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Equine Motor Neuron Disease: A Review of Clinical and Experimental Studies

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Epidemiological, pathological, laboratory, and experimental studies all support the hypothesis that equine motor neuron disease is an oxidative disorder associated with prolonged vitamin E deficiency. The role that pro-oxidants play in the disease has not been determined. All horses without access to green forage and/or with low plasma vitamin E levels should be supplemented with vitamin E.
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Equine motor neuron disease (EMND) is a neurodegenerative disorder of the somatic lower motor neurons of horses. The disease was first described in 11 horses in 1990.[1] Since that first report, a goal of our laboratory has been to find the cause of EMND so that it can be prevented. The purpose of this paper is to review the epidemiologic, pathological, clinical, and laboratory findings of EMND, in addition to reporting the recent experimental reproduction of the disease and some previously unpublished information from naturally occurring EMND cases. A review of these data provides strong support of a causative factor, and guidelines are provided for prevention of the disease.

Clinical Findings

Horses with acquired EMND are 2 years of age or older.[2,3] There is generally an acute onset of muscle trembling, a short-strided gait, almost constant shifting of weight in the pelvic limbs when standing, and excessive recumbency (Fig. 1). Muscle wasting is noticeable, and, in retrospect, owners frequently remark that weight loss was apparent before the trembling being observed.[2] Ocular fundus examination reveals brown reticular discoloration (Fig. 2) in nearly 40% of cases, although visual impairment is rarely reported.[4] The tail head is often carried in an elevated position and the head and neck in an abnormally low position.[2] In a smaller percentage of cases, trembling and constant shifting of weight either may not occur or may not be observed and the predominant clinical sign may be muscle wasting. A summary of clinical signs seen in horses with EMND is given in Figure 3. Although the clinical signs are characteristic for EMND, other neuromuscular disorders, especially some chronic myopathies and equine dysautonomia, may look clinically similar. A biopsy of the *sacrocaudalis dorsalis medialis* (tail head) muscle (Fig. 4) or spinal accessory nerve can be useful in confirming the diagnosis (sensitivity >90%).[5,6] Approximately 40% of horses with EMND continue to deteriorate and are euthanized within 4 weeks of onset of signs. A similar proportion have marked improvement in clinical signs within 4 to 6 weeks following either relocation to another stable or administration of antioxidants, whereas the remaining 20% survive with permanent and noticeable atrophy.

Laboratory Findings

The only consistently abnormal laboratory finding on routine hematologic and serum chemical analyses is a mild to moderate elevation in serum muscle enzyme (creatine kinase and aspartate aminotransferase) activity.[2] Plasma vitamin E values are consistently low (<1 μg/mL), selenium is normal, vitamin A is slightly low to normal, and serum ferritin is frequently high in horses with EMND.[7]

In the spinal cord of EMND affected horses, copper is increased compared with controls,[8] and vitamin E is low (Fig. 5) (Jackson C, Kayden HJ, Traber M, personal communication). Hepatic concentrations of copper are normal (mean 4.48 ppm), iron is frequently elevated (mean 540 ppm), and vitamin E is consistently low (mean 0.91 μg/g). Normal published ranges for the nutrients are: copper (2-10 ppm wet

