CASE REPORT

Unusual presentation of Sjögren's syndrome

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SUMMARY

We present a case of a 67-year-old woman admitted from the neurology clinic for further investigations of progressive ataxia and sensory symptoms. Neurological examination showed reduced pinprick and absent vibration sensations in the lower limbs. Motor system examination was normal. Her antinuclear antibodies titre was 1:100 with positive Ro antibodies. Her initial nerve conduction studies were normal. However, the lower limb somatosensory-evoked potentials (SSEP) demonstrated impairment of central sensory conduction pathway. Rheumatology review revealed a history of fatigue and Sicca symptoms and her Schirmer's test was strongly positive. This led to the diagnosis of ganglionopathy associated to Sjögren's syndrome. She had an excellent response to intravenous methylprednisolone followed by oral prednisolone and intravenous cyclophosphamide infusions. This case highlights that dorsal column involvement can precede the diagnosis of primary Sjögren's syndrome.

BACKGROUND

The most common presenting symptoms of Sjögren's syndrome (SS) are dry eyes, dry mouth, joint pain and fatigue. However, dorsal column involvement, reported as the most uncommon neuropathy in SS, was the presenting manifestation of SS in this case. As such SS should be considered as differential diagnosis in patients presenting with sensory ataxia.

CASE PRESENTATION

We present a case of a 67-year-old woman referred to neurology clinic with a 3-month history of unsteadiness and progressive sensory disturbance.

She had a medical history of hypertension, lichen sclerosis, peptic ulcer and hiatus hernia. She also had previous hysterectomy for endometrial carcinoma, and cholecystectomy.

She described progressive asymmetrical pins and needles sensation in her hands and lower legs. There was no motor weakness, and otherwise she systematically felt well. She became unsteady over the past few months prior to her admission and had few falls.

She is a non-smoker and rarely drinks alcohol.

On physical examination, her lower limb neurological examination revealed normal power, absent knee and ankle reflexes, downgoing plantars, reduced pinprick and absent vibration sense. She walked with a broad-based gait and Romberg's test was positive.

INVESTIGATIONS

Laboratory investigations showed normal full blood count, renal and liver function tests, bone profile,

vitamin B12/folate and thyroid function test. C reactive protein level was 10 mg/L (normal <5 mg/L).

Radiological investigations including chest X-ray, MRI (brain and spine) and CT scan (chest, abdomen and pelvis) were also within the normal limit. Her cerebrospinal fluid analysis was normal including oligoclonal bands and viral PCR.

Initial nerve conduction studies were normal, in particular lower limb sensory potentials were normal ruling out a large fibre neuropathy. However, the lower limb somatosensory-evoked potentials (SSEP) demonstrated a delay in the P40 component indicating that central sensory conduction pathway is impaired.

Her autoimmune profile showed antinuclear antibodies (ANA) titres of 1:100, with positive Ro antibodies. Anti-double stranded DNA and antineutrophil cytoplasmic antibody were negative and immunoglobulins were normal.

Rheumatology review was requested; and revealed a history of Sicca symptoms for a few years and fatigue for a few months. She denied any arthralgia, skin rashes, mouth ulcers, hair loss or any other systemic symptoms. Schirmer's test was strongly positive. The rest of the musculoskeletal and systemic examination was normal.

This led to the diagnosis of SS presenting with dorsal column involvement, most likely ganglionopathy.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis should incorporate other causes of ganglionopathies including vasculitic causes, HIV infection and paraneoplastic syndromes (especially mediated by anti-Hu antibodies). Our patient was screened for paraneoplastic syndrome. Clinical assessment in addition to radiological investigations did not show any evidence of an underlying malignancy. She also had negative onconeural antibodies testing including anti-YO, anti-HU, anti-RI. Additionally she was tested for myelin-associated glycoprotein and glutamic acid decarboxylase antibodies and they all came back negative.

Other causes include: sensory variant of acute and chronic inflammatory demyelinating neuropathy, IgM paraproteinaemic neuropathy and drug induced (cisplatin, pyridoxine). These causes were also excluded in the case of our patient.

