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Brief report

Antiphospholipid syndrome mimicking multiple sclerosis in two patients

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Abstract

Antiphospholipid syndrome can sometimes mimic multiple sclerosis symptoms and, therefore, present difficulties at the time of diagnosis. We describe the cases of two young women with recurrent neurological deficiencies, the presence of antiphospholipid antibodies in serum, and typical demyelinating lesions on magnetic resonance imaging. Initiation of anticoagulant therapy did not result in any new neurological events in either patient.

Keywords: Antiphospholipid syndrome; Anticardiolipin; Multiple sclerosis

1. Introduction

Antiphospholipid syndrome (APS) is defined as the presence of arterial and/or venous thrombosis and/or recurrent fetal loss in the presence of antiphospholipid antibodies (aPL) on two occasions over a period longer than 6 weeks. Diverse neurological syndromes have been reported in APS, despite there being no causal relationship between aPL and some of these manifestations.

Several cases have been published over the past years about a syndrome that simulates multiple sclerosis (MS) in the presence of aPL. These patients usually experienced a good clinical response after the initiation of anticoagulation [1–4].

We describe two new patients with APS whose clinical symptoms were indistinguishable from those of MS.

2. Case reports

2.1. Case 1

In 1995, a 21 year-old woman experienced a sudden weakness in her right arm and leg. An examination revealed hemiparesis 4/5, as well as tactile and algesic hemihypoesthesia. She complained of occasional migraines and claimed to smoke 10 cigarettes daily. Routine analysis of hematology, biochemistry, complement levels, antinuclear antibodies (ANA), anti-DNA and anti-extractable nuclear antigen (ENA) antibodies revealed normal results. Cerebrospinal fluid (CSF) had 3 leukocytes per high-power field, with normal values for other parameters. Results were negative for bacteria and mycobacteria, and oligoclonal bands were absent. Electrocardiogram (ECG), echocardiography, and visual, auditory, and somatosensory evoked potentials were all normal. Cerebral magnetic resonance imaging (MRI) showed slight T2-weighted hyperintensity in the bilateral periventricular white matter. The patient recovered completely with no therapy.

Six years later, she displayed dizziness that increased with movements of the head, accompanied by nausea and

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unsteadiness, followed by right hemiparesia and hemihypoesthesia 12 h later. An analysis showed a prolonged, activated partial thromboplastin time (aPTT) of 45 s and positive IgM anticardiolipin antibodies (ACA) with a titer of 93 uMPL/ml. This result was confirmed over three subsequent analyses. No episodes were noted after anticoagulation treatment. Lesions observed on MRI remained unalterable.

2.2. Case 2

In 1985, a 26 year-old woman experienced four episodes of sudden itching with numbness and weakness in her lower limbs over a 6 month period. She recovered from each episode 1 week later without any treatment. She had been smoking 10 cigarettes daily, taking contraceptive pills, and had had a previous gestation with normal childbirth. Examination demonstrated central facial palsy and power 4/5 in the right lower limb. A hemogram, coagulation, biochemical tests, and complement were normal. Serologic testing for syphilis was negative. CSF showed 8 white cells per high-power field, with normal values of glucose and proteins. Cultures were negative. ECG, computed tomography (CT), an electroencephalogram, and brainstem, visual, and somatosensory evoked potentials but did not show any alterations. Use of contraceptives was suspended.

Twelve years later, she presented occasional transitory neurological deficiencies. At that time, ANA (titer 1/640) and ACA (IgG 47 uGPL/mL) yielded positive results, while anti-DNA and anti-ENA were negative. CSF did not show oligoclonal bands. Cerebral MRI revealed T2-weighted multiple areas of hyperintensity with ovoid morphology in the deep white matter and both semioval centers (Fig. 1). The patient was given aspirin therapy.

Four years later, she developed metrorrhagia and had hematomas spread all over her body. Blood tests showed 2000 platelets with antiplatelet antibodies. Aspirin was stopped and steroids were initiated. One month later, she suddenly developed central facial palsy with left hemiparesis 3/5 and tactile hypoesthesia. A cranial CT showed an area of ischemia in the basal nuclei. Transesophagic echocardiography did not show pathological findings. ACA IgM were positive at a titer of 37 uMPL/mL. The patient began oral anticoagulation.

Since then, she has not developed any new neurological events, ACA and ANA were found to be positive, and MRI showed the same unchanged lesions described previously.

