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 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 B₁₂ (679 pg/ml) were normal. The serum concentration of γ -globulin was increased (24.9%). Serum antinuclear antibody (speckled type $\times$ 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 μ V, 3.74/6.52 μ V, and 14.7 μ V, 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/cm² (age matched controls; 141–277/cm²). 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 ¹²³I-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 $\times$ 1200 for light microscopy and $\times$ 7600 for electron microscopy), the densities of small myelinated fibres, large myelinated fibres, unmyelinated fibres, and denervated Schwann cell clustering were 2591/mm² (mean (SD) 4130 (844)), 2590/mm² (3257 (889)), 7294/mm² (27 866 (5820)), and 5230/mm² (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 ($\times$ 2500). Furthermore, there was a marked reduction in the number of nerve terminals and unmyelinated axons around the secretory coils ($\times$ 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 anhidrosis.

We thank Dr Shinji Oono, Department of Ophthalmology, Saga Medical School, Japan, for his help and advice in the examination of pupils.

HIROFUMI GOTO
HIDENORI MATSUO
TAKAYASU FUKUDOME
NORITOSHI SHIBUYA

Department of Neurology, Kawatana National Hospital, Shimoguni-gou 2005-1, Kawatana, Higashisonogi-gun, Nagasaki, 859-3615, Japan

AKIO OHNISHI
Department of Neurology, University of Occupational and Environmental Health

HIDEKI NAKAMURA
First Department of Internal Medicine, Nagasaki University School of Medicine

Correspondence to: Dr H Goto
goto@kawatana.hosp.go.jp

- 1 Mellgren SI, Conn DL, Stevens JC, *et al*. Peripheral neuropathy in primary Sjögren's syndrome. *Neurology* 1989;39:390-4.
- 2 Gemignani F, Marbini A, Pavesi G, *et al*. Peripheral neuropathy associated with primary Sjögren's syndrome. *J Neurol Neurosurg Psychiatry* 1994;57:983-6.
- 3 Gemignani F, Manganelli P, Pavesi G, *et al*. Polyneuropathy in Sjögren's syndrome. A case of prevalently autonomic neuropathy with tonic pupil and hypohidrosis. *Funct Neurol* 1988;3:337-48.
- 4 Ross AT. Progressive selective sudomotor denervation. A case with coexisting Adie's syndrome. *Neurology* 1958;8:809-17.
- 5 Griffin JW, Cornblath DR, Alexander E, *et al*. Ataxic sensory neuropathy and dorsal root ganglionitis associated with Sjögren's syndrome. *Ann Neurol* 1990;27:304-15.

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

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 (μ m/profile)	173 (55)	122 (88-156)
Area of transverse profile (μ m 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 μ m of perimeter of transverse profiles.

showed that the patient in fact had spasmodic torticollis which we think was the cause of the rotary subluxation at C1/C2.

A 37 year old man presented in November 1997 with a history of an insidious onset of progressive deformity of the neck associated with spasm of the left sternocleidomastoid and trapezius muscles and occipital pain from April of that year. He had had mild neck pain for several years. The occipital pain was left sided and became increasingly severe. Electromyography was not performed. He had been off work for 6 months and found it increasingly difficult to sleep in a comfortable position. The only relevant history was one of "anxiety attacks".

On examination there were no signs of rheumatoid arthritis. The patient had a classic "cock robin" deformity with his head tilting to the left and turning to the right. This was associated with spasm and tenderness, but no obvious hypertrophy, of the left sternocleidomastoid and trapezius which was thought to be voluntary as it subsided when he was relaxed. Plain radiography of the atlantoaxial region was essentially normal and thus CT was obtained under a general anaesthetic as the patient was extremely anxious. After the induction of the general anaesthetic, the element of spasm and tilting of his neck which was thought to be due to psychological overreaction disappeared and examination showed persistence of the "cock robin" deformity. Spinal CT in the neutral position confirmed a C1/C2 rotary subluxation which reduced with the head turned towards the left but was exaggerated by turning to the right. There was no history of recent neck injury, rheumatoid arthritis, or pharyngeal infection and thus a cause for the C1/C2 rotary subluxation was not apparent at that stage. In view of the severity of the pain surgical stabilisation of C1/C2 was suggested.

