CASE REPORT

Psychiatric manifestations of primary Sjögren's syndrome: a case report and literature review

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SUMMARY

A 54-year-old woman diagnosed with primary Sjögren's syndrome in 2007 presented with a 1-year history of visual hallucinations requiring admission to a psychiatric unit. The hallucinations resolved while on olanzapine and hydroxychloroquine but recurred when they were stopped. Despite restarting olanzapine, her visual hallucinations persisted. When she started a tapering dose of prednisolone, all the hallucinations resolved. This report adds to the small literature on psychiatric manifestations of Sjögren's syndrome and provides evidence that low-dose corticosteroids may be an effective treatment for this manifestation.

BACKGROUND

Sjögren's syndrome is the second most common autoimmune rheumatic disease after rheumatoid arthritis.¹ Central nervous system (CNS) involvement in primary Sjögren's syndrome (CNS-SS) is a rare but significant complication² and can manifest with focal or diffuse neurological deficits including psychiatric disorders.

CASE PRESENTATION

A 54-year-old woman, with a medical history of treatment for breast cancer (1993), was admitted in 2006 to a psychiatric unit with a 6-week history of visual hallucinations. She described seeing coloured rings and blotches throughout her visual field, and experienced hallucinations of a religious nature. She was discharged on olanzapine 10 mg, and she had a complete resolution of her psychotic symptoms. Following discharge, she developed a prolonged depressive episode which eventually responded to treatment with sertraline 100 mg daily.

In 2007, she developed numbness in her hands extending up to the wrists, and 2 months later numbness in both feet to the ankles. Over the subsequent 6–9 months, the numbness became more intense but remained in the same distribution. Nerve conduction studies revealed a severe fairly symmetrical demyelinating sensorimotor neuropathy consistent with chronic inflammatory demyelinating polyneuropathy.

Autoimmune screen revealed: antibodies to SSA (Ro) weakly positive, rheumatoid factor of high titres: 517 U/mL (human latex equivalent) and 272 U/mL (animal RAPA equivalent), coeliac IgA antitissue transglutaminase antibody 171 U/mL (high titre). Erythrocyte sedimentation rate (ESR) was elevated at 30 mm/h, C reactive protein (CRP) was normal (<5 mg/L). Antibodies to SSB (La), antineuronal, antinuclear, antineutrophil

cytoplasmic, double-stranded DNA and thyroid antibodies were all negative; complement was within normal range. Cerebrospinal fluid (CSF) and serum showed oligoclonal IgG but of different electrophoresis patterns. Infection screen for HIV, treponemal antibody, hepatitis B and C virus was negative. Porphyrin screen and white cell enzymes were negative.

MRI of the brain and spinal cord were normal apart from the presence of a few non-specific T2 hyperintense foci in the cerebral white matter, not in excess for her age, and in keeping with minor small vessel ischaemic change.

Rheumatology review at that time thought that there were no clinical features of systemic lupus erythematosus. Schirmer's test was found to be dry and she had dry mouth symptoms. These features with a positive rheumatoid factor, positive anti-Ro antibodies, polyclonal hyper-γ-globulinaemia, raised ESR and normal CRP and the presence of neuropsychiatric features were suggestive of Sjögren's syndrome. She was started on hydroxychloroquine 200 mg daily at this stage. Salivary gland biopsy was not performed.

Repeat nerve conduction studies in March 2008 demonstrated a marked improvement in the sensorimotor conduction times, in keeping with the patient's clinical improvement, her sensory symptoms had completely resolved. A repeat MRI of the brain showed no significant interval change and no increase in the extent or distribution of T2 hyperintensities.

After a psychiatric review in 2008 it was decided to taper and stop olanzapine and sertraline. Hydroxychloroquine was also stopped at that time. She remained well for over 2 years except for occasional episodes of acute visual hallucinations.

In August 2011, while on holiday in Spain, she developed visual hallucinations again, as well as auditory hallucinations. On her return to the UK, her husband found her running up and down the street. She was admitted to hospital; a CT scan of the brain was normal. She was restarted on olanzapine 15 mg and clonazepam 1 mg twice daily as well as hydroxychloroquine.

MRI of the brain including T2-flair sequences showed no interval change; ESR was slightly elevated at 28 mm/h and CRP 11 mg/L.

CSF findings were unchanged from the CSF analysis in 2007 and CSF protein, glucose ratio and viral PCR were normal and there were no cells.

EEG in October 2011 showed findings similar to that of 2008, with minor theta activity over the temporal areas consistent with small vessel disease;

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there was no paroxysmal activity and no evidence of epileptogenicity; the findings were not suggestive of an encephalitic or encephalopathic process.

Antineuronal antibodies to Purkinje cell (anti-Yo) and neuronal antibodies 1 and 2 (anti-Hu and anti-Ri), voltage-gated potassium channel antibodies, ant glutamic acid dehydrogenase antibodies and N-methyl-D-aspartate receptor antibodies were all negative.

Antibodies to CV2/CRMP5 were positive, suggestive of a paraneoplastic syndrome.

