ORIGINAL ARTICLE

DEMYELINATING DISEASE IN A PATIENT WITH PRIMARY SJÖGREN'S SYNDROME: A CASE REPORT

DOENÇA DESMIELINIZANTE EM PACIENTE COM SÍNDROME DE SJÖGREN PRIMÁRIA: RELATO DE CASO

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ABSTRACT

This report describes the case of a patient with primary Sjögren's Syndrome (SS) associated with demyelinating neurological involvement. Data were obtained using medical records, patient interviews, photographic documentation of imaging exams, and a brief literature review. Neurological manifestations of SS are rare and present a wide clinical spectrum, including demyelinating features that resemble multiple sclerosis and neuromyelitis optica. Treatment of the neurological manifestations is often based on an extrapolation of other autoimmune diseases, including rheumatoid arthritis and systemic lupus erythematosus. Management may require oral or intravenous immunosuppressive therapy, depending on symptom severity.

Keywords: Neurological Manifestations; Neuromyelitis Optica; Sjogren Syndrome

RESUMO

Relatamos o caso de uma paciente portadora de Síndrome de Sjögren Primária com manifestações neurológicas de característica desmielinizante. As informações foram obtidas por meio de revisão do prontuário, entrevista com a paciente, registro fotográfico dos exames de imagem e, por fim, breve revisão da literatura. As manifestações neurológicas da Síndrome de Sjögren são raras e apresentam um amplo espectro clínico, incluindo manifestações desmielinizantes que simulam a esclerose múltipla, além de neuromielite óptica. O tratamento dos sintomas neurológicos se baseia numa extrapolação de outras doenças autoimunes, como a artrite reumatoide e lúpus eritematoso sistêmico, e preconiza o uso de imunossupressores orais e venosos, a depender da gravidade dos sintomas.

Palavras-chave: Manifestações neurológicas; Neuromielite óptica; Síndrome de Sjögren

INTRODUCTION

Sjögren's syndrome (SS) is an autoimmune epithelitis, defined by lymphocytic infiltration of exocrine glands and the presence of specific antibodies. This condition mainly affects women aged between 40 and 55 years. Besides the ocular and oral dryness, typical symptoms of SS, patients may present extraglandular manifestations involving the kidneys, lungs, hematologic system, skin, and nervous system.[1] Neurological involvement may include sensory and motor impairment, along with central nervous system (CNS) manifestations, such as myelitis, cerebral vasculitis, seizures, organic brain syndrome, and neuromyelitis optica spectrum disorders (NMOSD).[2,3]

The etiopathogenesis of SS involves an autoimmune reaction potentially initiated by environmental factors (e.g., viral infections) in genetically susceptible patients. This reaction may cause dysregulation and hyperactivity of B lymphocytes, leading to lymphocytic infiltration of the exocrine glands, and possible degeneration, necrosis, and atrophy of the acinar glands. Clinically, this glandular damage impairs lacrimal and salivary function, which contributes to xerophthalmia and xerostomia, present in about 95% of patients.[4]

Diagnostic criteria for SS have not yet been established. However, the diagnosis should be considered in patients with sicca symptoms combined with at least one of the following conditions: (a) positive serologic testing for anti-SS-A or anti-SS-B antibodies; (b) a positive salivary gland biopsy demonstrating lymphocytic inflam-

matory infiltration in exocrine glands; or (c) systemic extraglandular manifestations.[5]

