Vestibular and ventilatory dysfunction in sensory and autonomic neuropathy associated with primary Sjögren’s syndrome

Subacute sensory neuropathy was described by Denny-Brown in association with carcinoma and has recently been described in association with primary Sjögren’s syndrome (SS). The primary pathology is in the dorsal root ganglia and consists of lymphocytic infiltration and neuronal cell destruction. We describe a patient with primary SS with sensory and autonomic neuropathy and the previously undescribed clinical features of vestibular and ventilatory dysfunction.

A 38 year old man presented with difficulty with walking for one month. He also complained of pain and tingling in the feet and hands, patchy areas of abnormal sensation on the trunk and perioral paraesthesiae. He had experienced grittiness and dryness of the eyes and a dry mouth for 6 months and had keratoconjunctivitis sicca on ophthalmological examination about 4 months before his neurological presentation. His pupils reacted sluggishly to light but the visual fields and optic fundi were normal. There was reduced sensation in all divisions of the fifth cranial nerve bilaterally, although there was some sparing of the perioral region, and the corneal reflexes and corneal sensation were reduced. In the limbs the power was normal. The deep tendon reflexes were absent. In the upper limbs there was reduction of pinprick and light touch sensation in a distal distribution and loss of vibration sense and proprioception up to and including the wrists. In the lower limbs, pinprick sensation was reduced in the toes, light touch was absent up to the thighs and vibration sensation was absent below the iliac crests. There was severe impairment of proprioception up to and including the knees. Romberg’s sign was positive and the gait was severely ataxic. There was bilateral punctate keratitis in the interpalpebral distribution and the Schirmer’s test was 14 mm on the right and 4 mm on the left (normal > 5). On later examination, the Schirmer’s test revealed no lacrimadon from either eye.

The significant results of investigations were that the RA latex test was negative, anticardiolipin antibody level was 8 (normal < 20) and smooth muscle antibody titre was 1:40. Screening for other autoantibodies, including extractable nuclear antigens, was negative. CSF protein was initially 660 mg/L (normal < 400), CSF IgG was 55 mg/L (normal 10-60) and CSF IgG/albumin was 0.14 (normal < 0.11). On a later occasion the CSF protein level was 1,100 mg/L. CSF electrophoresis did not reveal oligoclonal bands. Motor nerve conduction velocity was normal but sensory action potentials were absent in the right median, ulnar and sural nerves. A sural nerve biopsy showed axonal degeneration, with loss of large diameter fibres, and a sparse perivascular lymphoid infiltrate around occasional perineurial vessels. Biopsies of the lip and conjunctiva were normal. No evidence of malignancy was found. Autonomic function was tested using bedside techniques on six occasions. Initially the patient showed an abnormal heart rate response to the Valsalva manoeuvre, deep breathing and to standing. Later he also showed postural hypotension and reduction in the blood pressure response to hand grip.

Because of the xerophthalmia and xerostomia, and the finding of punctate keratitis on Rose-Bengal staining, a diagnosis of primary SS causing sensory and autonomic neuropathy was made. He was treated with intravenous methylprednisolone (500 mg per day for 5 days) and then given oral prednisone (100 mg/day). His gait improved and there was some improvement in joint position sense, although the numbness of the limbs and painful dysesthesiae persisted. After one month the steroid dose was tapered. When the prednisone dose was reduced to 80 mg/day he became worse and developed tight band-like sensations about the trunk. He developed dyspnoea and tachypnoea with resting respiratory rates up to 30 per minute. At this time he showed no signs of anxiety or emotional distress. Spirometry was normal and a chest radiograph was normal. Blood gas analysis showed a compensated respiratory alkalosis. Ten weeks after the first course, he was given a further course of 5 days of 500 mg/day of intravenous methylprednisolone and then continued on reducing doses of
oral prednisone and he was treated with azathioprine (125 mg/day). Despite this, he then complained of blurred vision and intermittent oscillopsia. On examination, horizontal nystagmus was present for several weeks. Electronystagmography showed absent responses to caloric stimulation on two occasions. CT and MRI scans of the brain were normal. He was treated with both plasma exchange and intravenous gamma globulin and continued on prednisone and azathioprine for 8 months. At review 18 months after his first presentation, he continued to have severe ataxia of gait and widespread sensory loss with no remaining normal pain sensibility. His pattern of breathing had changed so that he no longer had tachypnoea, but had episodes when he noticed that he had ceased breathing.

His wife noticed periods of apnoea lasting several minutes during sleep. A recording of respiration during sleep was performed on one occasion but apnoeic episodes were not observed.

Our patient had primary Sjögren’s syndrome and had clinical and electrophysiological evidence of a subacute sensory neuropathy which has been well described in primary SS. He also had bilateral trigeminal sensory neuropathy and evidence of autonomic dysfunction which are also reported to occur in primary SS. There was no evidence of CNS disease, which is described in SS.

The new features in this patient are the vestibular and ventilatory abnormalities. The ventilatory problems consisted of dyspnoea and tachypnoea but later changed to intermittent apnoea. We propose that this may have been due to involvement of primary sensory neurons of pulmonary stretch receptors in the nodose ganglia by the neuropathic process. The pulmonary stretch receptors mediate the Hering-Breuer reflex which results in the termination of inspiration and the initiation of expiration. The initial dyspnoea and tachypnoea may have occurred as an irritative phenomenon while the later apnoea may have been due to neuronal loss. Similar involvement, in the nodose ganglion, of the primary sensory neurons of the carotid and aortic body chemoreceptors may also have contributed to the ventilatory disturbance. Slowing of respiration has been observed in rabbits with experimental allergic encephalomyelitis, where there is major pathology in the dorsal root ganglia, and has been attributed possibly to lesions in the nodose ganglia interrupting the Hering-Breuer reflex.

Our patient’s oscillopsia may be due to a peripheral vestibular lesion as electronystagmography showed absent caloric responses and there was no evidence of a central lesion on CT or MRI. We suggest that his vestibular dysfunction represents an extension of the pathological process to include the primary sensory neurons of the vestibular (Scarpa’s) ganglia. Vestibular neuropathy has not previously been reported in subacute sensory neuropathy.

In our patient, high dose corticosteroid treatment was beneficial, but the patient relapsed when the dose was reduced. Treatment with azathioprine, and intravenous gamma globulin were of no apparent benefit. After the end of treatment he remained stable. The clinical response of this patient suggests that benefit can be obtained by immunosuppressive treatment during the initial phase of inflammation.

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5 Pender MP, Sears TA. The pathophysiology of acute experimental allergic encephalomyelitis in the rabbit. *Brain* 1984;107:699-726.