

## Peripheral Nerve Lesions in a Case of Equine Motor Neuron Disease

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**ABSTRACT.** A male 14-year-old Arab horse was pathologically diagnosed as equine motor neuron disease (EMND), which was kept as a breeding horse on a farm in Tokachi district of Hokkaido in Japan. On examination of the peripheral nerves, the most characteristic feature was Wallerian-type degeneration revealed by myelinoclasts associated with myelin ovoids which were sometimes infiltrated by macrophages. The other abnormalities were axonal swellings which were surrounded by thin myelin sheaths. Ultrastructurally, the axonal swelling was due to an accumulation of neurofilaments, and was accompanied by a thin and degenerating myelin sheath. In teased nerve fiber preparations, the most conspicuous change was myelinoclasts represented by segmentation into myelin ovoids or balls. Occasionally, segmental demyelination and axonal degeneration characterized by multifocal axonal swelling were observed.—**KEY WORDS:** equine, motor neuron disease, peripheral nerve.

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Equine motor neuron disease (EMND) is an acquired neuromuscular disease of horses, which is characterized pathologically by degeneration of motor neurons in the ventral horns of the spinal cord and in selected brain stem nuclei [1, 11, 12]. Degeneration or death of motor neurons results in secondary axonal degeneration and denervation atrophy of skeletal muscle. EMND is fatal disorder, which shows progressive weakness and wasting. It has already been pointed out that the clinical and pathologic features in EMND are similar to amyotrophic lateral sclerosis (ALS) in man [1, 11, 12]. Most of cases of EMND have occurred in the United State [1], however, cases have been reported in Canada [12], the United Kingdom [5], and Switzerland [8]. In 1994, the first case of EMND in Japan has been reported by Kuwamura *et al.* [7], which was a 9-year-old male Anglo-Arab horse kept in Okayama Prefecture in Japan. We describe here the pathology of the peripheral nerve lesion in the Arab horse diagnosed as EMND, since only few details were presented in the previous papers. Also, it is the purpose of this report to present the data of a occurrence of an additional case in Japan.

The animal used in this study was a male 14-year-old Arab horse which was kept as a breeding horse on a farm in Tokachi district of Hokkaido in Japan. Clinically, the horse revealed weakness and a short-strided gait first. Ordinarily, the head was placed under the body. Muscle fasciculation at the both femoral parts was frequently observed. At this time, the animal was clinically diagnosed as femoral nerve paralysis. The animal progressively had developed weight loss and weakness despite a normal appetite. No abnormalities were seen in general blood and serum examination. Its prognosis was diagnosed as being less favorable and the animal was euthanatized four weeks later after the onset of the clinical abnormalities.

No gross abnormalities were found in the visceral organs, nervous system and skeletal muscles.

Histopathological lesions were confined to the nervous system and skeletal muscles. Neuronal degeneration, which was represented by central chromatolysis and depletion of Nissle substance (ghost cell) was observed in the ventral

horn of the spinal cord at the all levels, although loss of neuron or gliosis as scar could not be detected. Occasionally, such degenerative neurons contained single or multiple eosinophilic inclusions (Fig. 1). In silver-impregnated sections, a few number of axonal degeneration or axonal swelling (or spheroids) was observed in the ventral horn of the spinal cord, especially around the degenerative neurons (Fig. 2). Axonal degeneration was also present in the vestibulospinal and rubrospinal tracts in the brain stem, and in the hypoglossal, facial and abducent nuclei. In the spinal ganglia and trigeminal ganglion, nodules of Nageotte were occasionally observed, which were evident where satellite cell proliferation replaced lost cell bodies. Although there was little evidence of degenerating fibers, severe fibrosis or profuse Renault body formation were present in the ventral and dorsal spinal roots at all levels examined. In paraffin sections, the fascicles of the peripheral nerves (N. medianus, N. ulnaris, N. radialis, N. peroneus communis, N. tibialis) revealed well populated with myelinated fibers, although mild abnormalities were seen in almost all nerves examined. Myelin ovoid and axonal degeneration were diffusely scattered. Some fascicles contained numerous Renault bodies. On semithin sections using paraformaldehyde-fixed specimens of the peripheral nerves, the most characteristic feature was Wallerian-type degeneration revealed by myelinoclasts associated with myelin ovoids which were sometimes infiltrated by macrophages (Fig. 3). Also seen were remyelinating fibers, which were surrounded by thin myelin sheaths. The other abnormalities were axonal swellings which were surrounded by thin myelin sheaths (Fig. 4). Ultrastructurally, the axonal swelling was due to an accumulation of neurofilaments, and was accompanied by a thin and degenerating myelin sheath (Fig. 5). In teased nerve fiber preparations, the most conspicuous change was myelinoclasts represented by segmentation into myelin ovoids or balls (Fig. 6b). Occasionally, segmental demyelination and axonal degeneration characterized by multifocal axonal swelling were observed (Figs. 6c, d). On the examination of fresh frozen sections taken from the skeletal muscles of the whole

