CASE REPORT

Obstructive coronary artery disease in patient with acute thrombotic thrombocytopenic purpura

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SUMMARY

Thrombotic thrombocytopenic purpura (TTP) affects essentially all organ systems. Myocardial injury in TTP is often attributed to microthrombi formation. We present the first case report in the literature of an acute TTP patient with concomitant obstructive coronary artery disease (CAD) and acute myocardial infarction who underwent successful percutaneous coronary intervention (PCI). A 70-year-old female patient who was diagnosed with acute TTP required plasma exchange. The patient also experienced episodes of angina pectoris, elevated cardiac enzymes and global ST segment depressions on ECG. A subsequent non-invasive ischaemia workup revealed significant ischaemia. Coronary angiography revealed obstructive CAD in her right coronary artery, requiring PCI with a bare metal stent placement and dual antiplatelet therapy. The patient tolerated antiplatelet therapy well. At 6 months of follow-up, she had no recurrent angina. This case highlights the potential co-existence of obstructive CAD and acute TTP requiring careful differential diagnosis and treatment.

BACKGROUND

Thrombotic thrombocytopenic purpura (TTP) is a multisystem disease affecting almost every organ in the human body.¹ Cardiac involvement of TTP is common and cardiac death has become one of the most common causes of mortality in patients with TTP. Despite autopsy studies showing cardiac arrest and myocardial infarction to be the most common immediate causes of death in this population, major epicardial arteries are often spared from the disease process.² TTP mostly affects the microvasculature of the heart, with platelet microthrombi forming at the level of arterioles and capillaries, instead of at major coronary branches. Cardiac workup and treatment for these patients often tend to avoid invasive approaches. There exists no report of TTP patients with concomitant obstructive coronary artery disease (CAD) treated with percutaneous coronary intervention (PCI), and no recommendations on how these patients should be managed. Due to the high prevalence of severe anaemia, coagulopathy, thrombocytopaenia and platelet dysfunction, and renal insufficiency associated with acute TTP, there would understandably be increased risk for complications if these patients undergo invasive workup for CAD and acute myocardial infarction (AMI), for example, cardiac catheterisation and PCI.

Thrombocytopaenia and platelet dysfunction in TTP also pose greater risks of haemorrhage with dual antiplatelet therapy in patients with CAD and AMI.

We present a case of a patient who was admitted with acute TTP, and required plasma exchange (PLEX) therapy with clinical symptoms consistent with obstructive CAD and AMI instead of the common microthrombi-caused myocardial injury. A non-invasive stress test and a myocardial perfusion study revealed territorial myocardial ischaemia, and invasive coronary angiography confirmed obstructive CAD in the right coronary artery (RCA). Due to recurrent Canadian Cardiovascular Society (CCS) IV angina symptoms despite optimised medical therapy, the patient underwent successful percutaneous revascularisation with bare metal stent (BMS) placement and achieved satisfactory symptom resolution while she was treated with PLEX for acute TTP. To our knowledge, this is the first case report in literature illustrating successful interventional management of acute AMI in the setting of concomitant acute TTP.

CASE PRESENTATION

A 70-year-old woman presented to the outside hospital with 2-week history of worsening epigastric pain and indigestion, and was not responding to over-the-counter antacids. On the day of admission, her pain worsened significantly with severe squeezing sensation in the middle of her chest radiating to her left arm. On initial presentation to outside ED, her vital signs were stable, and physical examination showed diffuse petechial rash across her upper and lower extremities. Blood work revealed a platelet count of 11 ($10 \times 9/L$), haemoglobin 9.3 (g/dL), creatinine 0.77 (mg/dL), total bilirubin to 3.1 (mg/dL), lactate dehydrogenase (LDH) 1278 (U/L), and mildly elevated troponin (0.25 ng/mL). A peripheral blood smear revealed the presence of schistocytes. The initial ECG did not show acute ischaemia. The patient was seen by a local haematologist with concern for acute TTP. She received 2 units of fresh frozen plasma with a dose of intravenous steroids. She was transferred to our institute for emergent PLEX. The patient experienced intermittent chest pain symptoms on arrival, and a repeated ECG showed ST depressions in multiple leads (figure 1, top panel red arrows) with ST elevation in lead aVR (figure 1, top panel green arrow). Repeated blood work was comparable except for worsening LDH to 4758 (U/L). Her troponin trended up and