Fluorodeoxyglucose positron emission tomography-CT (PET-CT) from the skull base to upper thighs showed no evidence of occult malignancy. A focus of increased uptake was seen in the sigmoid colon. A flexible sigmoidoscopy performed to the mid-transverse colon, well beyond the focus of increased uptake, was found to be normal and biopsies excluded malignancy. Mammography and breast ultrasonography did not show any recurrence of breast cancer.

TREATMENT

On clinical review at the end of 2011, she was continuing to experience visual and tactile hallucinations, but no auditory hallucinations. In addition, she also reported sicca symptoms. She was started on a tapering dose of prednisolone starting at 15 mg, reducing by 2.5 mg/week to 10 mg daily.

OUTCOME AND FOLLOW-UP

Within 2 weeks of starting low-dose prednisolone there was a complete resolution of all her hallucinations apart from occasional flashes in her visual fields similar to a camera flash. Prednisolone was continued at 10 mg daily for a month and reduced to 7.5 mg daily thereafter. The steroids were stopped in August 2012. At a recent review in 2013, she has remained well with no psychiatric or rheumatological symptoms.

DISCUSSION

Cases of primary Sjögren's syndrome and psychiatric presentations have been previously reported. One patient manifested with major depression and after treatment with prednisolone (10 mg/day) for 1 month, her depressive symptoms as well as symptoms of dry eyes and dry mouth improved. The patient was maintained on 7.5 mg of prednisolone per day.³ A second patient was diagnosed with panic disorder with agoraphobia and was treated with a tapering dose of prednisolone for 2 months, starting at 40 mg/day. Her psychiatric as well as symptoms of Sjögren's syndrome resolved. The patient was maintained on prednisolone 20 mg/day.³ In addition, a patient with Sjögren's syndrome developed a progressive dementia which completely resolved with high-dose corticosteroids.⁴ In our case, symptoms of hallucination resolved with a tapering dose of prednisolone, starting at 15 mg/day.

The pathological mechanism of Sjögren's syndrome are unknown; however, CNS disease in Sjögren's syndrome may be immunologically mediated.⁵ There has been contrasting evidence for the role of antineuronal antibody in CNS-SS. Spezialetti *et al*⁶ did not detect serum or CSF autoantibodies to ribosomal P peptide or neuronal antigens in patients with CNS-SS. In another study, antineuronal antibodies were found to be present in patients with neurological complications.⁷ However, there is no consensus on the definition of CNS involvement in Sjögren's syndrome.⁵

In a recent paper, schizophrenia was found to be associated with an increased risk of autoimmune diseases such as Graves'

disease, psoriasis, pernicious anaemia, coeliac disease and hypersensitivity vasculitis. Gender-specific variation was found for Sjögren's syndrome.⁸ Schizophrenia was found to be associated with a large range of autoimmune diseases in a review of Danish national registers.⁹

The presence of CV2/CRMP5 antibodies raised the possible alternative diagnosis of a paraneoplastic encephalomyelitis as the cause of her neuropsychiatric symptoms, and the presence of unmatched oligoclonal bands would support this.

Anti-CV2/CRMP5 antibodies are associated with breast cancer, small-cell lung cancer and thymoma. Anti-CRMP5/CV2 antibodies are also associated with paraneoplastic sensory or sensorimotor peripheral neuropathies, cerebellar ataxia, chorea, uveoretinal and myasthenic syndrome and more recently with a neuromyelitis optica type syndrome.^{10–12}

The presence of onconeural antibodies is tightly associated with the underlying malignancy. However, the clinical syndrome in our patient was confined to hallucinations and delusions, and she had no short-term memory deficits, no seizures or stupor and no cerebellar signs. In addition the time course (initial symptoms in 2007 responding to antipsychotics and hydroxychloroquine without steroids), the normal MRI, EEG and the absence of a pleocytosis or elevated protein on CSF would be somewhat against a diagnosis of paraneoplastic syndrome.¹³ PET-CT and further imaging and investigation did not reveal any occult malignancy. The specificity of CV2/CRMP5 antibodies to an underlying malignancy is unknown; the presence of anti-Hu antibodies is reported to be associated with an underlying malignancy in 99% of cases, this was negative in our patient. She has regular breast screening mammography as indicated by her age and history of breast cancer.

A limitation of our report is that the diagnosis was made on clinical grounds. Our patient had anti-Ro antibodies, positive rheumatoid factor, symptomatic mouth dryness and had undergone dry Schirmer's test, but she did not have a salivary gland biopsy or symptomatic dry eyes, which are required to fulfil the classification criteria for Sjögren's syndrome according to Vitali *et al*.¹⁴ Nevertheless, in the absence of an alternative diagnosis, Sjögren's syndrome was a reasonable diagnosis on clinical and serological grounds.

Learning points

- ▶ This case report adds to the literature on psychiatric manifestations of primary Sjögren's syndrome and the presentation can be similar to that seen in neuropsychiatric lupus.
- ▶ It provides evidence that low-dose corticosteroids are an effective treatment option.
- ▶ Sjögren's syndrome should be considered in patients who present with unexplained neuropsychiatric symptoms.

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