Mononeuritis multiplex is characterized by multiple isolated neural injuries. Typically, these injuries result from ischemia, traumatic injury, compression, or connective tissue disease. Peripheral nervous system involvement is rarely found in antiphospholipid antibody syndrome (APS), and the association with asymmetric distal axonal polineuropathy is even rarer; the latter is more frequently found in systemic lupus erythematosus and in certain types of vasculitis as polyarteritis nodosa or vasculitis associated with anti-neutrophil cytoplasmic autoantibodies (ANCA)s.¹ ³ In this article, we report the case of a patient with mononeuritis multiplex associated with antiphospholipid antibodies. Our objective is to highlight this clinical manifestation associated with the presence of these antibodies, which is actually not considered as part of the classification criteria for APS or even the “extra criteria” manifestations, as well as the serology found and the treatment provided.

CASE REPORT

A 43-year-old male patient with no significant medical history applied to the clinic for evaluation of a six-week history of paresthesia symptoms in the first, third and fourth fingers of his left hand, with involvement of dorsal region of his right arm, with no apparent trigger. He previously received treatment with vitamin complexes and pregabalin without improvement. A written informed consent was obtained from the patient.

Physical exam was relevant for diminished muscle strength in flexor muscles of the right arm, absent tendon reflexes at right biceps and brachioradialis as well as sensory loss in both hands. Distal pulses were present with normal capillary refill time. There was no livedo reticularis or Raynaud’s phenomenon and the rest of physical exam was normal.

Initial general laboratory tests were normal. Thyroid function tests, viral hepatitis serology...
and human immunodeficiency virus serology were negative. A thoracoabdominal angiotomography was performed and resulted negative for vascular anomalies. Magnetic resonance imaging of the spine and brain was normal. Nerve conduction velocities were compatible with mononeuritis multiplex with left median nerve injury and right musculocutaneous nerve injury.

Cerebrospinal fluid analysis was normal and antiganglioside antibodies were within normal limits. Antinuclear antibodies and specific ANCAs were negative, and complement levels were within normal limits. Coagulation tests showed a prolonged activated partial thromboplastin time (PTT). Lupus anticoagulant (LA) was positive, with PTT LA screen positive and a positive hexagonal phase confirmation. Anti-phosphatidylserine antibodies were positive for immunoglobulin (Ig) G and IgM; anti-beta 2-glycoprotein I (anti-B2GPI) and anticardiolipin antibodies were within normal limits. Table 1 shows the summary of the tests performed.

The initial treatment was performed with high-dose steroids, which was subsequently tapered to suspend. We decided to add mycophenolate mofetil (MMF) as well as anticoagulation therapy with low molecular weight heparin, and subsequently with warfarin; patient has also received physical therapy with an excellent response. He was actually treated with oral anticoagulant and MMF, and is progressing favorably.

**DISCUSSION**

Antiphospholipid antibody syndrome is a prothrombotic disease mediated by immunologic phenomena that may affect venous or arterial circulation of any organ or tissue. Neurological manifestations have been classified as thrombotic (e.g. ischemic stroke, transient ischemic attack) and non-thrombotic (e.g. cognitive dysfunction, migraine, myelitis, seizure, chorea, leukoencephalopathy, Guillain-Barré syndrome, multiple sclerosis like syndrome).4-5 Besides ischemic stroke, myelitis and some of the non-thrombotic features, other neurologic manifestations are rare, mainly thus related to the peripheral nervous system; nevertheless, they may involve a greater morbidity if diagnosis and treatment are not performed in a timely manner. Mononeuritis multiplex development has been rarely associated with antiphospholipid antibodies; as far as we know, there are only three cases reported. This has not been clearly associated with diagnosis of APS, but with positive serology. Pathophysiology of this manifestation may be caused by anticoagulation state with low molecular weight heparin, and subsequently with warfarin; patient has also received physical therapy with an excellent response. He was actually treated with oral anticoagulant and MMF, and is progressing favorably.

**Table 1. Laboratory and other tests**

<table>
<thead>
<tr>
<th>Test Category</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood count</td>
<td>Hemoglobin 17 g/dL, Hematocrit 51%, White Blood Cells 4400, Neutrophils 53%, Lymphocytes 30%, Monocytes 13%, Band Cells 1%, Platelets 265,000.</td>
</tr>
<tr>
<td>Blood chemistry</td>
<td>Glucose 83 mg/dL, Creatinine 0.84 mg/dL.</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>pH 7, Density 1.006, White Blood Cells (-), Proteins (-), Erythrocytes (-).</td>
</tr>
<tr>
<td>Inflammatory markers</td>
<td>ESR 3 mm/h, C-reactive protein 0.020 mg/dL.</td>
</tr>
<tr>
<td>Immunologic</td>
<td>Rheumatoid factor 11 IU/mL (negative), ANA and specific ANCA-negative, complement levels within normal limits.</td>
</tr>
<tr>
<td>Nerve conduction velocity</td>
<td>Compatible with mononeuritis multiplex with left median nerve injury and right musculocutaneous nerve injury.</td>
</tr>
<tr>
<td>Tests compatible with antiphospholipid antibody syndrome</td>
<td>PT-14.6” (14”), PTT-46.5” (28.3”), INR-1.044.</td>
</tr>
</tbody>
</table>
Mononeuritis Multiplex Associated With Antiphospholipid Antibodies

Diagnosis predicts the need of immunosuppressive therapy in patients with vasculitis without poor-prognosis factors. It is relevant that mononeuritis multiplex is not recognized as an extra criteria manifestation of APS, but this could represent a no traditional clinical feature.

Apart from conventional biological markers for APS (LA, anticardiolipin antibodies and anti-B2GPI of either IgG or IgM), numerous other markers of APS have been studied. These antibodies are known as non-conventional and include the anti phosphatidyl-ethanolamine, phosphatidylserine/prothrombin, anti-vimentin, anti-annexin, and antibodies directed against domain I of the B2GPI molecule. Particularly, anti-phosphatidylserine antibodies have been related as a strong risk factor for arterial and venous thrombosis and have a very strong correlation with LA positivity as it occurred in this case.

Regarding the treatment, corticosteroids and other immunosuppressant therapies have been reported in some studies to decrease titers of LA and anticardiolipin antibodies. Even though immunosuppressive treatment is not indicated in the management of APS except in the presence of catastrophic APS, there is no consensus or formal recommendation in the treatment of these type of affections; thus the rationale for administering immunosuppressive therapy used in this case was solely based on expert opinion.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES


