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A Rare Case of Neuromyelitis Optica Spectrum Disorder Secondary to Primary Sjögren's Syndrome in an Older Woman

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Abstract: Primary Sjögren's syndrome is an autoimmune disorder that is characterized by lymphocytic infiltration of salivary and lacrimal glands. The extra-glandular manifestations might be arthritis, myalgia, glomerulonephritis, skin rashes, and neurologic involvement. One of the uncommon neurologic manifestations is neuromyelitis optica spectrum disorder (NMOSD). In the present case, an older woman is reported that was diagnosed with NMOSD secondary to keratoconjunctivitis sicca, which is rare in geriatric practice.

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Introduction

Primary Sjögren's syndrome (PSS) is an autoimmune disorder, most commonly presenting with dry mouth and eyes, that is characterized by lymphocytic infiltration of the exocrine glands. There are also extra-glandular involvements such as arthritis, myalgia, glomerulonephritis due to mixed cryoglobulinemia and amyloidosis, skin rashes, interstitial pneumonitis and gastrointestinal manifestations (Fox, 2011). The prevalence of neurologic manifestations in PSS is estimated to range from 8 to 49% (Margaretten, 2017). Neurological involvements of PSS vary widely and are divided into peripheral and central nervous system manifestations. While peripheral neuropathies can be seen as sensory, sensorimotor, autonomic or cranial neuropathy, central nervous system involvement might be present in different spectrums including focal cerebral lesions, multiple sclerosis-like involvement, aseptic meningitis or encephalitis, ataxia due to cerebellar involvement, cognitive dysfunction and depression (Margaretten, 2017). Neuromyelitis optica spectrum disorder (NMOSD) is frequently seen in the third and fourth decades. NMOSD cases seen after the age of 50 are defined as late onset, while NMOSD cases seen after the age of 70 are defined as very late onset. Very late onset NMOSD are extremely rare (Hu et al., 2022). The frequency of NMOSD in patients with PSS is also very rare. As far as we know, the co-existence of NMOSD and Sjögren's syndrome has been reported in an older patient (Shahmohammadi et al., 2019).

In this case report, an older woman with NMOSD after PSS will be presented.

Case report

A 74-year-old female patient was admitted to our outpatient geriatric clinic with complaints of dry mouth, stinging and burning in the eyes, and numbness in the hands bilaterally. The patient, who had known diagnoses of hypertension and diabetes mellitus, applied to the rheumatology department at another center about four years ago due to dry mouth and dry eyes. Lymphocytic infiltration was detected in the minor salivary gland biopsy. Positive for ANA titer (+++; cytoplasmic pattern) and negative for rheumatoid factor (RF), anti-SSa, anti-SSb were measured simultaneously. She was diagnosed with PSS at four years ago. The patient was followed up without medicine during this period. Then, two years ago, she was admitted to the neurology department due to dizziness and widespread paresthesia throughout the whole body. On neurologic examination glove-sock-shaped sensory deficit, dysdiadochokinesia and cerebellar dysmetria in addition to bilateral paresthesia were detected. No acute pathology was detected on cranial imaging. The spinal magnetic resonance imaging of the patient showed an edematous appearance in the spinal cord at the cervical and thoracic levels, and staining lesions showing long segment involvement in the spinal cord (Figure 1). In the patient