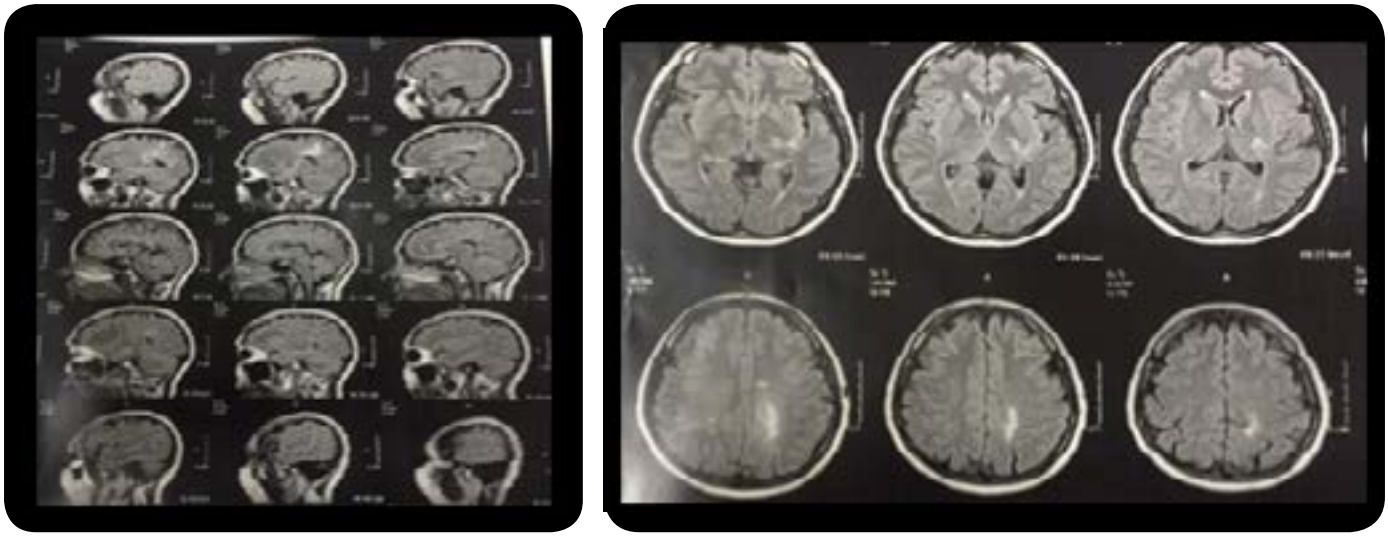
The following recommendations of the European League Against Rheumatism (EULAR) should be considered when managing patients with systemic disease: (a) adapt the management of the systemic disease according to organ-specific severity using the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) (EULAR Grade C, Level 4); (b) use the minimum effective dose and shortest duration needed of glucocorticoids to control active systemic disease (EULAR Grade C, Level 4); (c) consider the use of synthetic immunosuppressive agents as corticosteroid-sparing options (EULAR Grade C, Level 4); (d) consider B-cell-targeted therapies for patients with severe refractory systemic disease, with no evidence supporting one treatment over the other (EULAR Grade B, Level 1b); (e) after sequential (or combined) use of glucocorticoids, immunosuppressants, and biologic medications, an organ-specific systemic intervention may be considered (EULAR Grade D, Level 5).[7]

This report described a clinical case involving primary SS presenting with demyelinating neurological manifestations and provides a review of concepts related to this topic.

CASE REPORT

E.B.S., a 49-year-old female, initially reported headache, paresthesia, and eventual limb weakness. Magnetic resonance imaging (MRI) revealed hyperintensities in the corticospinal tract at the level of the cerebral peduncles, periventricular and subcortical white matter, and the corpus callosum. A cavitated lesion was also observed, extending from the subependymal region to the subcortical area of the inferior parietal lobe, suggesting multiple sclerosis. Then, the patient developed blurred vision and ocular hyperemia, predominantly in the right eye. A diagnosis of optic neuritis was established and treated with intravenous methylprednisolone pulse therapy. Despite treatment, the condition progressed to visual loss in the right eye and right-sided hemiparesis, requiring plasmapheresis and cyclophosphamide therapy.

Due to the persistent motor and visual impairments, rituximab therapy was initiated, followed by maintenance therapy with azathioprine. The motor function improved; however, visual loss in the affected eye persisted. Follow-up MRI revealed hyperintense lesions in the white matter of both cerebral hemispheres and signal alterations in the spinal cord at the C6 and C7 levels (Figures 1, 2, and 3). Oligoclonal band testing in cerebrospinal fluid (CSF) and serum anti-aquaporin-4 antibody (AQP4-IgG) yielded negative results. Given the presence of ocular and oral dryness symptoms, an investigation for SS was conducted. The results included positive anti-Ro/SSA antibodies, an antinuclear antibody (ANA) titer of 1:320 with a fine speckled nuclear pattern (FSNP), and a salivary gland biopsy consistent with chronic lymphocytic sialoadenitis, confirming the diagnosis.



Figures 1 and 2. Brain MRI in fluid-attenuated inversion recovery (FLAIR) sequence showing hyperintense signal in the corticospinal tract at the level of the cerebral peduncles, periventricular white matter, and corpus callosum. A cavitated lesion extends from the subependymal region to the subcortical area of the inferior parietal lobe.

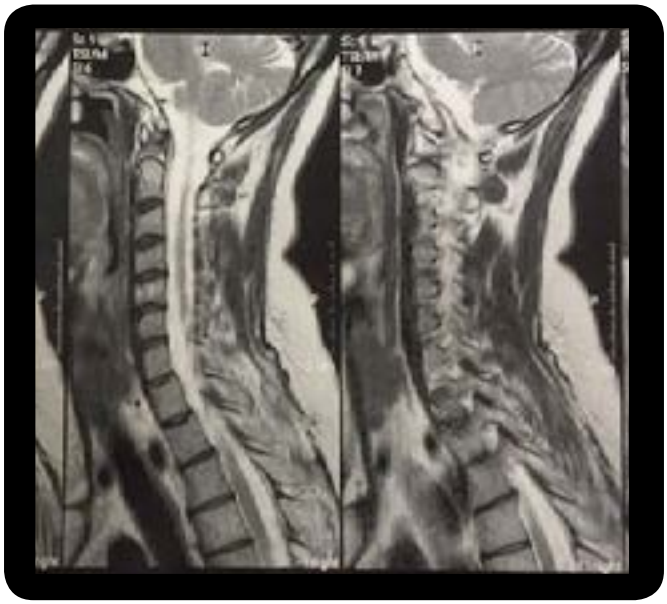


Figure 3. T2-weighted brain MRI: Signal alteration in the spinal cord at the C6 and C7 levels.

