CASE REPORT

Unilateral Optic Neuritis in Primary Sjögren Syndrome Onset – a Case Report

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Abstract

Introduction. *Primary Sjogren's syndrome (pSSj) is a chronic, autoimmune disease that predominantly affects the lacrimal and salivary glands but is also responsible for extra-glandular disturbances. Although rare, optic neuritis (ON) may appear as initial manifestation and may be responsible for visual loss if diagnosis is delayed. The aim of the paper is to report a case of pSSj-induced ON as disease debut.*

Case presentation. *A 35-year-old patient with xerophthalmia presented an episode of sudden decrease in visual acuity of the left eye. Examination of the fundus revealed papillary edema, tortuous retinal vessels, non-reflex macula improved after methylprednisolone pulse-therapy. Immunological testing revealed high titer antinuclear antibodies (ANA) and intensely positive anti-Ro antibodies. Schirmer test was positive and parotid gland ultrasound was compatible with pSSj. Central nervous system damage is heterogeneous as clinical phenotypes in patients with pSSj. Prompt distinction between non-specific ON and pSSj-related eye involvement is mandatory for successful therapeutic strategy.*

Conclusions. *pSSj is a rare cause of ON that requires a detailed medical history, autoantibody determination, and minor salivary gland biopsy for confirmation. The ON response to methylprednisolone is promising and may improve patients' prognosis.*

Keywords: optic neuritis, xeropthalmia, primary Sjögren's syndrome, autoimmunity, autoantibodies.

Introduction

Primary Sjogren's syndrome (pSSj) is a chronic, progressive, autoimmune disease that predominantly affects the exocrine glands, namely the lacrimal and salivary glands, but almost half of patients can also experience extra-glandular manifestations [1].

The mechanism responsible for the glandular damage is the inflammatory process induced by lymphocytic infiltration and B cell hyperactivity [2].

SSj has a prevalence ranging from 1 to 3% in the general population. It is classified as primary (pSSj), if the sole condition or secondary (sSSj) if accompanied by other chronic conditions like rheumatoid arthritis, systemic lupus erythematosus or autoimmune thyroiditis [3]. However, both conditions mainly affect female patients aged over 50 years old, with an estimated gender ratio of 9:1 [4].

Systemic manifestations can target the skin, lungs or kidneys but also the peripheral nervous system, leading to the widely

described peripheral neuropathy, especially sensory polyneuropathy, mononeuropathies or cranial nerve symptoms [5].

Since first described in 1980, neurological manifestations in pSSj have been intensely studied because of the disease's distinct feature to cause painful small-fiber neuropathy or damage of the dorsal root ganglia, being top ranked among other autoimmune diseases in inducing a pure sensory neuropathy [6]. The prevalence of peripheral nervous system (PNS) involvement in pSSj varies widely from 2% to 50% and the percentage heterogeneity is due to various clinical display of nervous symptoms and study designs [7].

Despite available knowledge on PNS manifestations in pSSj, information on central nervous system (CNS) anomalies is scarce and still waiting to be clarified. Its frequency is lower, affecting around 2 to 25% of SSj patients [7]. The most frequent CNS disorders are transverse myelitis, cognitive symptoms, aseptic meningitis, headache or optic neuritis (ON). ON may appear as a manifestation of onset but is rare and may be responsible for blindness if the diagnosis is delayed [8].

Case presentation

We report the case of a female patient, 35-year-old, with a 5-year history of xerophthalmia that was not further investigated at the time. She denied smoking, chronic drug intake at the time or Raynaud-like changes. She reported intermittent headaches for more than seven years, but her medical history had no history of autoimmune disease.

Patient experienced an episode of 24-hour sudden decrease in visual acuity of the left eye. Emergency examination revealed that the visual acuity (VA) in the left eye was 0.2, and 1.0 in the right eye with normal ocular pressure. Exploration of the fundus revealed papillary edema, tortuous retinal vessels and a non-reflex macula. Optical coherence tomography was not initially available for examination.

No other systemic symptoms like fever, adenopathies or arthritis were obvious at the time. Three-day pulse therapy with one gram methylprednisolone was administered, with slight improvement of the papillary edema and a VA of 0.9 on discharge.

Ophthalmologic examination was followed by cerebral magnetic resonance imaging (MRI) that revealed no significant changes of the brain, no tumoral masses of the orbits or sinus area and symmetrical optical nerves. Arterial Doppler ultrasound was normal.

