Wetherbee Ail*

Documentation of a neurological disease in a Vermont family 90 years later

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SUMMARY *The neuropathological findings of a Farr family member consist of neuronal loss in the anterior horns and dorsal nuclei of Clarke, neuronal intracytoplasmic inclusions and posterior and lateral column demyelination. This report supports the role of familial amyotrophic lateral sclerosis as a link between common motor neuron disease and classical spinocerebellar degeneration.*

RÉSUMÉ: *Les découvertes neuropathologiques chez un membre de la famille Farr sont les suivantes: Perte neuronale dans les cornes spinales antérieures et les noyaux dorsaux de Clarke, inclusions neuronales intracytoplasmiques, et démyélination des faisceaux spinaux postérieurs et latéraux. Ce rapport soutient le rôle de la sclérose amyotrophique latérale familiale comme lien entre l'atrophie musculaire progressive et la dégénérescence spino-cérébelleuse classique.*

Dr. William Osler, in 1880, published a paper entitled "On Heredity in Progressive Muscular Atrophy as Illustrated by a Vermont Family". He described a progressive, fatal disease characterized by fasciculations, weakness and atrophy that affected 13 members of the family within two generations. The case reported below is the first description of the neuropathology of a member of this Vermont family and illustrates the debate over the nosology of this disease.

CASE REPORT

M.Y., a 35 year old woman, began to experience weakness in the left leg one year before her terminal admission. She then gradually developed weakness and atrophy of the left hand, right lower extremity and right hand. One month before admission she developed dyspnea which steadily worsened and she was admitted because of severe ventilatory insufficiency secondary to muscle weakness. On admission, in April 1972, there was poor respiratory excursion, atrophy of all extremities, areflexia and, except for slight movement of the left shoulder and right foot, quadriplegia. Sensation was normal for all modalities and no Babinski sign was present. The patient died on the second hospital day. At autopsy there was severe denervation-type atrophy of all muscles. The only gross neuropathologic finding was gray atrophy of the lumbar and cervical anterior roots. Microscopic neuronal changes included a moderate loss of neurons from the hypoglossal nuclei and dorsal motor vagal nuclei, severe neuronal loss from the anterior horns of cervical and lumbar cord with reactive gliosis, eosinophilic intracytoplasmic inclusions in many of the remaining lumbar anterior horn cells

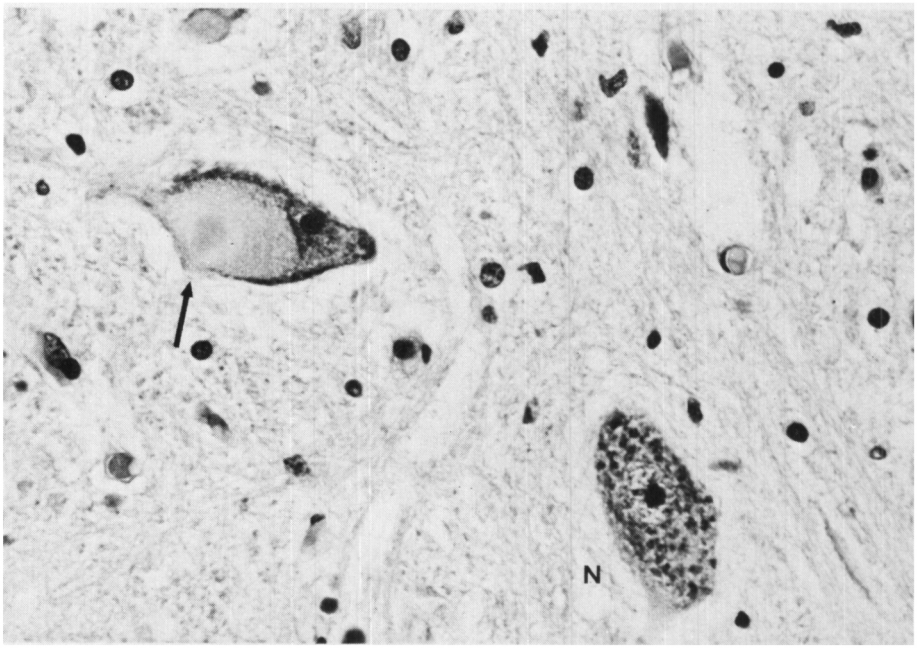

Figure 1. A lumbar anterior horn neuron with an eosinophilic, intracytoplasmic inclusion (arrow) lies adjacent to a normal neuron (N). Hematoxylin-eosin, x 100.