The patient was placed in halo-traction for a week, and further CT was performed. This showed significant improvement but not total correction of the rotary subluxation. As reduction was not total, it was decided not to perform transarticular screw fixation of C1/C2 but a posterior modified Gallie fusion was performed in the position of maximum reduction. A halo-vest was applied. Check radiography was satisfactory and the patient reported a very pleasing relief of the pain and spasm which he had preoperatively. The halo-vest was maintained for 10 weeks during which his pain and spasm had completely resolved. However, shortly after removing the halo, he had a recurrence of the pain and spasm in the left sternocleidomastoid although the severe occipital pain was still completely relieved. His neck posturing was now variable and typical of spasmodic torticollis with no residual "cock robin" deformity. There was rotation to the right, tilt to the left, and left shoulder elevation. Check radiography showed no loss of the previous position.

At this point a diagnosis of spasmodic torticollis was made with a torticollis severity score as described by Tsui *et al* of 15 indicating moderately severe deformity.¹ Five hundred units (200 mU/ml) of botulinum toxin A (Dysport—Ipsen) were injected into the left sternocleidomastoid (250 mU) and trapezius (250 mU). The first injection itself produced a 50% reduction in pain and spasm. Three further injections of the same dose over a year produced further improvement and at latest follow up 16 months after surgery his torticollis score had fallen to eight. His posture was similar in nature but much less pronounced

and variable. The occipital pain remains absent and he has achieved a solid fusion.

Atlantoaxial rotary subluxations were first described by Wortzman and Dewar in 1968² and further clarified by Fielding and Hawkins in 1977.³ The maximum normal rotation of the atlantoaxial joints is 45–47 degrees. Beyond this the lateral inferior facet of the atlas rocks over the lateral superior articular facet of the axis.³

Rotary atlantoaxial subluxation can be caused by severe twisting injury of the neck, usually associated with violent sport and vehicular accidents.⁴ It has been reported as a result of a greater than 90 degree rotation of the neck under general anaesthesia.^{4,5}

In this case the common causes of C1/C2 rotary subluxation were absent and we suggest that the subluxation was caused by the spasmodic torticollis over time. Surgery and application of the halo abolished the occipital pain and the spasm was reduced, possibly due to the extra somatosensory input from the halo (a mechanical geste antagonistique). Removal of the halo was followed by recurrence of the dystonic spasm but the occipital neuralgia remained absent due to the stabilisation of the atlantoaxial complex.

In this case it was not possible to determine at what stage the rotary subluxation occurred. It is possible that the subluxation was the primary event leading to malposition of the neck and muscle spasm—a type of "post-traumatic" dystonia. However, in patients with atlantoaxial rotary subluxation, the normal neck deformity is the classic "cock-robin" deformity and activation of sternocleidomastoid and trapezius does not occur. The surgical treatment in this case resolved the "cock robin" deformity and occipital pain but the typical clinical findings of spasmodic torticollis reappeared once the halo was removed. It is most likely that the halo provided sufficient somatosensory input to inhibit the sternocleidomastoid spasm during the length of time the halo was in position. The evolution of the clinical findings with relief of occipital pain and "cockrobin" deformity followed by a more typical appearance of spasmodic torticollis strongly suggest that it was the dystonia which caused the rotary subluxation.

Spasmodic torticollis is a focal and usually idiopathic dystonia with cervical muscle spasm causing involuntary neck posturing and movement. It can occur at any age. Chemical denervation of the overactive muscles with botulinum toxin is now the usual treatment and is effective in most patients.⁶

Dystonia can cause subluxation or dislocation at various joints. For instance, the temporomandibular joints can undergo recurrent or chronic dislocation in idiopathic or tardive oromandibular dystonia.^{7–9} Angelini *et al* described subluxation of the subaxial cervical spine resulting in a cervical myelopathy in a child with spastic dystonic cerebral palsy¹⁰ and Tunkel *et al* reported cervical subluxation causing improvement in the dystonia in a patient with longstanding idiopathic torsion dystonia.¹¹ To our knowledge adult onset spasmodic torticollis causing and presenting as a rotary atlantoaxial subluxation has never been reported in the literature. Prolonged rotation beyond the physiological limit is likely to be the cause of this subluxation.