TREATMENT

Our patient was treated with three doses of 1 g intravenous methylprednisolone followed by oral prednisolone and had seven cycles of intravenous cyclophosphamide infusions.

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OUTCOME AND FOLLOW-UP

The patient had an excellent response to the treatment, with significant improvement in her sensory symptoms and ataxia. Her deep tendon reflexes returned to normal in her lower limbs 5 months after starting cyclophosphamide. Her upper limb reflexes were back but remained reduced. After 1-year follow-up she remained in remission.

DISCUSSION

SS is an autoimmune disease characterised by an exocrinopathy predominantly affecting salivary and lacrimal glands. SS can be primary or secondary (in association with other connective tissue diseases).

In the case of our patient, the diagnosis of primary SS was based on the 2012 American College of Rheumatology criteria. She had sicca symptoms, strongly positive Schirmer's test, positive ANA and anti-RO antibodies. Hence, labial gland biopsy was not considered to be essential.

Over the past decades a number of reviews of SS-associated neuropathies have described the wide spectrum of its neurological features involving central and peripheral nerve systems.

The exact prevalence of neurological manifestations in patients with SS is still unknown. In general, the majority of studies reported neurological complications in 5–20% of patients with the disorder.^{1–9}

Dorsal column involvement has been reported as the most uncommon neuropathy in SS, typically seen in less than 5% of patients.^{5 10–19}

Interestingly, Mori *et al* in their large cohort reported that 36 of 90 patients developed ganglionopathies. Experts believe that this series, conducted in highly selected populations within a specialised neuromuscular centre, cannot provide accurate figures with regards to the frequency and prevalence of neuropathic syndromes in patients with SS in general.¹¹

Neurological symptoms may precede the onset of sicca symptoms.⁶

Ganglionopathy clinically presents with paraesthesia, impaired proprioception, preserved power, reduced or absent reflexes, sensory ataxia and positive Romberg's sign.

Other causes of ganglionopathies should be considered including vasculitic causes, HIV infection, paraneoplastic syndromes (especially mediated by anti-Hu antibodies), sensory variant of acute and chronic inflammatory demyelinating neuropathy, IgM paraproteinaemic neuropathy and drug induced (cisplatin, pyridoxine).¹⁰

Mori *et al*⁶ demonstrated that 53% and 11% of patients with SS-associated sensory ganglionopathies, had anti-SSA and anti-SSB respectively. In other reviews, Anti-SSA and/or anti-SSB were found positive in 10–55% of patients with SS-associated neuropathy.^{20–24}

Positive Schirmer's test was reported in 93% of patients with ganglionopathies.⁶

Nerve conduction studies typically reveal impaired sensory nerve action potentials, with preservation of compound motor action potentials.^{6 25}

In patients with sensory ataxic neuropathy, their spinal cord MRI may show T2 hyperintensities in the fasciculus cuneatus and gracilis.²⁶

With regards to the treatment of SS-associated ganglionopathy, there is no clear consensus and number of immunosuppressive regimens have shown to be effective in many isolated case reports. Kastru *et al*²⁷ reported the benefit of pulsed cyclophosphamide in this type of neuropathy.

Our patient had significant functional improvement with intravenous methylprednisolone followed by pulses of cyclophosphamide.

In another series, the use of intravenous immunoglobulin in severe ataxic neuropathy, mainly where steroids and plasmapheresis have failed, resulted in significant functional improvement.²⁸

Learning points

- ▶ Dorsal column involvement can precede the diagnosis of primary Sjögren's syndrome. As such Sjögren's syndrome or other connective tissue diseases should be considered in patients presenting with sensory ataxia.
- ▶ Appropriate immunosuppressive therapy can improve symptoms and function in these patients.
- ▶ The accurate prevalence of this manifestation is variable from one series to the other.
- ▶ Controlled trials are needed to better characterise the pathophysiology, clinical manifestations and therapeutics of this type of neuropathy.

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