Letters to the Editor

A new variant of sensory ataxic neuropathy with autosomal dominant inheritance

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Abbreviations: HSAN = hereditary sensory and autonomic neuropathy; SAP = sensory action potentials

We read with interest the description of a family with sensory ataxic neuropathy of autosomal dominant inheritance (van Dijk et al., 1995). Unfortunately, the Dutch authors omitted to discuss our report of a family with similar features which appeared in a Dutch journal (Marbini et al., 1994), classified as hereditary sensory and autonomic neuropathy (HSAN) with ataxia and late onset.

The proband was a 66-year-old man who complained of unsteady gait, especially during walking in the dark, by age 60 years. Neurological examination showed severe hearing loss, normal limb muscle bulk and strength, absent deep tendon reflexes in the ankles and marked sensory loss in the extremities, especially for the position sense, with severe sensory ataxia. Investigations, including CT and MRI brain scans, were unremarkable except for sensorineural hearing loss and abnormal autonomic function tests. Neurophysiological study showed normal EMG, extremely reduced or absent sensory action potentials (SAP), but only minor alterations in the motor nerves. Median and peroneal somatosensory evoked potentials were normal. Sural nerve biopsy showed a severe loss of myelinated fibres of all calibres (622/mm²), whereas the unmyelinated fibre population was relatively less involved (7772/mm²; control 32000/mm²). Biopsy of the peroneus brevis muscle showed normal findings.

The patient’s brother, aged 62 years, who also complained of swaying for the last few years, showed marked sensory ataxia, absent Achilles tendon reflexes, and deficit in all sensation modalities in the lower limbs, with normal EMG and electroneurography of the motor nerves, but extremely decreased amplitude or absence of the SAPs.

Loss of balance with onset in the sixth decade was also reported in the father and in another brother, both deceased. Neurological examination was normal in the proband’s sons, aged 18–40 years, as were clinical and electrophysiological study and autonomic function tests in the 35-year-old daughter of the patient’s 62-year-old brother.

The paper of van Dijk et al. (1995), and ours, clearly define a form of HSAN characterized clinically by sensory ataxia and late onset in the fifth or sixth decade, documented in two generations, consistent with autosomal dominant inheritance. A form of HSAN characterized by late onset sensory ataxia was reported in another Dutch family (Staal and Mechelse, 1978) which, however, showed a recessive mode of inheritance, whereas Robinson et al. (1977) described an autosomal dominant form of HSAN with ataxia, but with onset usually in the first two decades. Additional features were represented by deafness in our family, and oculomotor disorder in the Dutch family. This probably reflects a multisystem involvement, as other patients with HSAN and ataxia showed deafness (Robinson et al., 1977) or oculomotor dysfunction (Staal and Mechelse, 1978). Sural nerve biopsy findings were similar in our case and in the Dutch patient, showing severe loss of myelinated fibres, and moderate changes of the unmyelinated fibres. The most remarkable difference was in the somatosensory evoked potentials, which were severely affected in three members of the Dutch family, but normal in our proband. This would point to involvement of dorsal root ganglia sensory neurons and distal involvement in the peripheral nerves, respectively. It is also possible, however, that since the disease focuses on the peripheral sensory neurons, as suggested by Dyck (1993), degeneration involves either the peripherally and centrally directed axons of the dorsal root ganglion cells, or just the peripheral axons (Thomas, 1982).

In our opinion, these cases may represent a subset of autosomal dominant HSAN, or HSAN I described by Dyck (1993). This form is usually characterized by acrodystrophic symptoms with onset in the 2nd–3rd decade, but there is great variability in the onset and progression of the disease (Dyck, 1993). Our morphometric findings of profound loss of myelinated fibres with a relative preservation of unmyelinated fibres do not fit with previous data on HSAN I by Dyck (loss of unmyelinated fibres and small myelinated fibres) and by Danon and Carpenter (1985) (uniform loss for every fibre type), but rather resemble the pathological features of HSAN II (Nukada et al., 1982). A minor involvement of the unmyelinated nociceptive fibres could explain the absence of acrodystrophy, and this could result, in turn, in a delayed manifestation of the disease. Whether the differences between dominant HSN with ataxia and the classical form of HSAN...
I are due to phenotypic variability, or are expressions of different diseases, it is not known, but it will possibly be settled by molecular genetic investigations.

References


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Reply
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