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The Neurological Manifestations as an Onset Symptom of Anti-Phospholipid Syndrome: Report of Two Cases

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Introduction

The Antiphospholipid Syndrome (APS) is defined by the occurrence of multiple venous and arterial thrombosis. In this condition, the presence of anti-phospholipid antibodies (aPL), namely lupus anticoagulant (LA), anti-Cardiolipin antibodies (acl) or anti-beta 2 glycoprotein 1 antibodies is necessary for diagnosis[1,2].

The prevalence of aPL seropositive ranges between 1-5% in the general population, but only a minority of these individuals develop the APS[1]. For the definite diagnosis of APS at least one clinical feature such as vascular thrombosis or pregnancy morbidity and one laboratory abnormality must be observed. The laboratory abnormalities must be present on two or more occasions at least 12 weeks apart[3].

The cerebral involvement in APS is common and characterized by different clinical manifestations; they could be the first presenting feature or appear in the course of the disease. The reported manifestations of the cerebral involvement are: cerebral ischemic events such as CVA and TIA, epilepsy, dementia, cognitive deficit, headache, psychiatric disorders, chorea, MS-like syndrome, transverse myelitis and ocular symptoms. It is notable to mention that the presence of aPL in patients without criteria for APS may also be associated with neuropsychiatric and cognitive disturbances.

First Case

The first patient is a-57-year old woman who suffered of a chronic cervical pain. She had the right side sensory deficit and right side hemiparesis for about less than a day and a recurrent persistent headache. Brain and cervical MRI investigations were performed. On the brain MRI she had hyper intense foci in the left subcortical area (figure.1). On the cervical MRI she had a hyper signal focus at the level of C4-C5 (figure.2). The result was in favor of Multiple Sclerosis (MS) therefore, disease modifying drugs (DMD) was initiated. Then due to the chronic recurrent persistent headache, she was referred to us. The age of the patient and the severe persistent headache was not familiar to MS and the transient paresthesia and weakness lead us to rule out TIA for this patient. Therefore, we examined her for other clinical diagnostic possibilities. We did para-clinic studies to check other autoimmune causes which could represent with multiple neurological deficits and make assurance about the diagnosis of MS. We did the lumbar puncture examination and analyzed the CSF for oligo-clonal bands (OCB) as well. The OCB was negative. The collagen vascular disease tests such as ANA, Anti ds-DNA, Anti SS-A, Anti SS-B, RF, Anti NMO Ab, and Anti MOG Ab were negative, but the anti-phospholipid Ab IgG (screening) was 10.7(positive), Anti-Cardiolipin Ab IgG was 15.8 (positive). For more evaluation, the aPL was rechecked around 3 months later, and again those tests were found to be positive. The clinical findings and laboratory data supported the diagnosis of anti- phospholipid syndrome[2,4]. This patient had no history of fetal losses or stroke. After the diagnosis of APS the anti-platelet agents has been started and DMD was discontinued as well. Her headaches become better and less frequent after using antiplatelet agent.

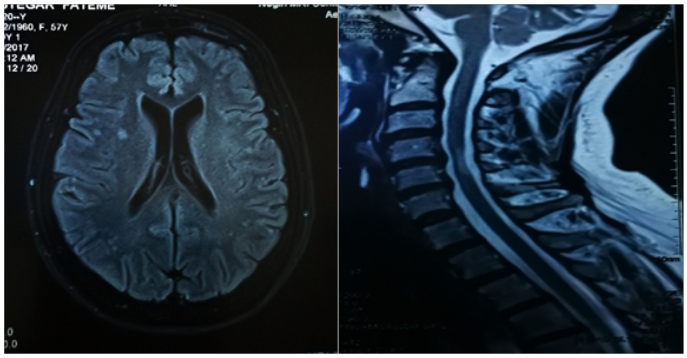

Figure 1 Figure 2

Figure 1-2: The brain and cervical MRI mimicking MS in a patient who presented by paresthesia and headaches