Further blood tests showed microcytic hypochromic anemia (Hb 10g/dl), mild inflammatory syndrome (erythrocyte sedimentation rate ESR 39mm/h, laboratory range under 20 and C-reactive protein 6.5 compared to a normal of 5 mg/L). Patient presented no lymphopenia, complement levels (C3, C4) were within range and rheumatoid factor was slightly elevated (20 versus laboratory 14 UI/mL).

Infectious diseases were brought into discussion, but negative results came back negative for Toxocara canis, Brucella, Bartonella henselae, Chlamydia trachomatis, Toxoplasma gondii. Syphilis, hepatitis B and C, HIV testing were also negative.

Despite a positive result of the Quantiferon Gold test, the chest X-ray had no abnormalities and the pneumologist ruled out tuberculosis as a potential cause for ON.

Despite being asymptomatic, an electromyography was performed in upper limbs, but no notable changes were observed.

The immunological tests presented high-titer antinuclear antibodies (ANA) titer 1/5120 and intensely positive anti-Ro autoantibodies with a speckled aspect on indirect immunofluorescent staining. Screening for antiphospholipid syndrome was negative, as well as p-anti-neutrophil cytoplasmic antibodies (ANCA), c-ANCA. Anti-aquaporin 4 antibodies were not

available for determination and cryoglobulins were absent. Antibodies suggestive of multiple sclerosis could not be determined.

Raising the suspicion of a pSSj despite the unusual onset with ocular involvement, a Schirmer's test was performed and confirmed a positive result, with a value of 6mm in the left eye and 4mm in the right eye. Ultrasound of the parotid glands identified multiple cystic lesions, some confluent, with a chronic appearance.

Minor salivary gland biopsy was not performed because of patient's disagreement with the procedure.

The presence of xeropthalmia, positive Schirmer's test, high-titer anti-Ro/SSA antibodies in the context of unilateral optic neuritis are compatible with the diagnosis of pSSj, according to the American-European Consensus Criteria for SSj [9].

Treatment with hydroxychloroquine and topical agents was initiated with favorable outcome and no added ocular events in the following two-year follow up interval.

Discussion

Primary SSj is characterized by dryness of eyes and mouth due to lymphocytic infiltration of the exocrine glands but is can also affect the skin or other mucosal surfaces. Patients can also suffer from extra-glandular manifestations that can delay the diagnosis or lead to a poorer disease prognosis. Central nervous system damage is rarer in patients with pSSj and has not benefited from extensive studies until recently when increasing prevalence has been noted. In up to half of SSj patients, CNS involvement is associated with PNS manifestations like neuropathies [10].

Classification of CNS anomalies divides focal forms including acute transverse myelopathy, multiple-sclerosis-like lesions or ON and diffuse forms like cognitive impairment, seizures, encephalopathy, or aseptic meningitis. Usually, this patient population has positive anti-SSA antibodies, and some might associate vasculitis or cryoglobulinemia [11].

Optic neuropathy is thought to be caused by intricate of vasculitis and demyelination of optic nerve, leading to visual loss. ON can be the initial manifestation of pSSj in about 25% of cases and identifying the diagnosis of SSj is challenging since patients can be otherwise asymptomatic [12].

A study published in 2013 aimed to investigate particularities in the clinical and therapeutic features of ON induced by pSSj. Authors retrospectively identified 8 patients that presented with acute visual disturbances, being initially diagnosed with non-specific or idiopathic ON. In the absence of sicca symptoms, detailed immunological testing showed positive ANA, anti-SSA or RF and further parotid ultrasound and labial biopsy confirmed the diagnosis of pSSj [13].

The presented case report was firstly diagnosed with ON despite complaining for mild xeropthalmia for more than five years. Patient's immunological changes stand in line with published literature data, but minor salivary gland biopsy would have been of help to acknowledge histopathological changes.

Placing the correct diagnosis while excluding potential mimickers is essential for further therapeutic strategies, since SSj-related ON may benefit from immunosuppression and high-dose corticosteroids, namely methylprednisolone [14]. Results from a retrospective study published in 2012 suggested that rituximab, an anti-CD20 monoclonal antibody, is not effective on CNS manifestations caused by pSSj [15]. However, there is yet no standard-of-care in CNS involvement of pSSj patients.

