Chronic autonomic neuropathy in a patient with primary Sjögren's syndrome

Several investigators have described the autonomic neuropathy in Sjögren's syndrome.[1–3] However, only a few have documented the details of dysautonomia, or the pathology of nerves or of other organs such as eccrine sweat glands.[3] We report on a patient with Sjögren's syndrome in whom dysautonomia was the dominant feature, and describe histological findings for the sural nerves and the eccrine glands.

A 39 year old woman visited our hospital because of frequent fainting attacks and diminished sweating. Her history indicated attacks of dizziness on standing since the age of 27. At the age of 30, she experienced a fainting attack on standing. At the age of 36, she noticed dry eyes and focal loss of sweating on the left forehead. She developed amenorrhea at the age of 27. The family history was unremarkable.

She was 164.5 cm tall and weighed 36 kg (body mass index 13.4). Neurological examination showed bilateral ptosis and isocoric pupils (3 mm in diameter; measured using infrared photography) with an irregular margin. The light reflex was absent and the accommodation reflex was tonic. Muscle tone and power were normal. The tendon reflexes were absent and plantar responses were flexor. Sensation and coordination were normal. The skin was generally dry, and spontaneous sweating was present only over the right forehead and T-10 and T-11 dermatomes in hot circumstances. The urinary system was normal.

Results of routine laboratory examinations, CSF studies, an oral glucose tolerance test, and thyroid function tests were normal. Urinary porphobilinogen (0.5 mg/day), δ-aminolevulinic acid (1.8 mg/day), and serum vitamin B_{12} (679 pg/ml) were normal. The serum concentration of γ-globulin was increased (24.9%). Serum antinuclear antibody (speckled type×160), anti-SS-A, and rheumatoid factor were positive. Her compound muscle action potentials in the extensor digitorum brevis were 1.90/0.77 mV (right/left). Sensory nerve action potentials in the bilateral median, ulnar, and right sural nerves were 3.73/8.54 μV, 3.74/6.52 μV, and 14.7 μV, and their sensory nerve conduction velocities were 33.1/39.0 m/s, 29.8/32.7 m/s, and 30.0 m/s, respectively. Distal latencies for median and ulnar motor nerves were 3.24/3.02 ms and 2.46/2.50 ms. Brain MRI showed no abnormality.

The pupillary response to 2.5% methacholine chloride showed hypersensitivity; the miotic ratio was 43% (3.0 to 1.7 mm); there was also hypersensitivity (3.0 to 9.0 mm) to 1.25% adrenaline (epinephrine) and a sluggish response to tyramine. The density of active eccrine glands on the dorsal surface of the right foot shown by iontophoretically applied pilocarpine (1%) was 19/cm^2 (age matched controls; 141~ 277/cm^2). Staining with rose bengal disclosed erosion. Results of Schirmer's test and a chewing gum test were 2 mm and 8 ml respectively. Cardiographic R-R interval showed an expiration-inspiration ratio of 1.03. In a cold pressor test, her blood pressure did not change (112/80 to 112/80 mm Hg). In a head up tilting test at an angle of 60 degrees, her blood pressure decreased from 122/74 to 84/44 mm Hg within 3 minutes, without an increased heart rate (79 to 79 beats/min) and plasma noradrenaline (norepinephrine) concentration (58 to 52 pg/ml). In myocardial ^{123}I-metaiodobenzylguanidine (MIBG) scintigraphy, the heart to mediastinum ratio was 1.52.

