Sensory neuropathy with prominent ataxia reflecting kinesthetic sensory impairment is a well recognised form of neuropathy associated with Sjögren’s syndrome. Pathologically, T cell invasion of dorsal root ganglia, loss of large sensory neurons, and secondary large fibre degeneration is seen in this neuropathy. However, a form of neuropathy associated with Sjögren’s syndrome, presenting with pain and superficial sensory involvement without sensory ataxia has been described anecdotally and in a case report. Clinical-pathological details of the second form of neuropathy have not been elucidated. In this report we describe seven patients with Sjögren’s syndrome showing painful sensory neuropathy without sensory ataxia.

Patients studied were referred for painful neuropathy to Nagoya University Hospital and its affiliated institutions. All seven patients fulfilled diagnostic criteria for Sjögren’s syndrome by the American-European Consensus Group and showed painful peripheral neuropathy (table 1). Patients included six women and one man, ranging from 25 to 72 years old. In all patients initial symptom of neuropathy was paraesthesia or painful dysesthesia in the most distal portions of the extremities, later extending proximally to involve the entire legs and arms. The trunk became involved in three patients, and the trigeminal nerve was impaired in three patients. Asymmetry in sensory impairment was present in four patients. None of the patients showed sensory ataxia in the initial phase. Most patients retained essentially normal muscle strength, but patient 1 showed slight weakness in distal limb muscles. Painful sensation was the most characteristic, and this symptom compromised activities of daily living in all patients. Superficial sensation for pinprick and temperature was prominently impaired. Deep sensation such as joint position and vibratory sense was substantially well preserved. Sensory ataxia and Romberg’s sign was not present. Autonomic dysfunction was seen in four patients including Adie’s pupils, urinary disturbance, and loss of T1-MIBG cardiac accumulation. However, orthostatic hypotension was not present. Apparent hypohidrosis was seen in three patients. Thermal stimulation in two patients, resulted in absent sweating on the forehead, trunk, arms, and legs, with preserved sweat gland function on pirocarpine test. Thermography showed abnormal skin temperature gradient in four patients. Deep tendon reflexes were comparatively well preserved except in two patients. Motor nerve conduction studies showed no slowing (mean (SD) 52.3 (3.9) m/s in the median, 44.8 (6.1) m/s in the tibial nerves) and preserved compound muscle action potentials (CMAPs) (7.5 (3.5) mV in the median, 9.0 (6.3) mV in the tibial nerves). Sensory nerve conduction (50.1 (6.0) m/s in the median, 47.2 (10.4) m/s in the sural nerves) and sensory nerve action potentials (SNAPs) (13.6 (11.7) uV in the median and 9.0 (6.3) uV in the sural nerves) were generally well preserved; only in pain 4, SNAPs were not evoked. Somatosensory evoked potentials (SEPs) were also well preserved (mean (SD) 20.0 (1.1) ms at N20, 13.7 (1.2) ms at N13, and 9.3 (0.4) ms at N9). Sural nerve biopsy in five patients showed a variable degree of myelinated fibre loss, predominantly affecting small diameter fibres (table 1, fig 1). Unmyelinated fibre density was severely reduced. Axonal sprouting was essentially absent in all patients. In teased fibre preparations, degeneration was seen in 32% to 55% of axons, predominantly small diameter fibres. Vasculitis was not seen.

Patient 2 developed sensory ataxia in the legs over the next nine years, and more details of this patient are given below. Patient 4 developed localised sensory ataxia in the fingers of the right hand over 11 years. Other patients showed persistent painful sensory neuropathy with gradual extension of distribution over 4 to 11 years of follow up.

CASE REPORT
A 68 year old man had painful dysesthesia and numbness in the feet for about 10 years, with spread to the proximal of the legs and arms. When he was 56 years old, he noticed painful dysesthesia in the legs, and subsequently in the hands. Neurological examination demonstrated light touch and pinprick were disturbed, and painful dysesthesia was elicited in glove and stocking distribution. Vibration and joint position sense was comparatively well preserved for the first time. Sensory ataxia and Romberg’s sign were not seen. Deep tendon reflexes were well preserved in upper limbs, but mildly decreased in lower limbs. Muscle strength was normal. Autonomic disturbance was not present. Nerve conductions were nearly normal except for sensory conduction in the median nerve, 40 m/s. SNAPs were well preserved. Result of routine blood haematology and biochemistry screening tests were normal. CSF protein was 33 mg/dl with no cells. A sural nerve biopsy specimen revealed myelinated fibre loss predominantly involving small diameter fibres with axonal degeneration.

