Case reports

Acute Myocardial Ischaemia in the Presence of Thrombotic Thrombocytopenic Purpura: What Are the Treatment Options?

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ABSTRACT

We describe a case of severe myocardial ischaemia in the setting of thrombotic thrombocytopoenic purpura (TTP). In this report, we discuss the potential difficulties in the diagnosis and management of acute myocardial ischaemia with TTP, particularly relating to the use of antiplatelet agents. We also highlight the importance of careful monitoring during plasma exchange for TTP when acute myocardial ischaemia is present. The potential role for novel therapies in the management of TTP related myocardial ischaemia is also discussed. (**Critical Care and Resuscitation 2001; 3: 45-47**)

Key words: Thrombotic thrombocytopenic purpura, acute myocardial ischaemia, cardiac arrest

Thrombotic thrombocytopenic purpura (TTP) first described by Moschowitz[1] is characterised by fever, thrombocytopenia, haemolytic anaemia, renal dysfunction and fluctuating neurological signs.[2] It is caused by an acquired reduction in plasma von Willebrand factor – cleaving protease activity (due to an IgG auto-antibody)[2,3] leading to the binding of unusually large multimers to platelets resulting in platelet microthrombi. The latter leads to organ dysfunction. Microvascular thrombosis classically occurs in cerebral, renal and dermal microvasculature although it can occur in any organ.[4,5] Both clinical features and autopsy data suggest that the coronary microvasculature is also involved in the disease process more frequently than realised.[5] The cardiac involvement manifests as conduction defects or coronary occlusion.

We describe a case of TTP where the patient presented with left sided weakness and malaise but died of cardiac arrest due to myocardial ischaemia. The issues relating to management of coronary ischaemia in the setting of TTP are discussed.

CASE REPORT

A 60 year old woman presented to the emergency department with a one week history of generalised malaise, nausea, dry retching, constipation and left sided hemiparesis. Her past medical history included type II diabetes mellitus, coronary artery bypass surgery nine years ago and an acute myocardial infarction one year ago. Her regular medications included digoxin, aspirin, lisinopril and atenolol. The only ECG abnormality on admission was a previously documented left bundle branch block. The chest x-ray revealed clear lung fields but an increased cardiothoracic ratio.

Investigations on admission revealed a haemoglobin of 93 g/L, platelet count 13 x 10^9/L and white cell count 12 x 10^9/L. The peripheral blood picture was consistent with microangiopathic haemolysis, with fragmented red cells, an elevated reticulocyte count and a haptoglobin level of 0.0 g/L (normal range 0.35 - 2.00 g/L). The prothrombin time was 11 s (normal range 14 - 18 s), activated partial thromboplastin time 41 s (normal range 31 - 35 s), fibrinogen 3.3 g/L (normal range 1 - 5 g/L),

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and D-dimer 1.1 units. There was evidence of renal impairment with a urea of 15.7 mmol/L and creatinine of 0.12 mmol/L. The total bilirubin was 44 umol/L, conjugated bilirubin of 14 mmol/L and LDH of 754 IU/L. The creatinine kinase was 198 U/L (normal range < 140 U/L) with a troponin of 3.7 U/L (normal range < 0.1 U/L). A CT scan of the brain showed two small well-defined lacunar infarcts in the right basal ganglion region.

A provisional diagnosis of TTP was made. Her treatment included 4 units of fresh frozen plasma (FFP) whilst her aspirin was withheld. On day 2, she was noted to have a Glascow Coma Score (GCS) of 10. Plasma exchange with FFP was commenced on the ward within 24 hr of admission. Although there was neurological improvement, owing to haemodynamic instability, she did not complete an entire cycle of plasma exchange and was transferred to the intensive care unit for further management. On day 3, her neurological status was unchanged, the serum LDH and troponin increased to 980 IU/L and 28 U/L, respectively. On day 4 she became obtunded. She was noted to be tachypnoeic with atrial fibrillation at a rate 120 per minute and a blood pressure of 77/40 mmHg. She was intubated and mechanically ventilated, an infusion of 250 mL of Haemacell^{TM} was administered and an adrenaline infusion was commenced. Following this her arterial blood gases (F_IO_2 of 0.7) were, pH 7.44, pCO_2 27 mmHg and pO_2 344 mmHg. Soon after she suffered a cardiac arrest and was unable to be resuscitated. Serial ECGs through her admission did not reveal any new findings.

