1 Motor Neuron Disease: The Clinical Syndrome

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The nomenclature of disorders of anterior horn cells is confused. This confusion reflects ignorance of the underlying causes of these syndromes; indeed, the current terminology is based on clinical or pathological descriptions of the syndromes themselves, rather than basic mechanisms. Rowland (1982, 1988) has pointed out the importance of distinguishing between motor neuron diseases and motor neuron disease in discussions of anterior horn cell disorders. The confusion in terminology can be resolved by appreciation of the historical development of the concept of anterior horn cell disease as a cause of muscle wasting.

Progressive muscular wasting was a clinical syndrome well known to physicians in the early nineteenth century. McHenry (1969) notes descriptions by Sir Charles Bell, Marshall Hall and Todd; at about this time the motor function of the ventral spinal roots and the sensory function of the posterior roots were defined independently by Bell and Magendie. The term progressive muscular atrophy was used by Aran (1850), who believed this syndrome was a muscular disorder. Duchenne (1849) also gave a description of this disorder. Thus, by the middle of the nineteenth century there were two conflicting views. Bell, supported by Cruveilhier (1853), who noted the thinness of the anterior spinal roots, regarded progressive muscular atrophy as a myelopathic disorder, whereas Aran and Duchenne favoured a muscular cause. Degeneration of anterior horn cells in the grey matter of the spinal cord was recognised independently by Luys (1860) in Paris, and by Lockhart Clarke in London. Charcot (1869) brought together these observations by studying the clinical and pathological features of the disease and described the involvement of the corticospinal tract. Charcot proposed the term amyotrophic lateral sclerosis (ALS) and recognised a clinical syndrome consisting of progressive muscular atrophy, often beginning in the hands and involving bulbar muscles, fibrillar contractions, especially during the period of active muscular atrophy, and permanent spasmodic contraction. Further, he noted the absence of sensory loss and that the disease was not complicated by paralysis of bladder or rectum, and that there was no tendency to the formation of bedsores. The myogenic origin of other cases of progressive muscular wasting, e.g. limb-girdle muscular dystrophy, was defined subsequently by von Leyden, Landouzy and Dejerine, and Erb (1891) (see McHenry 1969). Progressive bulbar palsy (primary labio-glosso-laryngeal paralysis) was described by Duchenne (1860). Charcot & Joffroy (1869) recognised its relationship to amyotrophic lateral sclerosis when loss of motor neurons was noted in the bulbar motor nuclei in pathological studies at the Hôpital Salpêtrière. Pure syndromes of myelopathic muscular atrophy without corticospinal involvement, and of primary lateral sclerosis (Spiller 1904) but without muscular atrophy are rare, as noted by Kinnier Wilson (1940) but these syndromes, nonetheless, have always been regarded as related to the core syndrome of amyotrophic lateral sclerosis. The term
motor neuron disease was introduced by Brain in recognition of the relation between the syndromes of progressive muscular atrophy, amyotrophic lateral sclerosis and progressive bulbar palsy, as shown by the clinical variation of involvement of upper and lower motor neurons and by the topography of the anterior horn cell loss and thus of the muscular wasting (see Brain 1962). This term has become commonly used in the United Kingdom, although Charcot's designation amyotrophic lateral sclerosis is preferred in French-speaking countries, and in the United States.

Rowland (1982) recognised the utility of the term motor neuron disease (MND) in describing the whole clinical syndrome but stressed the importance of retaining the general usage of the term motor neuron diseases (plural) to describe all the diseases of the anterior horn cells and motor system, including the inherited spinal muscular atrophies which are clinically and pathologically distinct from motor neuron disease (MND) itself. Similarly, heredo-familial diseases causing upper and lower motor neuron involvement, e.g. familial spastic paraplegia, do not form part of the MND syndrome itself, but are separate entities. The clinical syndrome of MND is sufficiently distinct to allow recognition of familial cases of MND, but uncertainty still arises in considering certain atypical syndromes, such as monomelic motor neuron diseases, and some juvenile onset cases. These problems in classification are considered below.

Classification of Motor Neuron Diseases

Diseases affecting anterior horn cells and bulbar motor neurons may present at any age from infancy to the senium. Those diseases beginning in infancy, childhood or adolescence are usually limited to the anterior horn cells, but in adults other parts of the motor system, including the upper motor neuron, may be involved, as in MND itself. Certain viruses, particularly poliomyelitis, show a predilection to infect anterior horn cells but other viruses, e.g. Herpes zoster and Coxsackie viruses may also affect anterior horn cells. In most motor neuron diseases motor nuclei in the brainstem are also involved; the term spinal muscular atrophy (SMA), usually used to denote a familial disorder without corticospinal tract involvement, does not therefore exclude bulbar involvement.

The cardinal features of neurogenic disorders are muscular weakness and wasting. In addition, disorders of anterior horn cells and bulbar motor nuclei are often characterised by prominent fasciculation at rest. This is particularly evident in more rapidly progressive disorders, e.g. MND in adults and Werdnig–Hoffmann disease (SMA Type 1) in infants. When there is involvement only of the lower motor neuron the tendon reflexes are reduced or absent but in MND itself, in which lower and upper motor neuron degeneration coexists, the tendon reflexes are characteristically brisker than normal, even in wasted muscles. The major forms of spinal muscular atrophy and MND are clearly defined clinically and pathologically; and in spinal muscular atrophies also by their pattern of inheritance.

Spinal Muscular Atrophies

Spinal muscular atrophy consists of a syndrome of progressive muscular atrophy and weakness due to anterior horn cell degeneration without involvement of