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Figure 1, Twelve-lead ECG (top) and coronary angiography (bottom). ECG revealed ST depressions in multiple leads (red arrows) and ST elevations in lead aVR (green arrow). Coronary angiography of right coronary artery (RCA) revealed 95% stenosis in the distal RCA and proximal posterior descending artery (white arrows, bottom left panel), and stent placement achieved 0% residual stenosis (white arrows, bottom right panel). CAD, coronary artery disease.

peaked at 8.4 (ng/mL). She continued to complain of chest pain that transiently and briefly responded to nitroglycerin and morphine. The patient's past medical history was significant for hypertension, hyperlipidaemia and insulin-dependent diabetes mellitus type 2, peripheral vascular disease in lower extremities and carotid arteries status post left carotid endarterectomy, and a history of left heart catheterisation several years ago reported non-obstructive CAD. Her pertinent home medications included aspirin, clopidogrel, carvedilol, amlodipine, pravastatin, valsartan-hydrochlorothiazide and insulin. Patient reported 14 pack-year smoking. Her family history was positive for diabetes only. Patient had daily PLEX and rituximab for her acute TTP. The patient had a decreased ADAMTS13 (8%) consistent with acute TTP. Her cardiac presentation, myocardial injury evidenced with elevated troponin I, was consistent with non ST elevation myocardial infarction (NSTEMI) in the setting of acute TTP. The differential diagnosis of the aetiology of myocardial injury included acute microthrombosis of coronary arterioles or obstructive CAD of the epicardial artery. In addition to PLEX for acute TTP, the differential diagnosis of aetiology of the NSTEMI would alter the approach of clinical treatment. Without obstructive CAD, microthrombi-induced myocardial injury in acute TTP is treated conservatively without an ischaemia workup or antiplatelet therapy. However, due the patient's advanced age, multiple risk factors for atherosclerotic CAD, history of peripheral arterial disease and recurrent classic angina, positive cardiac biomarkers and abnormal ECG with evidence of ischaemia (ST depressions), the co-existence of obstructive CAD with acute TTP was suspected. The patient was recommended to undergo an ischaemia workup, with a non-invasive nuclear stress test with myocardial perfusion imaging for risk stratification and, subsequently, invasive coronary angiography.

INVESTIGATIONS

Echocardiography: normal left ventricular systolic function with ejection fraction around 60%–65%, and normal valvular structure and function.

Nuclear stress test with positron emission tomography myocardial perfusion imaging: reversible ischaemia in the apical inferior and mid inferior segments.

Cardiac catheterisation/coronary angiography: see below and figure 1.

DIFFERENTIAL DIAGNOSIS

Microthrombi-induced myocardial infarction.

Obstructive CAD causing myocardial infarction concomitant with acute TTP.

TREATMENT

During hospitalisation, patient received daily PLEX until platelets reached 150 ($10 \times 9/L$) and two weekly doses of rituximab. Her kidney function remained stable, and LDH trended down to normal values. After stabilising her acute TTP, and platelet counts recovering above 150 ($10 \times 9/L$), in the context of recurrent, classic angina pectoris, non-STEMI, and an abnormal nuclear stress test was suggestive for obstructive CAD. The patient was referred for a cardiac catheterisation, which revealed diffuse disease with 95% stenosis in distal segment of right coronary artery (RCA), as well as 90% lesion in proximal right posterior descending artery (PDA) (figure 1, bottom left panel) and mild-to-moderate disease in other epicardial coronary arteries. Given her recurrent CCS IV angina, and angiographic evidence of obstructive CAD, the RCA stenoses was successfully treated with placement of a bare metal stent (figure 1, bottom right panel). The patient was treated with dual antiplatelet therapy for the stent placement with aspirin and prasugrel. Prasugrel was chosen partially out of concern that clopidogrel may have precipitated her TTP.

OUTCOME AND FOLLOW-UP

Patient tolerated PCI well. Her haematological parameter recovered completely. She was discharged home on day 9 of hospitalisation with plan of a 3-week PLEX tapering programme and additional doses of rituximab. Her discharge medications included aspirin, prasugrel, beta blocker and angiotensin receptor blocker. The patient continued with dual antiplatelet therapy without interruption for 4 weeks without any bleeding complication or clinical ischaemic symptoms. On the last follow-up visit 6 months after the PCI, she was doing very well, and remained asymptomatic.