At autopsy, the heart was markedly enlarged and dilated, demonstrating left ventricular concentric hypertrophy. The coronary artery bypass grafts were identified and were patent. On histology there were fibrin platelet thrombi identified within intra-myocardial vessels. There was no histological evidence of recent myocardial infarction. Serial sectioning of the cerebral hemispheres, the diencephalon and the brain stem revealed no significant macroscopic pathology.

DISCUSSION

Although the patient deteriorated neurologically prior to her death, the terminal event was myocardial failure due to extensive myocardial necrosis documented by the increase in serum troponin levels from 3.7 U/L to 28 U/L. The autopsy findings of patent coronary artery bypass grafts and microvascular thrombosis in the intra-myocardial vessels on histology suggest that the likely aetiology for the myocardial failure was small vessel ischaemia.

Despite the publication of many reviews describing the aetiology and management of TTP,[2,6-8] there is little information on the management of myocardial ischaemia in the setting of TTP. The myocardial damage is a result of haemorrhagic necrosis from hyalinized arteriolar microthrombi rather than large vessel coronary artery thrombosis. As the myocardial involvement in TTP frequently involves the conduction system,[9] the classic ECG manifestations of an acute myocardial infarct may not be readily apparent. Ischaemia is due to small vessel involvement and can frequently present as unstable angina or a non-Q wave infarction; therefore monitoring serum troponin levels may provide an early warning of subclinical myocardial damage.[10]

Plasma exchange (to remove the IgG autoantibody) and FFP transfusions (to replenish the plasma von Willebrand factor – cleaving protease activity) remain the cornerstone of treatment for TTP.[2,11] However, both have to be used with caution in patients with coexisting myocardial disease as FFP may cause pulmonary oedema and plasma exchange may lead to hypotension, both of which may increase myocardial damage. Antiplatelet agents have a well established role in the management of ischaemic heart disease, and while it may appear that antiplatelet agents would be ideally suited to the management of TTP, particularly when associated myocardial ischaemia,[7] the use of platelet inhibitor drugs in TTP remains controversial. There have been several case reports where recovery has been attributed to the use of these drugs.[7] However, a number of investigators have reported bleeding complications with little therapeutic benefit. In our case aspirin was not used. The role of the thienopyridines (i.e. ticlopidine and clopidogrel) in these patients is limited by the fact that a number of studies have implicated them as a possible precipitating factor in the development of TTP.[12,13] Also, data are now emerging that abciximab also causes thrombocytopoenia, although the precise mechanism of this adverse effect has not been elucidated.[14]

Although anecdotal evidence exists of the usefulness of thrombolytic therapy in TTP,[15] in the absence of evidence to support the use of thrombolytic therapy in acute coronary syndromes in general, we believed that in the presence of severe thrombocytopaenia it would be hazardous. In a study of TTP patients, it has been demonstrated that protein C and antithrombin III (AT-III) levels are reduced in non-survivors compared with survivors.[16] The potential beneficial roles of both Protein C and AT-III infusions in improving sepsis associated purpura fulminans[17] and microangiopathy raise the question as to whether these drugs might be of therapeutic benefit in TTP. However, currently no data exist to support the use of either of these drugs in TTP.

We present this report to highlight potential difficulties in the diagnosis and management of acute

myocardial ischaemia in TTP. Treatment such as plasma exchange for TTP-related myocardial disease should be performed with careful monitoring.

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