopped because of bleeding complications which required a blood transfusion. Whether the patient takes an anticoagulant or an anti-platelet drug will depend on the disease causing the thrombocytopenia. For example, in the case of TTP, antiplatelet therapy is recommended after platelet count elevation over 50,000/μL, and in the case of PNH, anticoagulation with a vitamin K antagonist is recommended, however, there is insufficient evidence concerning MDS.

We experienced AMI caused by TMA complicated with MDS, and such a case is quite rare. With pancytopenia, whether taking anticoagulant and antiplatelet agents will be hard to decide, and will depend on the platelet count and function, bleeding complications, and treatment for MDS for each individual patient. We hope that further studies will be undertaken in the near future.

REFERENCES