Ethical aspects of this study followed the recommendations of resolution No. 510, dated April 7, 2016, of the Brazilian national health council, which establishes specific ethical guidelines for the human and social sciences. The study was approved by the research ethics committee of the Faculdade de Medicina de Olinda (no. 46365721.9.0000.8033).

DISCUSSION

This report described the case of a 49-year-old female who presented an acute neuro-ophthalmologic syndrome. Neuroimaging findings suggested a demyelinating disease within the multiple sclerosis spectrum. During diagnostic evaluation, the presence of xerostomia and xerophthalmia raised the suspicion of SS. The diagnosis was confirmed by positive anti-Ro/SSA antibodies, an ANA titer of 1:320 FSNP, and a salivary gland biopsy revealing chronic lymphocytic sialadenitis.

Neurological manifestations occur in about 20% of patients with primary SS, with CNS involvement occurring in about 3.6%.2 In 80% of patients with neurological symptoms, CNS involvement may precede the primary SS diagnosis by up to two years. These clinical presentations may range from asymptomatic MRI findings to symptomatic lesions, including meningitis, seizures, cerebral vasculitis, or myelitis.[8]

NMOSD is a group of CNS disorders characterized by severe immune-mediated inflammation, demyelination, and axonal damage. These disorders may occur as primary conditions or associated with autoimmune rheumatic diseases (e.g., SS and systemic lupus erythematosus), with or without the presence of AQP4-IgG. These antibodies target aquaporin channels, disrupting the regulation of intra and extracellular water balance. This process strongly affects the optic nerves and the spinal cord.5,9 Besides the optic nerve and spinal cord, the central medulla, diencephalon, hypothalamus (areas with high aquaporin-4 expression), and subcortical white matter may also be affected in up to 85% of cases throughout the disease. Pathogenic mechanisms include immune complex-mediated vasculitis and antiphospholipid antibodies associated with stroke, migraine, seizures, and transverse myelitis.5 Previous studies support the hypothesis that anti-Ro/SSA antibodies bind to endothelial cells and contribute to the inflammatory process.

Wingerchuk *et al.* (2015) established the International Panel for NMO Diagnosis (IPND) to revise the diagnostic criteria and support clinical decision-making. The new nomenclature distinguishes NMOSD based on the presence (or absence) of AQP4-IgG while also considering the exclusion of alternative diagnoses. When AQP4-IgG is positive, diagnostic criteria include clinical or MRI findings involving the optic nerve, spinal cord, area postrema, brainstem, diencephalon, or cerebrum. When AQP4-IgG is negative or testing is unavailable, diagnosis requires strict clinical criteria combined with characteristic neuroimaging findings.[3]

The combination of clinical presentation, CSF analysis with oligoclonal band testing, MRI findings, AQP4-IgG testing, and therapeutic response are key factors in distinguishing NMOSD from multiple sclerosis, its primary differential diagnosis.[3,7] Additional differential diagnoses include inflammatory, infectious, genetic, metabolic, and neoplastic disorders.[3,4]

The epidemiology of neurological manifestations of SS has not been fully elucidated due to selection biases in patient inclusion criteria. However, CNS manifestations are rare and may precede sicca symptoms. Among these

manifestations, NMOSD may occur as a manifestation of SS or as a coexisting condition. The main differential diagnosis includes multiple sclerosis, CSF, MRI, and antibody findings. Treatment encompasses corticosteroid therapy, plasmapheresis, immunoglobulin, cyclophosphamide, rituximab, azathioprine, and mycophenolate mofetil. In patients with demyelinating diseases who exhibit an inadequate therapeutic response, the diagnostic investigation must be expanded, as they may represent an initial manifestation of an autoimmune rheumatic disease, with an emphasis on SS.[2,3,8]

CONCLUSION

Although neurological manifestations are rare, their presence may indicate an underlying autoimmune condition, including SS. In the presented case, atypical CNS involvement, particularly NMOSD preceding sicca symptoms, raised the suspicion of an autoimmune disease. The detection of specific autoantibodies and salivary gland biopsy subsequently confirmed the diagnosis of primary SS.

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