When atlantoaxial subluxation appears after prolonged involuntary neck posturing an underlying diagnosis of dystonia should be considered. Botulinum toxin will not resolve the subluxation, but was necessary in this case to control the underlying dystonia. External

braces and collars rarely control the forceful movements of cervical dystonia, and the toxin may take some days or even weeks to work, so we recommend treatment as soon as dystonia is diagnosed. In theory botulinum toxin might enhance the effect of or interfere with recovery from acute muscle paralytic agents used in anaesthesia. However, no such reactions have been reported in 12 years of extensive experience worldwide with botulinum toxin, and therefore it is probably safe to give injections even before neck surgery. When a patient with spasmodic (variable posturing) torticollis develops a fixed and sufficiently extreme "cock robin" posture, the clinician should consider investigation by plain radiography and CT to exclude rotary subluxation, even if the muscle spasm is intermittent.

S DALVIE

A P MOORE

G F FINDLAY

Walton Centre for Neurology and Neurosurgery, Lower Lane, Fazakerley, Liverpool L9 7LJ, UK

- 1 Tsui JK, Eisen A, Stoessl AJ, *et al*. Double-blind study of botulinum toxin in spasmodic torticollis. *Lancet* 1986;ii:245–7.
- 2 Wortzman A, Dewar FP. Rotatory fixation of the atlanto-axial joint. Rotational atlanto-axial subluxation. *Radiology* 1968;90:479–87.
- 3 Fielding JW, Hawkins RJ. Atlanto-axial rotatory fixation. *J Bone Joint Surg* 1977;59:37–44.
- 4 Van Gilder JC, Menezes AH. The cranio-vertebral junction and its anomalies. New York: Futura, 1987:206–8.
- 5 Ono K, Yonenobu K, Fujii T, *et al*. Atlanto-axial rotatory fixation. A radiographic study. *Spine* 1985;10:602–8.
- 6 Moore AP, Blumhardt LD. A double-blind trial of botulinum toxin "A" in torticollis, with one year follow up. *J Neurol Neurosurg Psychiatry* 1991;54:816–6.
- 7 Ibrahim Y, Brooks EF. Neuroleptic induced bilateral temporomandibular joint dislocation [letter]. *Am J Psychiatry* 1996;153:293–4.
- 8 Bradshaw RB. Perphenazine dystonia presenting as recurrent dislocation of the jaw. *J Laryngol Otol* 1969;83:79–82.
- 9 Gray AR, Barker GR. Idiopathic blepharospasm-oromandibular dystonia syndrome (Meige's syndrome) presenting as chronic temporomandibular joint dislocation. *Br J Oral Maxillofac Surg* 1991;29:97–9.
- 10 Angelini L, Broggi G, *et al*. Subacute cervical myelopathy in a child with cerebral palsy. Secondary to torsion dystonia? *Childs Brain* 1982;9:35–7.
- 11 Tunkel AR, Pasupuleti R, Acosta WR. Improvement of idiopathic torsion dystonia following dystonia induced cervical subluxation [letter]. *J Neurol Neurosurg Psychiatry* 1986;49:957.

Ataxic form of Guillain-Barré syndrome associated with anti-GD1b IgG antibody

Richter¹ proposed an ataxic variant of Guillain-Barré syndrome, in which patients have severe ataxia of the cerebellar type at the onset of Guillain-Barré syndrome but no ophthalmoplegia or severe loss of proprioceptive sense. Patients with ataxic Guillain-Barré syndrome have distal paraesthesias, areflexia, and raised CSF protein concentrations. Kusunoki *et al*² reported that of 149 patients who had anti-GQ1b IgG antibodies without profound weakness, five had acute self limited ataxia without ophthalmoplegia. The nosology of these patients, however, was not discussed. Of our 340 consecutive patients who had anti-GQ1b IgG, six had no external ophthalmoplegia and one had minimal external ophthalmoplegia. The clinical features of these seven anti-GQ1b-positive patients were consistent with an "ataxic form of Guillain-Barré syndrome" (Yuki *et al*, unpublished observations). Tentative diagnoses made by the primary physicians were Guillain-Barré