Cerebral venous sinus thrombosis and antiphospholipid antibodies

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Summary
We report two cases of cerebral venous sinus thrombosis associated with an antibody to phospholipids, namely the lupus anticoagulant. Both patients later developed further immunologically mediated conditions. The importance of screening for the lupus anticoagulant in addition to anticardiolipin antibodies in this condition and the need for follow-up of such patients is discussed.

Keywords: cerebral venous sinus thrombosis, antiphospholipids, lupus anticoagulant, anticardiolipin antibodies

anticoagulant', or in serum, where anticardiolipin antibodies are detected by immunoassay. These methods identify different members of a group of antibodies with varying specificities for phospholipid (see figure 1). Cerebral venous sinus thrombosis is associated with hypercoaguable states and a number of immune-mediated conditions.² Reports of cerebral venous sinus thrombosis with antiphospholipid antibodies are, however, limited.³ We hereby report two such cases, both presenting with isolated raised intracranial pressure. The implications of their presentation, investigative findings and follow-up are discussed.

Case 1

The association of antiphospholipid antibodies with thrombotic episodes is well established. In the absence of other connective tissue disease such an association is known as the primary antiphospholipid syndrome.¹ In clinical practice antiphospholipid antibodies may be detected by one of two methods. In plasma, by prolongation of clotting time in phospholipid-dependent tests, this being termed the 'lupus

A 30-year-old man was admitted with a two-week history of morning headache, nausea and vomiting. Over the second week he had noted a deterioration in visual acuity in both eyes. Eighteen months prior to this admission he had been investigated for a monoarthropathy of the right knee. At that time his erythrocyte sedimentation rate (ESR) was elevated at 48; rheumatoid factor (RF) was negative. Eight

Figure 1 Action of the lupus anticoagulant on clotting pathways. It inhibits the interaction of coagulation factors with phospholipids, in particular the phospholipid portion of the 'prothrombin activator complex'.

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months prior to admission he developed an extensive left deep venous thrombosis and had been anticoagulated for six months.

General examination revealed a small residual effusion of the right knee. On neurological examination visual acuity was reduced to 6/36 on the left, 6/24 on the right with bilateral, non-haemorrhagic papilloedema. Visual fields and blind spots were normal to confrontation.

Investigations showed elevated inflammatory markers; ESR 38, C-reactive protein 61 mg/l. Computed tomography (CT) head scan was normal, cerebrospinal fluid (CSF) opening pressure greater than 40 cm water with normal microscopy and protein. Magnetic resonance imaging (MRI) and cerebral angiography confirmed a diagnosis of sagittal sinus thrombosis (figure 2). An auto-antibody screen (antinuclear factor (ANF), dsDNA, ANCA, RF, ENA and anticardiolipin) was negative. Partial thromboplastin time (PTT) was elevated at 1.2 s (normal 0.93–1.17), platelet count was normal. A prothrombotic screen showed normal levels of protein C, S and antithrombin III. The lupus anticoagulant was positive (as determined by the Exner and Russell Viper Venom methods).

The patient improved symptomatically with lumbar puncture, oral steroids and acetazolamide. In view of recurrent thrombotic episodes and a positive lupus anticoagulant a presumptive diagnosis of primary antiphospholipid syndrome was made and he was anticoagulated. Over four weeks his symptoms resolved, visual acuity returned to normal and fundal appearances settled.

Four months later he represented with oral and genital ulceration in association with a vasculitic rash on the left shin and reactivation of the right knee arthropathy. Biopsy of the rash revealed a fibrinoid vasculitis consistent with a diagnosis of Behcet's disease.

Case 2

A 42-year-old woman presented with three weeks of constant headache and vomiting. She had noted intermittent blurring of vision in the right eye which was worse when standing. She had undergone stripping of varicose veins six weeks previously.

General examination was normal. Neurological examination showed bilateral, nonhaemorrhagic papilloedema with retained visual acuity (6/6 bilaterally). Visual fields and blind spots were normal.

Investigations revealed a normal platelet count and inflammatory markers, negative auto-antibody screen (ANF, RF, ENA and anticardiolipin) and normal CT head scan. PTT was 1.16 s. CSF pressure was normal (17 cm water) as was microscopy and protein. MRI and cerebral angiography confirmed a left sigmoid sinus thrombus.