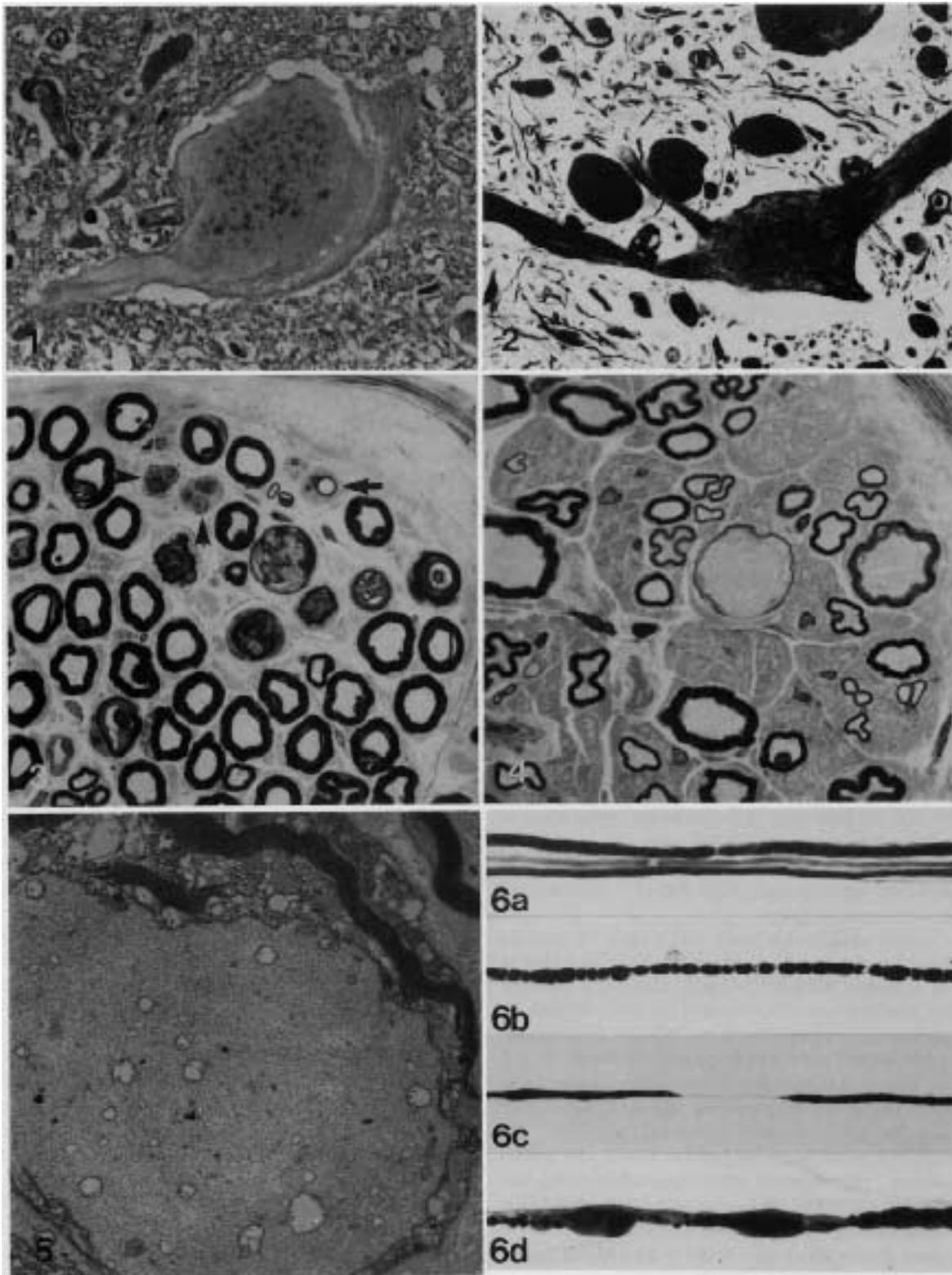


Fig. 1. Large, swollen neuron in the cervical ventral horn contains multiple intracytoplasmic inclusions. HE stain.  $\times 460$ .  
 Fig. 2. Numerous swollen axons (or spheroids) are seen close to the neuron in the cervical ventral horn. Bielschowsky stain.  $\times 450$ .  
 Fig. 3. A few Wallerian-type degeneration are present, which are revealed by myelinoclasts and myelin ovoids and are sometimes