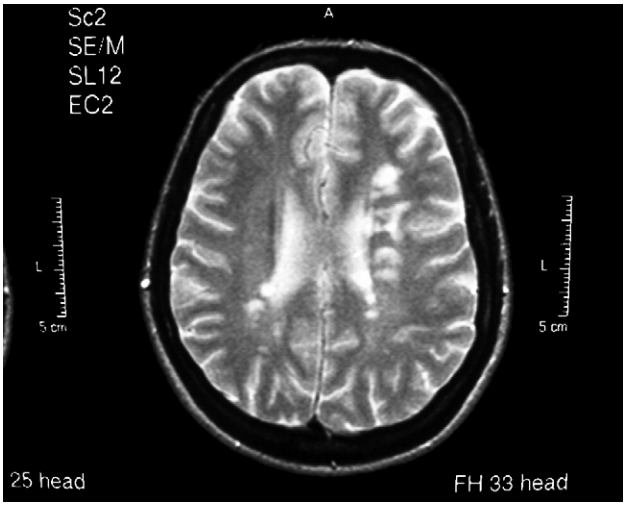

Fig. 1. Axial T2-weighted MRI revealing multiple areas of abnormal high signal intensity involving deep white matter.

3. Discussion

We describe two cases of young women who presented transitory neurological events, together with the presence of aPL and MRI compatible with demyelinating disease. We would further like to highlight the presence of ANA and autoimmune thrombocytopenia in the second patient. Initiation of anticoagulation resulted in no further events, which reinforces the diagnosis of APS in each case.

APS can sometimes simulate MS, and distinguishing the two can be very difficult. Yet, differentiation is important for their treatment and evolution. Anticoagulation is the therapy of choice in APS, although the optimal intensity remains unknown, and prognosis is better than in MS patients [5].

The most frequent clinical presentation of patients with APS that simulate MS is myelopathy, although other neurological deficiencies have also been described, such as cerebellar syndrome or optic neuritis [5]. Therefore, it is important to make an exhaustive anamnesis, with special attention to previous history of thrombosis or fetal loss, which could suggest the diagnosis of APS.

Blood tests do not provide a clear distinction between APS and MS. Cerebral MRI with gadolinium is considered to be the procedure of choice, although it cannot safely distinguish between the two entities. The most characteristic lesions are located in the white matter of both cerebral hemispheres at the periventricular site and are hyperintense in T2-weighted images [4,5]. We must bear in mind that, although these lesions are often interpreted as demyelinating, there are other diseases, such as ischemic injuries or vasculitis, that also present similar demyelinating lesions.

aPL are essential for the diagnosis of this entity. These antibodies have been demonstrated in 2–32% of MS patients, although only occasionally in some studies [5,6]. Some authors postulate that all patients with MS must be subjected to an aPL analysis [4]. Other authors [6], who did not find a high prevalence of aPL, disagree; they recommend aPL only when APS is highly suspected or clinical presentation of MS is not typical.

The persistent presence of aPL suggests the possibility of a thrombotic etiology as an explanation for the neurological symptoms, although its pathogenic role is still unknown. On the other hand, aPL has been found to react against myelin, since it is made up of phospholipids, which could suggest an

autoimmune mechanism. However, we do not know if aPL are an epiphenomenon or truly pathogenic. We must assume that the two mechanisms are not necessarily exclusive and that other pathogenic mechanisms could exist as well.

Learning points:

- APS can sometimes simulate MS. The medical history, together with the presence of aPL and the characteristic lesions seen on MRI, are the mainstay of the diagnosis.
- Differentiation is important because the choice of therapy in APS is anticoagulation.
- aPL should be ordered for all patients suspected of MS, especially if the clinical presentation of MS is not typical or if APS is highly suspected on the basis of the medical history.

References

[1] Scott TF, Hess D, Brillman J. Antiphospholipid antibody syndrome mimicking multiple sclerosis clinically and by magnetic resonance imaging. Arch Intern Med 1994;154:917–20.

[2] Siam AM, Hammoudeh M, Khanjar I. Multiple sclerosis-like picture in association with Hughes syndrome. Lupus 1998;7:367–9.

[3] Ijdo JW, Conti-Kelly AM, Greco P, Abedi M, Amos M, Provenzale JM, et al. Anti-phospholipid antibodies in patients with multiple sclerosis and MS-like illnesses: MS or APS? Lupus 1999;8:109–15.

[4] Cuadrado MJ, Khamashta MA, Ballesteros A, Godfrey T, Simon MJ, Hughes GRV. Can neurologic manifestations of Hughes (Antiphospholipid) syndrome be distinguished from multiple sclerosis? Analysis of 27 patients and review of the literature. Medicine (Baltimore) 2000;79:57–68.

[5] Karussis D, Leker RR, Ashkenazi A, Abramsky O. A subgroup of multiple sclerosis patients with anticardiolipin antibodies and unusual clinical manifestations: do they represent a new nosological entity? Ann Neurol 1998;44:629–34.

[6] Sastre-Garriga J, Reverter JC, Font J, Tintoré M, Espinosa G, Montalban X. Anticardiolipin antibodies are not a useful screening tool in a nonselected large group of patients with multiple sclerosis. Ann Neurol 2001;49:408–11.