Lupoid Sclerosis

What Is the Role of Antiphospholipid Antibodies?

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Abstract: A multiple sclerosis-like syndrome, also called lupoid sclerosis for having some lupus characteristics, has been described in a few reports. Recently, antiphospholipid antibodies have been demonstrated in patients with this syndrome, suggesting that they can participate in the etiopathogenic process, which can have therapeutic implications.

We report the case of a patient previously diagnosed with multiple sclerosis who later presented with ANA positivity and antiphospholipid antibodies, livedo reticularis, and deep venous thrombosis, leading her to be characterized as having lupoid sclerosis. The patient was anticoagulated. Antiphospholipid antibodies may be involved in the pathogenesis of lupoid sclerosis.

Key Words: multiple sclerosis, lupus, lupoid sclerosis, antiphospholipid syndrome

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Multiple sclerosis (MS) is recognized as a chronic, autoimmune inflammatory, and demyelinizing disease of the central nervous system (CNS). It attacks young adults and may occur from a benign to an incapacitating condition, being the second most frequent cause of neurologic incapacity, after trauma, in this age group.

The syndrome of antiphospholipid antibody (APS) is a prothrombotic disease that can follow a course with arterial and/or venous thrombosis, repetitive abortions, livedo reticularis, thrombocytopenia, hemolytic anemia, and neurologic involvement.

Vascular cerebral disease, chorea, epilepsy, migraine, cognitive alterations, transverse myelopathy, Devic syndrome, and a multiple sclerosis-like syndrome (also called lupoid sclerosis) are some of the neurologic manifestations associated with APS. To recognize the presence of the antiphospholipid antibodies in these neurologic complications can be important because of the treatment possibility that this raises.[1,2]

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CASE REPORT

A 28-year-old white woman presented in the year of 2001 immediately after delivery with sudden loss of vision in her left eye. There was partial and spontaneous recovery of the visual acuity. Six months later, she presented a right side hemiparesis associated with hypoesthesia, also on the right side.

The suspected diagnostic of multiple sclerosis was made, demyelinization plaques close to the callous body having been observed on magnetic nuclear resonance (MNR). The visual evoked potential test demonstrated optical neuritis bilaterally. The somatosensory evoked potential demonstrated sensory dysfunctions.

The evaluation of the cerebrospinal fluid was normal. With such findings, MS was diagnosed and the patient began the use of glatiramer acetate, evolving characteristically with periods of remissions and recurrence. In March of 2003, there was clinical worsening with intensification of fatigue and motor deficit on the right side.

A new MNR was performed, which demonstrated demyelinization areas in the deep white substance of both cerebral hemispheres, and cerebrospinal fluid showed oligoclonal bands. The patient was given pulses of methylprednisolone 1 g/d, for 5 days and treatment with interferon-β-1A was started. The presence of intense livedo reticularis in her legs and Raynaud phenomenon were noted.

There was an antecedent of a spontaneous fetal loss in the second quarter of gestation. These observations motivated a rheumatologic evaluation with ANA performed by indirect immunofluorescence (HEp-2), which showed a stippled fine positive pattern at 1/160. There was increased widened TTPA (1.59); positive lupus anticoagulant and positive IgM and IgG anticardiolipin antibodies in high titers. We initiated the use of oral anticoagulant and continued the interferon.

A anti-Ro, anti-La, anti-Sm, anti-RNP, and anti-DNA were negative. Despite beginning the anticoagulant in June 2004, the patient presented in September and in December 2004 with a progressive quadriparetsis.

In May 2005, while using warfarin 5 mg a day and with INR 2.15, a thrombosis was diagnosed in the left posterior

tibial vein. At this time, we opted for the use of rituximab, preceded by the use of a glucocorticoid and antihistamine.

At the end of the first hour of infusion (infusion of 50 mg/h), the patient presented fever, chills, tongue edema, dyspnea and hypertension, and the infusion was suspended. At this time, she has a persistent spastic tetraparesis with an associated neurogenic bladder.

DISCUSSION

APS was described in 1983 as a prothrombotic disease, with neurologic involvement among its clinical manifestations.[3,4] The mechanisms through which the neurologic damage occurs are not completely known. It is postulated that thrombotic and immunologic factors by cross-reaction of the antiphospholipid antibodies with cerebral structures may be involved.[5]

A multiple sclerosis-like syndrome, also called lupoid sclerosis, has been described as a rare neurologic manifestation in lupus patients and in people with primary APS. The presence of antiphospholipid antibodies in these patients suggests that they can participate in the etiopathogenic process.

Patients with APS who cross with MS-like syndrome usually present livedo reticularis, transverse myelitis associated or not to the optical neuritis, being clinically indistinguishable from the MS. These patients also do not differ by cerebrospinal fluid and MNR[6,7] aspect.

In 2005, Ferreira et al reported the difficulty in the differential diagnosis among the entities: multiple sclerosis, neuropsychiatric manifestations of lupus and APS. The authors comment on the controversy in relation to prevalence and the meaning of the antiphospholipid antibodies in the patients with MS. They report the importance of trying to differentiate these pathologies in view of the fact that they are diseases of different prognoses and treatment.[8]

In 2000, Cuadrado et al retrospectively studied 27 patients with probable or defined MS who, however, presented an atypical evolution.[9] These patients were directed to rheumatologic evaluation due to suggestive signals and symptoms of collagen disease, history of previous abortions, or by ANA positivity. In this population, all patients had positive antiphospholipid antibodies. Differences of the clinical point of view or the aspect of MNR were not found when compared with 25 patients with MS and negative antiphospholipid antibodies.[8] Additionally, in 1999, Ijdo et al studied 322 patients who had APS clinical suspicion. From these, 26 had MS or MS-like diagnosis; 23 had positivity for 1 or more antiphospholipid antibodies.

With the current patient, once the lupoid sclerosis diagnosis was made, anticoagulation with warfarin was introduced, in addition to interferon, gabapentin, baclofenac, fluoxetine, clomipramin, and clonazepan; but this produced no improvement in her condition. Despite the warfarin use and with an INR 2.15, the patient presented a deep venous thrombosis in her left leg.

We then opted to use rituximab, a chimerical monoclonal antibody against CD-20; however the collateral effects related to the infusion demanded its interruption. Such an option was based on a report of its use in a case of refractory autoimmune hemolytic anemia, with improvement of the hematological patterns and decrease of the titers of antiphospholipid antibodies.[10] Additionally, this medication has also been suggested as a therapeutic option in the cases of multiple sclerosis that do not have a satisfactory course with the immunomodulators commonly used.[11,12]

Recently, Monson et al[13] published the effect of the depletion of B lymphocytes in the blood of 4 patients with MS and in the cerebrospinal fluid of 2 of these patients. There was significant depletion of CD19 cells in all the patients' peripheral blood.

Return of CD19 cells to the pretreatment levels was observed within 14 to 18 weeks after the use of the medication. CD19 B lymphocyte counts in the cerebrospinal fluid before and after the use of the rituximab was obtained in only 2 patients: significant depletion of these cells was not observed on them.

We emphasize the importance of the description of a lupoid sclerosis case associated to APS, particularly for being a disease that attacks young patients and is frequently incapacitating. It is suggested that the presence of antiphospholipid antibodies may participate in the development of small vascular occlusions and consequent damage to the nervous tissue.

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