body, mild to moderate lesions were observed symmetrically in almost all of the skeletal muscles. The characteristic changes consisted of solitary or multiple fascicles of small angular fibers among normal-sized fibers. However, such lesions, histochemically examined using ATPase reaction, revealed no fiber-type grouping. Also seen were targetoid fibers which were characterized by core-like structures in the central portion of the fibers in some muscles. NADH-TR activity was absent in the central zone of such targetoid fibers.

The pathological alterations reported in EMND were degeneration and loss of motor neurons in the spinal cord and brain stem resulted in axonal degeneration in the ventral roots and peripheral and cranial nerves and denervation atrophy of skeletal muscle. The pathological findings in our case were in good agreement with the observations previously reported [1, 11, 12]. In chronic cases of EMND, neuronal loss with resultant glial scarring may be the predominant lesion in the central nervous system [11–13]. Although statistical examination was not done, there was no decrease in the number of the neurons and no glial scarring in the spinal cord in the present case. These differences might be reflected in the duration of the disease: namely, our case might be in early phase or the initial stage of the disease. Also, our observations of the peripheral nerves and skeletal muscles might be consistent with the course of the disease, which revealed only scattering of degeneration, and no large group atrophy, respectively.

On the other hand, while relatively severe lesions were observed in the ventral horn of the spinal cord and the ventral spinal roots, the peripheral nerves revealed only scattering of myelinoclasia associated with axonal degeneration and there were no indication of chronic reactions including fiber loss or fibrosis. Although small and large group atrophy, as seen in severely affected muscles in EMND cases, is pathognomonic of denervation atrophy, no evidence of reinnervation (fiber-type grouping) is observed [12]. The present findings and those previous observations confirms that the degeneration of the axon begins close to the perikaryon of the motor neuron and migrate centrifugally into more distal regions of the peripheral nerves and skeletal muscles. However, as has already been pointed out [1, 12], the degenerative involvement of the trigeminal ganglion, spinal ganglia and dorsal spinal roots indicates that sensory peripheral nerve pathology is present in EMND. This fact of a parallel involvement of motor and sensory neurons suggests a more widespread metabolic disturbance in EMND than simply "sick" motor neurons.

In EMND cases reported [1] and the present case,

Wallerian-type degeneration was the most frequent change in the peripheral nerve. In addition to this alteration, axonal swellings composed of neurofilament accumulation were observed in the present case. The later changes are observed close to the cell bodies of motor neurons in motor neuron disease including in EMND [1, 10]. Although further studies are needed to confirmation, Wallerian-type degeneration represented by myelinoclasia might be induced by such axonal structural changes resulting from abnormalities in the synthesis, processing, organization, or transport of components necessary for the maintenance of the normal axonal cytoskeleton [10].

Although the etiology of EMND has not been determined, a deficiency in the lipid antioxidant vitamin E (alpha-tocopherol) have been recently suggested one of risk factors [2–4]. The white muscle disease in foal due to deficiency of tocopherol and selenium has been reported in Hidaka and Tokachi districts in Hokkaido, Japan [6, 9]. These facts do not exclude the possibility that the cases of EMND will continue to occur in Japan.

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infiltrated by macrophages (arrow heads). Also seen are remyelinating fibers, which are surrounded by thin myelin sheaths (arrow). N. medianus. Epon section. Toluidine blue stain.  $\times 520$ .

Fig. 4. Axonal swelling is present, which were surrounded by thin myelin sheaths. N. radialis. Epon section. Toluidine blue stain.  $\times 900$ .

Fig. 5. Electron micrograph of swollen axon showing accumulation of neurofilaments associated with a thin myelin sheath.  $\times 5,000$ .

Fig. 6. Teased fiber of N. radialis. (a) Control fiber. (b) Myelinoclasia represented by segmentation into myelin ovoids or balls. (c) Segmental demyelination. (d) Multifocal axonal swelling.  $\times 160$ .

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