Her symptoms settled spontaneously and the papilloedema resolved. She was treated with aspirin and at discharge the diagnosis was thought to be of cerebral venous sinus thrombosis, possibly secondary to recent surgery. She remained well on follow-up for nine

Figure 2 Patient 1: MRI scan (A) showing thrombus in the posterior sagittal sinus (arrowed). In the same patient a venous phase angiogram (B) confirms a filling defect in this region.

months. She then presented to the dermatological department with cold urticaria; a disorder of unknown aetiology, thought to be immunologically mediated. Further screening at this time revealed negative cryoglobulins and cold agglutinins but a positive test for the lupus anticoagulant (determined as in patient 1). She was commenced on cypheptadine for urticaria but has not been anticoagulated, she remains well 18 months from her initial presentation.

Discussion

Antibodies to phospholipids, first described in association with systemic lupus, are present at low titre in approximately 4% of the general population.⁴ Persistent high titres, in particular of IgG anticardiolipin, are clearly associated with thrombosis at multiple sites. In the absence of connective tissue disease the antiphospholipid syndrome has been associated with a number of neurological presentations including chorea, seizure disorder, psychiatric disturbance, and transverse myelitis.^{1,5} The two cases presented here illustrate the association of antiphospholipid antibodies with cerebral venous sinus thrombosis.

Cerebral venous sinus thrombosis: features
<ul style="list-style-type: none">• chronic: symptoms of raised intracranial pressure papilloedema• acute: impaired consciousness seizures focal symptoms/signs

Cerebral venous sinus thrombosis: causes
<ul style="list-style-type: none">• abnormalities of blood (eg, polycythaemia, myeloproliferative disorders, prothrombotic tendencies)• abnormalities of flow (eg, dehydration, sinus compression by tumour, arteriovenous malformations)• abnormalities of vessel wall (eg, local sepsis, malignant infiltration)

The first patient had a past history suggestive both of a prothrombotic tendency and a possible immunologically mediated arthropathy. Subsequently he developed Behcet’s disease, an independent risk factor for cerebral venous sinus thrombosis⁶ and previously described in association with antiphospholipid antibodies. In the second patient, sigmoid sinus thrombosis occurred six weeks after varicose vein surgery. Though cerebral venous sinus thrombosis has been described post operatively this is generally in the immediate postoperative period. The later presentation with an immunologically mediated skin disorder and lupus anticoagulant indicate this to be the probable specific causative agent. In both patients the marginal prolongation of PTT at presentation suggests the presence of a circulating anticoagulant.

In our patients it is notable that a full auto-antibody screen, including anticardiolipin and ANF, was negative and in patient 2 inflammatory markers were not raised. The prolongation of PTT or thrombocytopenia may not always be found in these patients and the presence of the lupus anticoagulant may not therefore be suspected. It is important to recognise that though both the lupus anticoagulant and anticardiolipin antibodies are often present in an individual (70% concordance), each may be present in isolation, as in these two patients.

Both patients presented with symptoms and signs of raised intracranial pressure and had normal CT head scans. Such findings are characteristic of the syndrome of benign intracranial hypertension, though both patients would have been atypical for such a diagnosis in terms of age and build. The chronic presentation of cerebral venous sinus thrombosis may mimic benign intracranial hypertension, CT head scans are often normal in these patients, and this diagnosis should be considered in cases

Cerebral venous sinus thrombosis: management options
<ul style="list-style-type: none">• treatment of underlying condition• heparin/warfarin in acute presentations• acetazolamide/steroids for raised intracerebral pressure• anticonvulsants for seizures• antiplatelet agents

Summary/learning points
<ul style="list-style-type: none">• in unexplained cerebral venous sinus thrombosis antiphospholipid antibodies should be sought by assays for both anticardiolipin antibodies and the lupus anticoagulant• in patients atypical for benign intracranial hypertension (presenting with symptoms and signs of raised intracranial pressure and a normal CT head scan) cerebral venous sinus thrombosis should be considered. MRI and MRI angiography are the investigations of choice

of benign intracranial hypertension occurring in patients not obviously at risk for this condition. The investigation of choice in this situation is now MRI and MRI angiography.

These two cases demonstrate the importance of screening for antiphospholipid antibodies in patients presenting with cerebral venous sinus thrombosis. In patients where such antibodies are identified clinicians should be aware not only of the risk of recurrent thrombosis but also of the possible later development of associated immunologically mediated conditions.

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