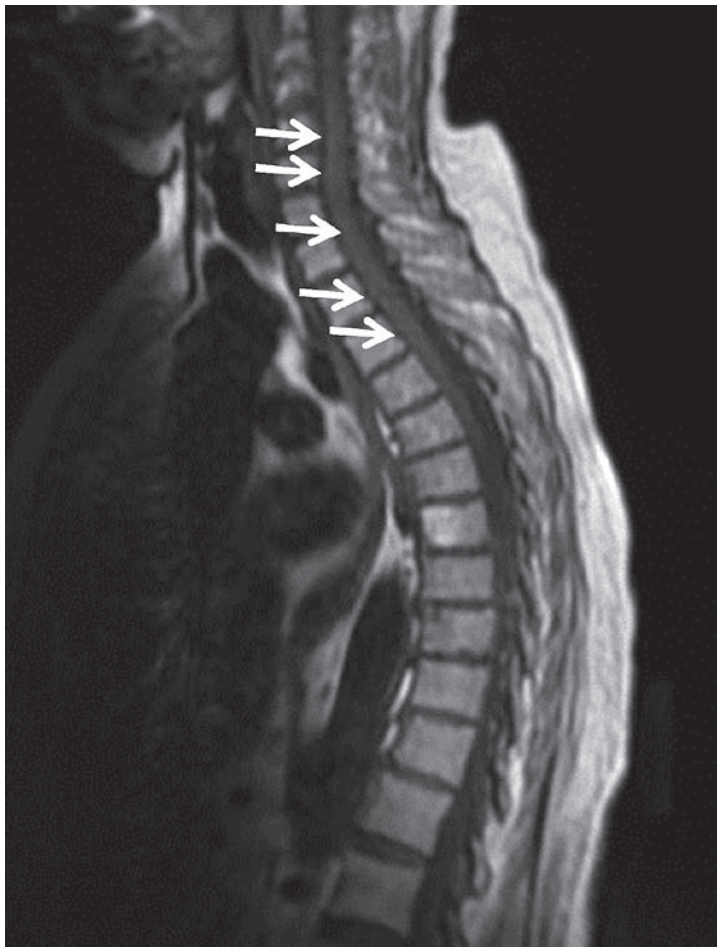

Figure 1 – Cervical and thoracal T2 magnetic resonance image demonstrates edema and longitudinally extending hyperintensity in the cervico-thoracal junction indicating acute myelitis.

who had no signs of optic neuritis, transverse myelitis was primarily considered. Cerebrospinal fluid assessment revealed high protein levels. Serum anti-NMO (neuromyelitis optica) antibody was detected positive. Multiple sclerosis was not considered in the differential diagnosis because the clinical course was not primarily relapsing-remitting, no oligoclonal bands were seen in the cerebrospinal fluid sample, no multiple lesions were found in the spinal MRI (magnetic resonance imaging), and NMO-specific antibody positivity. In addition, since there was no history of infection or immunization before the neurological symptoms, the diagnosis of myelin oligodendrocyte glycoprotein antibody associated disease was excluded. Additionally, since the symptoms develop in a chronic process, acute myelopathies were excluded. She was started on high dose intravenous methylprednisolone (1 gram daily for three consecutive days) for the treatment of acute attacks. When no significant clinical response was observed, intravenous immunoglobulin (1 g/kg daily for five

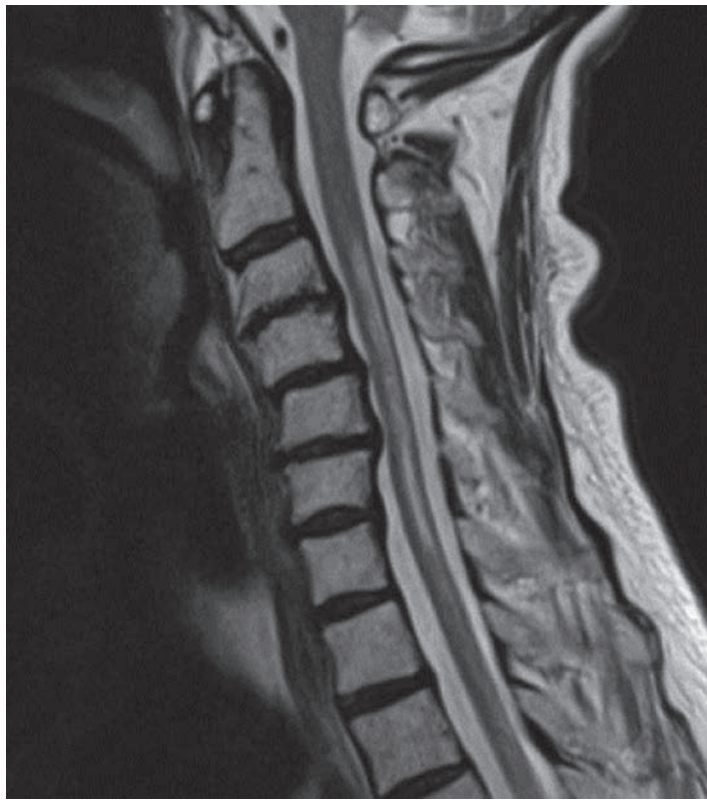

Figure 2 – Cervical and thoracal T2 magnetic resonance image (2 years later) revealed bright longitudinal lesions indicative for sequale of demyelinisation and chronic transverse myelitis.

consecutive days) was applied as second-line treatment. There was no need for plasma exchange for the patient, who received a clinical response after intravenous immunoglobulin treatment, and maintenance treatment was planned as rituximab. During the follow-up, her neurological complaints not sicca symptoms regressed, and no myelitis recurrence was observed and her control MRI only showed some chronic alterations (Figure 2). She has suffered from dry mouth and dry eyes started again for six months ago and were admitted to our geriatric clinic. In comprehensive geriatric assessment, she had forgetfulness, which did not affect her daily life activities, recurrent falls in a year, polypharmacy and widespread body pain. The medications were recorded as lercanidipine 20 mg/day, nebivolol 5 mg/day, olmesartan 20 mg/day, levothyroxine sodium 50 mg/day, sitagliptin 100 mg/day, gliclazide 60 mg/day, gabapentin 600 mg/day, esomeprazole 40 mg/day. In physical examination, there was orthostatic hypotension, minimal paresthesia and no disorientation on neurological examination. Cerebellar examination was normal. Schirmer test was bilaterally less than 5 mm of strip wetting in 5 minutes. Laboratory tests revealed anemia (hemoglobin level: 10.8 g/dl), increased erythrocyte sedimentation rate (66 mm/h), and estimated glomerular filtration rate according

to MDRD (Modification of Diet in Renal Disease) was 23 ml/min/1.73 m^2. Vitamin B12 and 25-hydroxyvitamin D levels were normal. Treatment and recommendations were made for polypharmacy and orthostatic hypotension, and the patient was referred to the rheumatology department with a diagnosis of PSS. Azathioprine treatment was started due to the risk of NMOSD relapse, and pilocarpine treatment was also performed due to severe dry mouth. She is followed up in our geriatric outpatient clinic in terms of geriatric syndromes. This case report, which is very rare in geriatric practice, is made to contribute to the literature.