Figure 1  [A] Transverse section of a sural nerve specimen from a control subject. [B] Specimen from a patient of painful sensory neuropathy with predominant small fibre loss associated with Sjögren’s syndrome (patient 1). Small diameter myelinated fibres are more noticeably involved and no axonal sprouting. Bars=25 µm.
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<th>Patient Age/sex</th>
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<td>Controls (mean (SD), n=9)</td>
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*+, Positive findings; –, negative findings. Muscle weakness, atrophy, and painful sensation: +3, severe; +2, moderate; +1, mild; –, absent. Distribution of sensory involvement: F, facial; T, trunk; L, limbs. Sensory signs: –3, severe; –2, moderate; –1, mild; –, absent. Nociception was evaluated by pin pricking. Autonomic dysfunction: 1, Adie’s pupils; 2, loss of 123I-MIBG cardiac accumulation; 3, urinary disturbance; 4, hypohidrosis. SS-A, anti-SS-A antibody; SS-B, anti-SS-B antibody; RB, Rose Bengal test for Sjögren’s syndrome. For nerve biopsy findings, large >6.73 µm; small <6.73 µm in fibre diameter; As for typical sensory ataxic neuropathy with Sjögren’s syndrome, large myelinated fibre density was 660 (714) (median (SD)), small myelinated fibre density was 3263 (2390), and small/large fibre ratio was 14.6 (19.0) for 20 cases. ND, not determined. †Sensory ataxia developed in the legs 9 years later, in the right hand 11 years later respectively. ‡Result of second sural nerve biopsy examined 12 years later.
In the next nine years, involvement of deep sensation gradually developed. At 68 years old, he showed sensory ataxia in the legs and positive Romberg's sign without muscle weakness. The deep tendon reflexes were almost preserved. Motor nerve conduction velocities were still preserved, but sensory nerve action potentials were not elicited in the median and sural nerves. At this time, sicca symptoms were obvious, and a Rose Bengal test was positive. A lip biopsy specimen showed periacinar lymphocytic infiltration. Second sural nerve biopsy on the other side showed severe large fibre loss as well as small fibre loss without axonal sprouts.

**DISCUSSION**

The most well recognised form of Sjögren's syndrome associated neuropathy has been sensory ataxic neuropathy associated with profound impairment of kinesthetic sensation.\(^{1,4–6}\) Neuropathologically, T cell invasion in the dorsal root ganglion as well as loss of large ganglion neurons and their large axons have been verified.\(^7\) However clinicopathological findings in our patients differed remarkably from those of sensory ataxic neuropathy. Painful sensation and hyperalgesia in our patients suggested involvement of small nociceptive nerve fibres as has been demonstrated.\(^8\)

Indeed, in sural nerve of our patients, small myelinated and unmyelinated fibres were predominantly involved; electrophysiologically, amplitudes of SNAPs were comparatively preserved, particularly in contrast with sensory ataxic neuropathy. Findings in the dorsal root ganglion in this neuropathy have not been described, but predominant small fibre loss, extremely rare axonal sprouts, lack of vasculitis, lack of motor involvement, and fairly well preserved SEPs suggest that small dorsal root ganglion neurons can be involved. As demonstrated by the clinical course of our patients, some patients show persistent symptoms or a slowly progressive course while remaining limited to a painful small fibre type of neuropathy, while others, including one of our patients, may later develop sensory ataxic neuropathy presumably involving large sensory neurons. Additionally, one of our patients developed localised unilateral sensory ataxia in the fingers, suggesting that some patients may develop localised sensory ataxia. These observations suggest that painful sensory neuropathy with predominant small fibre loss and sensory ataxic large fibre neuropathy are elements of a spectrum of sensory neuropathy in Sjögren's syndrome.

In summary, these patients suggest that painful sensory neuropathy with predominant small fibre loss is an identifiable subtype of Sjögren's syndrome associated neuropathy.

**REFERENCES**

The harsh realities facing the use of SPECT imaging in monitoring disease progression in Parkinson’s disease

Dr Snow is right to be cautious in his optimism concerning the use of functional imaging markers in neuroprotection studies in Parkinson’s disease\(^1\) as storm clouds gather\(^2\) over the methods and interpretation of CALM-PD and REAL-PET. The concerns, however, are not limited to the effect of drug treatment on ligand uptake. Most importantly we need to ask the weight that should be placed on the result of functional imaging studies when these are not supported by the accompanying clinical data. In addition, there are concerns about the ability of the methods for accurately monitoring progression. The key requirements for a PET or SPECT method to be used in assessing progression are sensitivity to clinical change and reproducibility.\(^3\) There are no data concerning either from the study of Winogrodzka\(^4\) within the first year a significant number of patients have learned dopamine transporter binding, and show which radioisotope is optimal for performing progression studies.

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References

CORRECTIONS
There were two mistakes published in the table of the short report, Sjögren’s syndrome associated painful sensory neuropathy without sensory ataxia, by K Mori, M Iijima, M Surgiara et al in the September issue of JNNP (2003;74:1320-2); the digit 9 was added to the eleventh column head by accident and the second entry in the final column should read 12, not 2.

The authors of the letter entitled Menin- goma of the optic nerve sheath: treatment with hydroxyurea, published in the September issue of JNNP (2003;74:1348–50) were listed in the incorrect order. The author order should read as follows: S Paus, T Klockgether, H Urbach, U Schlegel.