Conclusions

Primary SSj is a rare cause of ON that requires a detailed medical history, autoantibody determination and minor salivary gland biopsy for confirmation. ON can precede the diagnosis of pSSj, thus clinicians need to be aware to investigate the

presence of autoimmune diseases in the presence of eye involvement. Despite the lack of therapy standardization, ON response to methylprednisolone pulse therapy is promising and may improve the short-term prognosis of these patients. Recurrences should be carefully investigated, and immunosuppression should be discussed if necessary. A multidisciplinary approach with a team of rheumatologists and ophthalmologists should care for pSSj-related ON for a better patient management.

Author Contributions:

C.C. conceived the original draft preparation. C.C., M.D., and R.I. were responsible for conception and design of the review. C.C., M.D., and R.I. were responsible for the data acquisition. M.D., and R.I. were responsible for the collection and assembly of the articles/published data, and their inclusion and interpretation in this review. C.C., M.D., and R.I. contributed equally to the present work. All authors contributed to the critical revision of the manuscript for valuable intellectual content. All authors have read and agreed with the final version of the manuscript.

Compliance with Ethics Requirements:

The authors declare no conflict of interest regarding this article.

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References

[1] Tincani A, Andreoli L, Cavazzana I, Doria A et al. Novel aspects of Sjögren's syndrome in 2012. *BMC Med.* 2013;11(1):93.

[2] García-Carrasco M, Fuentes-Alexandro S, Escárcega RO, Salgado G, Riebeling C, Cervera. R. Pathophysiology of Sjögren's syndrome. *Arch. Med. Res.* 2006;37(8):921–932.

[3] Jonsson R, Vogelsang P, Volchenkov R, Espinosa A, Wahren-Herlenius M, Appel S. The complexity of Sjögren's syndrome: Novel aspects on pathogenesis. *Immunol. Lett.* 2011;141(1):1–9.

[4] Patel R, Shahane A. The epidemiology of Sjögren's syndrome. *Clin. Epidemiol.* 2014;6(1):247.

[5] Fox RI, Fox CM. Extraglandular Manifestations of Sjögren's Syndrome (SS): Dermatologic, Arthritic, Endocrine, Pulmonary, Cardiovascular, Gastroenterology, Renal, Urology, and Gynecologic Manifestations. S*jögren's Syndr.* 2011:285-316.

[6] McCoy SS, Baer AN. Neurological Complications of Sjögren's Syndrome: Diagnosis and Management. *Curr. Treat. options Rheumatol.* 2017;3(4):275–288.

[7] Morreale M, Marchione P, Giacomini P et al. Neurological Involvement in Primary Sjögren Syndrome: A Focus on Central Nervous System. *PLoS One* 2014;9(1):84605.

[8] Fauchais AL, Magy L, Vidal E. Central and peripheral neurological complications of primary Sjögren's syndrome. *Presse Med* 2012;41(9):e485–e493.

[9] Shiboski SC, Shiboski CH, Criswell LA, Baer AN, et al. American College of Rheumatology Classification Criteria for Sjögren's Syndrome: A Data-Driven, Expert Consensus Approach in the SICCA Cohort. *Arthritis Care Res. (Hoboken)* 2012;64(4):475.

[10] Cafaro G, Bursi R, Chatzis LG, et al. One year in review 2021: Sjögren's syndrome. *Clin. Exp. Rheumatol*. 2021;39(6):S3–S13.

[11] Soliotis FC, Mavragani CP, Moutsopoulos HM. Central nervous system involvement in Sjögren's syndrome. *Ann. Rheum. Dis.* 2004;63(6):616–620.

[12] Sun JY, Liu Z, Zhao P, Liu T. Optic neuritis as an initial presentation of primary Sjögren syndrome: A case report and literature review. *Medicine (Baltimore)* 2016;95(44):E5194.

[13] Tang WQ, Wei SH. Primary Sjögren's syndrome related optic neuritis. *Int. J. Ophthalmol* 2013;6(6):888.

[14] Ozgocmen S, Gur A. Treatment of central nervous system involvement associated with primary Sjogrens syndrome. *Curr. Pharm. Des.* 2012;14(13):1270–1273.

[15] Mekinian A, Ravaud P, Hatron PY, Larroche C et al. Efficacy of rituximab in primary Sjögren's syndrome with peripheral nervous system involvement: Results from the AIR registry. *Ann. Rheum Dis.* 2012;71(1):84–87.