Discussion

Dry mouth is one of the common symptoms in older adults. In community-dwelling elderly, the reported prevalence ranges from 17 to 40% (Liu et al., 2012). The most common cause of dry mouth in geriatric practice is medication-related. Xerostomia may develop especially due to polypharmacy and antipsychotic, antimuscarinic, antihistamine, sedative or opioid analgesic drugs that have anticholinergic burden (Prado-Mel et al., 2022). In addition, dry mouth is a problem that can affect malnutrition, dysphagia dental problems, oral hygiene disorders and daily living activities in elderly individuals (Barbe, 2018). Other causes of dry mouth in the elderly including a history of radiation to the head and neck area, psychiatric problems, and Parkinson's disease (Barbe, 2018). Dry eye can also be related to anticholinergic medication in elderly individuals, and it frequently develops after surgery or due to age-related vision problems (Prado-Mel et al., 2022). PSS, which is known to present with dry mouth and dry eyes, is generally seen in middle-aged women. Elderly-onset Sjögren's syndrome (Eo-SS) is a rare condition (Fulvio et al., 2023).

The average prevalence of neurological involvement in PSS is 20% (Margaretten, 2017). Neurological presentation in PSS is quite broad. It may be asymptomatic, such as white matter changes may be detected incidentally on cranial imaging. They may also present with clinically evident neurological symptoms and findings. While peripheral neuropathy is the most common, multiple sclerosis-like lesions, encephalitis, cognitive dysfunction, ischemic stroke and psychiatric symptoms can be listed (Margaretten, 2017). In general, the underlying mechanisms are immune-mediated vasculopathy, vasculitis or demyelination (Alexander, 1993). NMOSD is extremely rare in association with Sjögren's syndrome. NMOSD has been differentiated from MS (multiple sclerosis) soon after the discovery of a highly specific serum autoantibody (NMO-IgG) which targets aquaporin-4: the main channel regulating water transport in CNS (central nervous system). The spectrum embraces five subgroups: idiopathic NMOSD (previously known as Devic disease) optic neuritis or longitudinally myelitis associated with systemic autoimmune disease; optic neuritis or longitudinally myelitis associated with brain

lesions; Asian optic-spinal MS and limited forms of NMO (Jarius et al., 2023). The common clinical features of NMOSD are ocular pain with impaired vision, severe symmetrical paraplegia, sensory loss and bladder dysfunction. In the present case, bilateral paresthesia without optic neuritis occurred. NMOSD usually affects women in their third and fourth decades. As in our case, NMOSD cases with an onset age over 70 years are known as very old onset NMOSD and are very rare (Hu et al., 2022). Additionally, the co-existence of NMOSD and PSS is mostly associated with anti-SSa/SSb positivity (Berkowitz and Samuels, 2014); however, there are cases also without anti-SSa/SSb positivity (Akaishi et al., 2021). In our case, SSa/SSb antibodies were observed as negative, which differs from the literature in this respect.

When NMOSD develops in patients diagnosed with PSS, treatment should be started as soon as possible. IV pulse methylprednisolone treatment should be started as the first choice. Plasmapheresis should be considered in cases unresponsive to steroids. Azathioprine, rituximab or mycophenolate mofetil should be planned for maintenance treatment (McCoy and Baer, 2017). Our patient responded to IV pulse steroids and rituximab was started as maintenance treatment. Although her symptoms including dry mouth and dry eyes regressed during the treatment, sicca symptoms started again because she gave up the treatment for an unknown reason. Our patient was referred to the rheumatology department with a maintenance immunosuppressive treatment plan in case of a recurrency of NMOSD. He continued to be followed up in the geriatric outpatient clinic in terms of geriatric syndromes.

Conclusion

A very rare case of NMOSD secondary to PSS has been reported in geriatric practice. Although the anticholinergic burden effect is often considered in older adults who are admitted to the hospital with dry mouth and dry eyes. When the patients are evaluated within the framework of comprehensive geriatric assessment, there may be an underlying rheumatological disease such as PSS. Even though elderly individuals are rarely seen in NMOSD regardless of its etiology, it may be associated with PSS. Moreover, it should be kept in mind that sicca symptoms may flare up again when treatment is stopped the maintenance treatment for NMOSD.

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