DISCUSSION

Autopsy studies show cardiac involvement in almost all patients with acute TTP with typically microthrombi being responsible for myocardial injury and sparing major epicardial arteries.^{2 3} Although large thrombus obstructing epicardial coronary artery with the absence of underlying atherosclerotic CAD has been reported in acute TTP,^{4 5} we report a patient presenting with acute TTP and classic acute coronary syndrome with recurrent angina pectoris. This patient underwent non-invasive and subsequently invasive diagnostic and treatment for her obstructive CAD with satisfactory results without complications.

From a cardiac standpoint, patients with TTP are challenging to manage as they often present with anaemia, thrombocytopaenia, platelet dysfunction and impaired kidney function. These comorbidities and complications make them poor candidates for anticoagulation, contrast studies and potential PCI. PLEX is the cornerstone of the treatment of acute TTP, with other therapies being less validated in clinical studies. An angiogram should be postponed if possible until lab values at least partially normalise. As TTP relapses, there is always a serious concern with double

antiplatelet therapy, which should be limited to a minimum. If percutaneous revascularisation is indicated, BMSs should be chosen for the reduction of the duration of dual antiplatelet therapy. The choice of antiplatelet agents remains controversial. Treatment and maintenance with aspirin has been shown to prevent microthrombi formation and future relapses.⁶ Several reports showed thienopyridine derivatives like clopidogrel and prasugrel to be potential inducers of TTP.⁷ In patients who develop TTP while taking one of these agents, it seems reasonable to select a different one in the future.

Troponin was shown to be a reliable biomarker for detection of cardiac involvement in TTP. Elevated level on admission has been shown to be a risk factor for death and refractoriness.⁸ In our opinion, all patients admitted for TTP should be screened for signs/symptoms of cardiac involvement, and should have troponin levels checked and an ECG done. A patient with documented cardiac involvement should be considered for further testing including echocardiogram and an ischaemic workup if

CAD risk factors, ischemic symptoms are present and underlying obstructive CAD is within the differential diagnosis.

Contributors XD was responsible for overall designing the project, interpreting data and critically revising and corresponding the manuscript. SLW was involved in collecting data, drafting the article and preparing for documentations.

Competing interests None declared.

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REFERENCES

- 1 Kiss JE. Thrombotic thrombocytopenic purpura: recognition and management. *Int J Hematol* 2010;91:36–45.
- 2 Nichols L, Berg A, Rollins-Raval MA, et al. Cardiac injury is a common postmortem finding in thrombotic thrombocytopenic purpura patients: is empiric cardiac monitoring and protection needed? *Ther Apher Dial* 2015;19:87–92.
- 3 Patschan D, Witzke O, Dührsen U, et al. Acute myocardial infarction in thrombotic microangiopathies-clinical characteristics, risk factors and outcome. *Nephrol Dial Transplant* 2006;21:1549–54.
- 4 Ho HH, Minutello R, Juliano N, et al. A rare cause of acute myocardial infarction: thrombotic thrombocytopenic purpura. *Int J Cardiol* 2009;133:e1–2.
- 5 Doll JA, Kelly JP. ST-segment elevation myocardial infarction treated with thrombolytic therapy in a patient with thrombotic thrombocytopenic purpura. *J Thromb Thrombolysis* 2014;38:124–6.
- 6 Myers TJ, Wakem CJ, Ball ED, et al. Thrombotic thrombocytopenic purpura: combined treatment with plasmapheresis and antiplatelet agents. *Ann Intern Med* 1980;92(2 Pt 1):149–55.
- 7 Jacob S, Dunn BL, Qureshi ZP, et al. Ticlopidine-, clopidogrel-, and prasugrel-associated thrombotic thrombocytopenic purpura: a 20-year review from the Southern Network on Adverse Reactions (SONAR). *Semin Thromb Hemost* 2012;38:845–53.
- 8 Benhamou Y, Boelle PY, Baudin B, et al. Cardiac troponin-I on diagnosis predicts early death and refractoriness in acquired thrombotic thrombocytopenic purpura. Experience of the French thrombotic microangiopathies reference center. *J Thromb Haemost* 2015;13:293–302.

Learning points

- ▶ Concomitant obstructive coronary artery disease (CAD) is possible in patients presenting with acute TTP, although microemboli is more common to cause myocardial injury,
- ▶ Patients with acute Thrombotic thrombocytopenic purpura (TTP), the presence of ischaemia symptoms, risk factors of CAD, elevated biomarkers, and an abnormal ECG warrant ischaemia workup and potential treatment.
- ▶ Bare metal stents are probably a better choice for patients who require percutaneous coronary intervention in the setting of TTP.

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