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The first lab data

test	result	unit	Reference intervals
ACE	43	IU/L	8-65
ANA	1/40	titer	Up to 1/40
Anti-ds-DNA	1	IU/mL	< 20:negative;borderline:20-25; > 25:positive
Anti-phospholipid Ab(IgG) (screening) *In this test the patient serum was screened for the presence of auto-antibodies against the following antigens: beta 2 glycoprotein1, phospholipid inositol.*	10.7	U/mL	Up to 10
Anti Cardiolipin Ab(IgG)	15.8	GPLU/mL	Up to 10: positive
NMO Ab(IgG)	negative	titer	Up to 1/10
Anti SS-A Ab	2.9	RU/mL	< 20:negative; >=20:positive
Platelet count	185000		150000 - 450000

The second lab data after 12 weeks

test	result	unit	Reference intervals
Anti Cardiolipin(IgG)	2.5	GPLU/mL	Up to 10:positive
Anti Cardiolipin(IgM)	57	MPLU/mL	Up to 10:positive
C.ANCA	3	U/mL	>18:positive;12-18: Borderline;< 12:negative
P.ANCA	1.3	U/mL	>18:positive;12-18: Borderline;< 12:negative
Anti beta- 2 glycoprotein(IgM)	37	MPLU/mL	Positive > 10
Anti beta- 2 glycoprotein(IgM)	2.6	GPLU/mL	Positive > 10
Lupus Anti coagulant	40	sec	30 - 45

Second Case

The patient is a-63-year old man who had chronic renal failure and presented by a stroke and a history of several TIAs. At the visiting time, we found a history of complex partial seizure. He suffers from inability to write because of sensory and motor deficit effecting hands, imbalance, chronic headache, memory problems and stuttering. During his admission he had psychological problems, such as talkativeness, loss of concentration and flight of idea with a mild disorientation to time, place and person, ataxia, sensory changes in his hands and upward plantar reflex in the left side. In his brain MRI, bilateral pre-ventricular hyper intense foci with involvement of subcortical area and basal ganglia were detected. (figure.3)

We tried to find out the cause of the repeated thrombotic events and multiple neurological dysfunctions. The anti Cardiolipin Ab IgG was 17.9 (positive) and the anti- phospholipid Ab IgM was 35.1(positive) as well. The aPL rechecked around 3 months apart and they were positive again. The other collagen vascular disease tests were normal. By the laboratory findings and the presence of multiple vascular events and other clinical findings the patient has been diagnosed as APS.

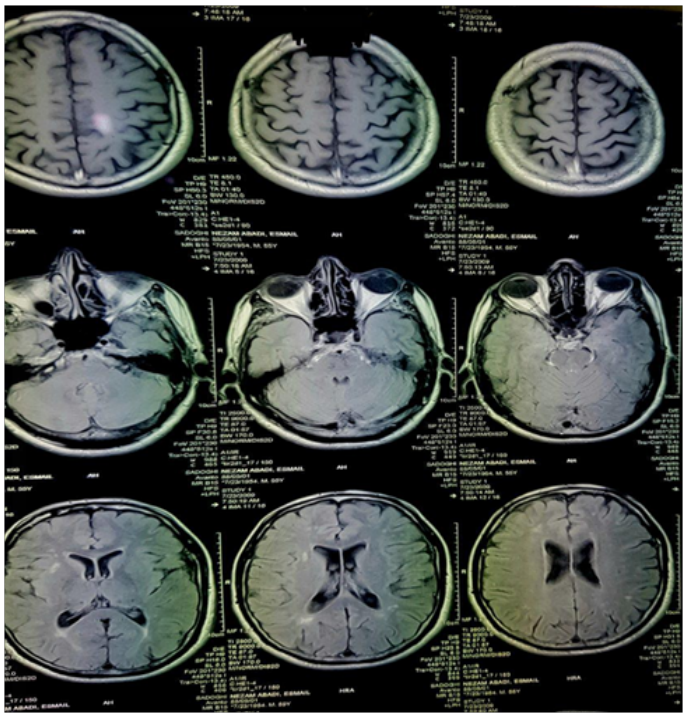

Figure 3: The brain MRI features in the patient with repeated TIAs and positive findings of aPL antibodies.

