

## EMERGENCY CASEBOOK

# Thrombotic thrombocytopenic purpura mimicking acute ischemic stroke

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Thrombotic thrombocytopenic purpura (TTP) is an autoimmune disorder characterised by thrombocytopenia, haemolytic anemia, fluctuating neurological deficits, fever, and renal impairment. This case report is about a young man who presented with acute onset right sided paralysis, dysarthria, and central facial paralysis, suggestive of cerebrovascular accident, but eventually diagnosed as TTP. In addition, the clinical presentation of TTP is discussed and some teaching points for the emergency physicians are emphasised.

Thrombotic thrombocytopenic purpura (TTP) is a rare disorder, and its clinical presentation mimics that of a variety of other diseases. Early diagnosis is important as TTP is a life threatening illness with mortality exceeding 90% in the absence of emergent, appropriate treatment.

## CASE REPORT

A previously healthy 36 year old man presented to our emergency department (ED) with right arm weakness, numbness on the right side of face, and difficulty speaking, which developed an hour before presentation. He had had a fever, cough, headache, and bleeding from the gums for 10 days. On examination, the patient's blood pressure was 160/100 mm Hg, pulse 94 beats/min, respiratory rate 14 breaths/min, and temperature 38.0 °C. Neurological examination revealed 2/5 right arm weakness, 4/5 right leg weakness, dysarthria, and right central facial palsy. There was no nuchal rigidity or cerebellar abnormalities.

After blood was drawn for laboratory tests, he underwent cranial computed tomography (CT) within 30 minutes. The CT scan did not show any intracranial or subarachnoid haemorrhage, or any signs of ischaemia. After another half an hour, his neurological findings resolved. A diagnosis of transient ischaemic attack was considered and admission to the neurology department planned. Results of the laboratory tests were unexpected: white blood cell count  $12\,000 \times 10^9$ , haemoglobin 74 g/l (7.4 g/dl), haematocrit 0.21 (21.1%), and platelet count  $11\,000 \times 10^9$ . Urea, creatinine, electrolytes, and liver function were normal. Urinalysis was remarkable with +3 erythrocytes. Levels of indirect bilirubin and lactate dehydrogenase were elevated. Intravascular haemolysis was suspected and a blood smear requested. Three hours after presentation, the previous neurological symptoms reappeared for an hour and then resolved again gradually. The blood smear was remarkable for fragmented erythrocytes (fig 1).

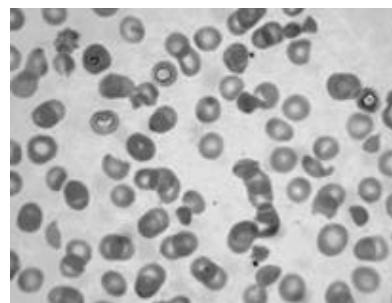
The intravascular haemolysis, thrombocytopenia, haematuria, fluctuant neurological findings, and fever were consistent with a diagnosis of TTP. The patient was admitted, and he underwent plasma exchange emergently. He did not have any neurological symptoms during the course of treatment. Complete remission was achieved on day 12 after admission, and he was discharged on day 16.

## DISCUSSION

TTP is a life threatening disease, characterised by thrombocytopenia, microangiopathic hemolytic anaemia, fluctuating neurological signs, renal failure, and fever. The condition is rare with an annual incidence in adults of 3.7 per million. It is seen predominantly in women, usually between 30 and 40 years of age.<sup>1</sup>

The pathogenesis of TTP is attributed to the presence of unusually large von Willebrand factor (vWF) multimers that lead to platelet clumping and subsequent microvascular thrombosis. These vWF multimers are normally cleaved into smaller protein units by a metalloprotease enzyme, the von Willebrand factor cleaving protease (ADAMTS-13). Impairment of ADAMTS-13 activity leads to an excessive accumulation of vWF, which then may lead to the onset of TTP. TTP is mostly idiopathic, but may be triggered by clinical situations such as bacterial or viral infections, pregnancy, drugs (for example, clopidogrel, ticlopidine, quinine, cyclosporin), and autoimmune disorders (systemic lupus erythematosus, thyroiditis, and antiphospholipid syndrome).<sup>2,3</sup>

Identification of the first acute TTP episode is challenging as no specific clinical symptom or biological criterion is available for the diagnosis. Suspicion of TTP relies on the association of several clinical symptoms and laboratory results. The brain is the commonest target for ischaemia, and abnormal neurological findings present in most cases of TTP. Patients usually develop headache, confusion, ataxia, seizures, and mental status and focal abnormalities. Other frequent symptoms are fever, weakness, arthralgia, myalgia, jaundice, nausea, vomiting, diarrhoea and abdominal pain. Skin and mucosal bleeding secondary to the thrombocytopenia is also common.<sup>2,3</sup> Patients may have renal abnormalities including oligoanuria, acute renal failure, albuminuria, and microscopic haematuria.<sup>2</sup> Consumption thrombocytopenia is present in most cases, with platelet counts often below  $20\,000 \times 10^9$ . The widespread deposition of fibrin in the vessels leads to mechanical trauma to the passing red blood cells, resulting in fragmented red blood cells on the blood smear. Haemoglobin is usually below 80 g/l (8 g/dl)



**Figure 1** Blood smear revealed fragmented erythrocytes suggesting intravascular haemolysis.

secondary to haemolytic anaemia. Elevated lactate dehydrogenase and bilirubin levels may represent intravascular haemolysis.<sup>1-3</sup>

Currently plasma exchange treatment is indicated for all adult patients with a clinical diagnosis of TTP. Since the availability of plasma exchange treatment, mortality has fallen from 90% to about 10%. As delay in the initiation of plasma exchange correlates with treatment failure, early diagnosis and treatment is essential.<sup>4</sup>

According to the 2005 American Heart Association guideline for cardiopulmonary resuscitation and emergency cardiovascular care, our patient was a candidate for thrombolytic therapy for ischaemic stroke within first two hours of presentation. However, right sided weakness, central facial palsy, and dysarthria have been reported to be associated with TTP.<sup>3</sup> These neurological manifestations of TTP can easily be mistaken for acute ischaemic stroke, which requires early thrombolysis. Administration of thrombolytic drugs to patients with TTP misdiagnosed as acute ischaemic stroke may lead to detrimental consequences. Therefore the laboratory test results of patients presenting with signs and symptoms of acute ischaemic stroke must be checked carefully, and TTP should be borne in mind as a differential diagnosis.

## CONCLUSION

Rapid diagnosis and treatment are necessary for decreasing the risk of fatal outcome in patients with TTP. Emergency physicians should be familiar with the clinical presentation and laboratory abnormalities of TTP to be able to make the diagnosis early on. In patients presenting with fluctuant

neurological findings, thrombocytopenia, haemolytic anemia, and fever, the diagnosis of TTP should be considered.

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