Histological examination of the left sural nerve showed no degenerating abnormality on teased fibre analysis. In epon embedded sections of the left sural nerve (toluidine blue staining ×1200 for light microscopy and ×7600 for electron microscopy), the densities of small myelinated fibres, large myelinated fibres, unmyelinated fibres, and denervated Schwann cell clustering were 2591 /mm^2 (mean (SD) 4130 (844)), 2590/mm^2 (3257 (889)), 7294/mm^2 (27 866 (5820)), and 5230/mm^2 (796 (687)), respectively. There were no onion bulbs, infiltrating inflammatory cells, or features of vasculitis. Light microscopical examination of the eccrine sweat glands of the lower posterolateral aspect of the left leg showed atrophic changes of the glands, but no infiltrating inflammatory cells (haematoxylin and eosin). Electron microscopical examination showed a reduction of the perimeter and area of the transverse profile of secretory coils compared with the controls, indicative of atrophy of the glands (×2500). Furthermore, there was a marked reduction in the number of nerve terminals and unmyelinated axons around the secretory coils (×12 500, table). Histological analysis of the minor salivary glands of the lip mucosa showed focal lymphocytic sialoadenitis with degeneration of the ductular epithelium (haematoxylin and eosin), suggesting coexistence of Sjögren's syndrome.

The patient was treated with oral prednisolone (40 mg/day) and l-threo-3, 4-dihydroxyphenylserine (200 mg/day). The dose of prednisolone was tapered to 20 mg/day. Fainting attacks on standing disappeared after the treatment.

Our patient had bilateral tonic pupils, bilateral Horner's syndrome, hyporeflexia, orthostatic hypotension, abnormal cardiovascular reflexes, reduced lacrimation, and segmental anhidrosis. Examination of the autonomic nervous system disclosed parasympathetic and postganglionic sympathetic injury including sudomotor involvement. Since Ross reported the presence of tonic pupils and progressive anhidrosis in his patient (Ross' syndrome),[4] several reports have confirmed that autonomic dysfunction in Adie's syndrome may be more widespread than previously recognised. However, severe orthostatic hypotension as seen in our patient is rare. The clinical condition of our patient seemed different from that of acute autonomic neuropathy, because the dysautonomia started insidiously and progressed slowly over many years. Our patient did not have any other systemic disease except Sjögren's syndrome. Peripheral neuropathy with Sjögren's syndrome may represent a distinct syndrome, in which sensory polyneuropathy predominates but there is some autonomic dysfunction or Adie's pupils.[1–3] Griffin *et al*[5] described autonomic deficits in patients with ataxic sensory polyneuropathy with Sjögren's syndrome. In their patients, histological examination of sural nerves showed a preferential loss of large myelinated fibres, which is different from the findings of our patient. We concluded that the diagnosis of our patient was a subtype of polyneuropathy with Sjögren's syndrome.

The marked reduction in the density of unmyelinated fibres seen in our patient may reflect damage of the postganglionic sympathetic efferent projection. We showed the severe degeneration of postganglionic sympathetic cholinergic nerves innervating the eccrine glands by histopathological morphometric analysis. Examination of the eccrine glands would provide useful information for assessment of autonomic function in patients with anhydrosis.

Electron microscopic morphometric evaluation of the transverse profiles of secretory coils in the skin and nerve terminals and unmyelinated axons around secretory coils

	Controls†	*Patient‡*
Perimeter of transverse profile (μm/profile)	173 (55)	122 (88–156)
Area of transverse profile (μm^2/profile)	2017 (1000)	990 (445–1445)
Nerve terminals (n)*	9.1 (4.8)	1.1 (0–2.4)
Unmyelinated axons (n)*	12.7 (6.2)	1.8 (0–3.7)

†Mean (SD) of six control subjects in whom 14–38 transverse profiles of secretory coils in each individual were morphometrically evaluated.
‡Mean of 38 transverse profiles of secretory coils. Minimum–maximum values are shown in parentheses.
*Number/100 μm of perimeter of transverse profiles.

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C1/C2 rotary subluxation due to spasmodic torticollis

Rotary subluxation of the atlantoaxial complex is encountered more often in children than in adults. It is usually associated with a clear history of cervical trauma, upper respiratory infection, recent head or neck surgery, or rheumatoid arthritis. This paper reports on an adult presenting with C1/C2 rotary subluxation in whom all of these causes were absent. The subsequent clinical course