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* Wetherbee was the name of the Massachusetts family described by Madelaine Brown (1951) as an example of familial progressive muscular atrophy.

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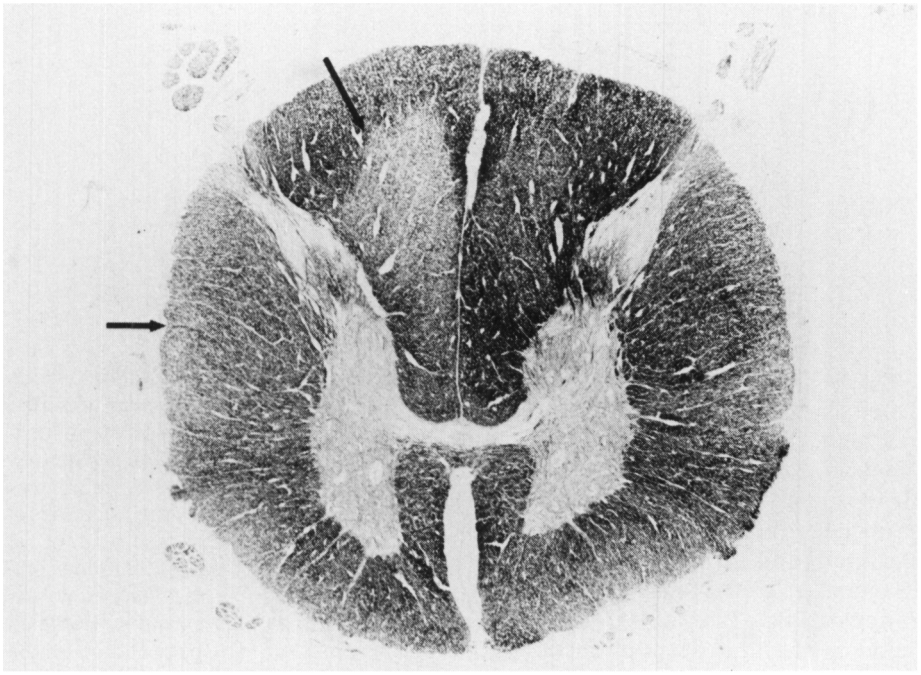

Figure 2. A section of lower thoracic spinal cord demonstrates asymmetrical posterior and lateral column pallor (arrows). Spielmeyer myelin stain, x 4.

(Fig. 1), and a moderate asymmetric loss of neurons from Clarke's column. Tract changes included severe asymmetric loss of axons and myelin throughout the cervical dorsal spinocerebellar tracts (Fig. 2) and lumbar posterior columns, with a moderate loss of axons and myelin in the lumbar lateral corticospinal tracts. Dorsal root ganglia were not submitted for examination.

DISCUSSION

The histologic changes in this case correspond exactly to the unique subgroup of familial amyotrophic lateral sclerosis described by Hirano et al. (1967). The neuropathologic findings indicate that these families can no longer be considered as hereditary examples of the common variety of motor neuron disease (Brown, 1951). Indeed, there are many striking pathological similarities between this disease and a recently reported spinocerebellar degeneration (Woods et al., 1972). This is an important nosologic consideration since there has been considerable interest in the possible role of virus infection in common motor neuron disease (McKann et al., 1973) while the spinocerebellar degenerations appear to result from a metabolic defect.

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