The first lab data

test	result	unit	Reference intervals
Anti Cardiolipin (IgG)	17.9	GPLU/mL	Up to 10:positive
Anti Cardiolipin (IgM)	35.1	MPLU/mL	Up to 10:positive
Antiphospholipid IgG(screening)	20.5	U/mL	Up to 10:positive
Anti beta-2 glycoprotein 1(IgM)	9	MPLU/mL	Positive >10
Anti beta-2 glycoprotein 1(IgG)	6	GPLU/mL	Positive >10
C.ANCA	0.1	U/mL	>18:positive;12-18: Borderline;<12:negative
P.ANCA	0.2	U/mL	>18:positive;12-18: Borderline;<12:negative
RF	negative		
ANA	9		>10: positive
platelet	262,000		150,000 - 450,000

The second lab data after 12 weeks

test	result	unit	Reference intervals
Anti Cardiolipin (IgG)	11	GPLU/mL	Up to 10:positive
Anti Cardiolipin (IgM)	24.8	MPLU/mL	Up to 10:positive
Lupus anticoagulant	20	sec	30 - 45

Discussion

In case 1, some of the clinical and imaging findings were in favor of multiple sclerosis. The coexisting of brain hyper intense foci and transverse myelitis was more characteristic for MS by the diagnostic criteria of this disease, other symptoms such as transient paresthesia and weakness lead us to the diagnosis of TIA. In addition to that, the age of the patient was not compatible with MS. Further on, the history of recurrent persistent headache was questionable and was needed more evaluations to rule out other causes of neurologic deficit in the patient. More important, the patterns of cortical lesions that were mainly subcortical, was thought to be more compatible with other causes than demyelinating disease.

The headache is one of the most often described neurological manifestation in patients with APS being presented either as chronic headache or episodes of migraine[5], and in fact case 1 referred to us because of chronic persistent headache as her chief complaint.

The MRI studies could lead us to make the correct diagnosis. The static lesions are more suggestive of APS but the dynamic lesions are more characteristic of MS which could find by magnetization transfer imaging compared with standard MRI studies. The elongated ovoid shaped lesions (Dawson fingers) and black holes are more characteristic of MS. The distribution of the lesions can be helpful, since sub-cortical lesions are more dominant in APS but periventricular and corpus callosum involvement in MS. Although transverse myelitis and optic neuropathy are rare manifestations of APS, it is recommended that SLE and secondary APS must be suspected in patients with those conditions[5]. In the first patient, lesions were in subcortical area and in the second case the involvement of the basal ganglia and periventricular area was present.

It is told that MS-like symptoms accompanied by aPL have remarkable clinical and preclinical improvements after anticoagulation or even antiplatelet therapy[5]. Interestingly, the case 1 had a good response to antiplatelet treatment and her headaches became better and less frequent, as well as she did not have any clinical response to DMD.

The second case was diagnosed with primary APS by the diagnostic criteria and showed repeated complex partial seizures with some personality changes[3]. Most often the occurrence of epilepsy in APS is understood to be sequels of the ischemic neuro-parenchymal insults[5]. High titer of aCL, anti-beta 2 GP1 and anti- thrombin antibodies have been presented in patients who suffer of epilepsy[5]. Cognitive dysfunction is a relatively uncommon neuropsychiatric manifestation in APS patients[5]. The second case had several psychological problems such as memory problem, loss of concentration and disorientation.

Finally, according to our observations, antiphospholipid syndrome could be presented by neurological dysfunctions. If we encounter unusual features in a case with neurologic symptoms, we have to be more cautious about differential diagnosis. In the first case, despite MRI positive criteria for MS; however, she has other unusual presentation for demyelinating disorder. The second case, has repeated TIAs accompanied by complex partial seizure as well as psychiatric personality changes, that all of them lead us to consider other causes of neurovascular dysfunction. Fortunately, with initiation of anticoagulants the clinical manifestations of the patient were also improved dramatically.

Conclusion

Anti-phospholipid syndrome could be presented by neurological dysfunctions. If we encounter unusual features in a case with neurologic symptoms, we have to be more cautious about differential diagnosis.

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