Neurological symptoms as the sole presentation of relapsed thrombotic thrombocytopenic purpura without microangiopathic haemolytic anaemia

Kay T. Htun; Amanda K. Davis
Department of Haematology, Alfred Health, Melbourne, Victoria, Australia

Dear Sir,
Thrombotic thrombocytopenic purpura (TTP) is a disorder which leads to the formation of von Willebrand factor-rich microthrombi in the arterioles and capillaries of multiple organs. Although the diagnosis is classically made upon a pentad of fever, thrombocytopenia, microangiopathic haemolytic anaemia (MAHA), renal failure and various neurological symptoms, it only requires the presence of thrombocytopenia and MAHA without an alternative cause. However, it is not often considered in the differential diagnosis in patients without features of overt microangiopathy. Without timely and effective treatment, TTP can lead to significant morbidity and mortality in up to 90% of cases (1). Recent advances in understanding the role of ADAMTS13 deficiency in the pathophysiology of idiopathic TTP (2-4) have shown this enzyme plays an important role in early diagnosis and treatment, especially in atypical presentations.

We describe two cases of relapsed idiopathic TTP, presenting with isolated neurological symptoms without microangiopathic haemolysis. Both patients consented verbally to publish their clinical data as a case report.

Case 1
A 72-year-old Caucasian female with stable rheumatoid arthritis was diagnosed with TTP in December 2012 after presenting with severe acute thrombocytopenia (platelets 15x10^9/l, normal range 150–400x10^9/l) and MAHA. She was on methotrexate 20 mg weekly with folic acid supplementation, irbesartan for hypertension and vitamin D. ADAMTS13 level was low at 13% (TECHNOZYME ELISA method) (normal range 40–130%). She responded well to six daily single volume plasma exchanges (TPE) and prednisolone 1 mg/kg daily. Platelet count, ADAMTS13 and LDH level normalised with resolution of MAHA on blood film. Prednisolone was rapidly weaned. Four months later, she represented with headache and bilateral visual impairment for two weeks. Full blood count revealed mild thrombocytopenia of 80 x 10^9/l with no evidence of MAHA on blood film and normal LDH. She had visual acuity of 6/60 bilaterally and right lower homonymous quadrantanopia. Computed tomography

References

Correspondence to:
Amanda K. Davis
Department of Haematology, Alfred Health
55 Commercial Road, Melbourne
Victoria 3004, Australia
Tel.: +61 03 9076 2000, Fax: +61 03 9076 3021
E-mail: am.davis@alfred.org.au

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(CT) scan of the brain showed multiple cerebral infarcts involving bifrontal and left parieto-occipital areas (Figure 1). Bilateral carotid Doppler ultrasound showed no stenosis and transthoracic echocardiogram revealed no intracardiac thrombus. The patient was in sinus rhythm with no known history of atrial fibrillation. Screening for antiphospholipid syndrome was negative. ADAMTS13 activity was severely reduced (<1%) with a positive inhibitor assay at 3.2 Bethesda Units/ml. Urgent TPE was commenced with subsequent stabilisation of visual symptoms. Platelet count and ADAMTS13 level normalised within two weeks. Prednisolone 1 mg/kg and weekly rituximab therapy (375 mg/m²) for three weeks were given to maintain remission. Prednisolone was slowly weaned over a period of four months. The patient’s visual impairment improved to 6/24 bilaterally in six weeks with complete resolution of right homonymous quadrantanopia. The patient has remained in remission.

Case 2

A 29-year-old Caucasian female presented with recurrent episodes of presumed immune thrombocytopenia (ITP) which first started in 2004. Thrombocytopenia responded well to systemic steroid therapy. In May 2009, the diagnosis was revised as TTP based on revisiting clinical history and blood films demonstrating microangiopathic haemolysis. ADAMTS13 level was low at <1% at the time of diagnosis. In September 2009, she presented with episodes of transient visual disturbance affecting both eyes, each episode lasting 2-3 minutes with complete resolution in between the attacks. The presumed diagnosis of ocular migraine was made after normal magnetic resonance imaging (MRI) and magnetic resonance angiogram (MRA) of the brain, normal transthoracic echocardiogram with contrast study and negative autoimmune and antiphospholipid antibody screening. In early 2010 she had a typical TTP relapse with acute thrombocytopenia, MAHA and ADAMTS13 activity of <1%. She achieved remission after being treated with TPE, systemic steroids and weekly rituximab for four weeks with normalisation of pla-

**Clinical events**

<table>
<thead>
<tr>
<th>Event</th>
<th>Platelet (150–400x10⁹/L)</th>
<th>LDH (125–255 U/L)</th>
<th>ADAMTS13 (40–130%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 2009 (TTP diagnosed)</td>
<td>270</td>
<td>168</td>
<td>0.3</td>
</tr>
<tr>
<td>March 2010 (TTP relapsed)</td>
<td>13</td>
<td>427</td>
<td>0.1</td>
</tr>
<tr>
<td>2011 (In remission)</td>
<td>374</td>
<td>168</td>
<td>78</td>
</tr>
<tr>
<td>January 2013 (TTP relapsed without MAHA)</td>
<td>300</td>
<td>170</td>
<td>0.1</td>
</tr>
<tr>
<td>February 2013 (In remission)</td>
<td>173</td>
<td>160</td>
<td>75</td>
</tr>
</tbody>
</table>

Figure 1: Table illustrating clinical events of the patient (case 2) together with platelet count, LDH and ADAMTS 13 activity and CT scans of the brain (case 1) demonstrating bifrontal and left parieto-occipital infarcts (see the arrows).
beit rare, in cases of thrombotic stroke or stroke like symptoms in the absence of traditional risk factors for cerebrovascular disease.

In conclusion, idiopathic TTP, either in relapse or even possibly as an initial presentation, can occur without concurrent thrombocytopenia and microangiopathic haemolysis. Testing for severe ADAMTS13 deficiency is crucial for early diagnosis when there is a clinical suspicion to allow timely treatment and hopefully favourable outcomes in such cases.

Conflicts of interest
None declared.

References