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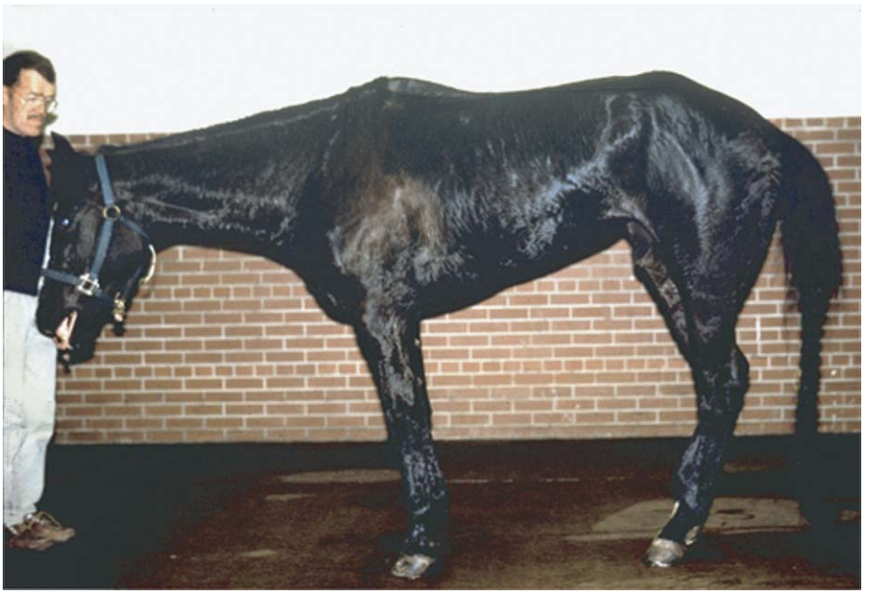

Figure 1 An adult horse with typical clinical appearance of EMND. The limbs are "camped" under the body, the neck is held lower than normal, and muscle wasting and excessive sweating are evident. Holding the horse is the late Dr. John Cummings, who first reported the disease in 1990.

weight), iron (200-500 ppm wet weight), and vitamin E (20-40 μg/g dry weight).

Oral glucose absorption tests performed on EMND cases have revealed a reduction in the rate and amount of glucose absorption in several cases.[2] Oral xylose absorption may also be slightly abnormal, but not to the same degree as glucose absorption. Red blood cell superoxide dismutase (SOD_1) activity was found to be lower in a group of EMND cases than controls, but there was no excessive polymorphism in the SOD_1 gene between the two groups.[9]

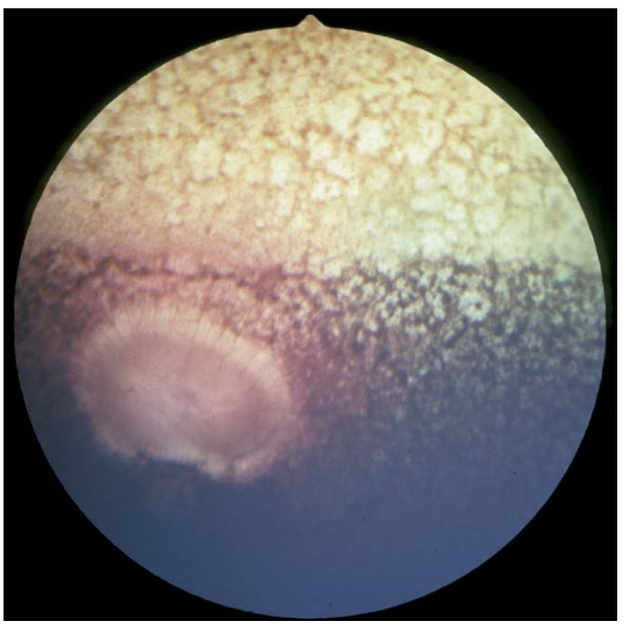

Figure 2 Fundus photograph of horse with EMND. The brown pigment is an abnormal ceroid-lipofuscin accumulation within the retinal pigment epithelium.

Pathology

Pathologic findings are generally limited to the lower motor neuron system.[1,10] In acute cases, there is noticeable neuronal degeneration (swollen, chromatolytic somata with distorted nuclei) and loss of somatic motor neurons in the spinal cord ventral horns. In more chronic, "arrested" cases, glial scars, consisting of astrocytes and lipofuscin-laden microglia and a paucity of motor neurons, may be the only noticeable microscopic finding. Loss of approximately 30% of somatic motor neurons must occur before clinical signs are obvious.[11] All brainstem cranial nerve somatic motor nuclei, except those of cranial nerves III, IV, and VI, have microscopic lesions, although clinical signs of cranial nerve deficits are subtle or nonexistent. There is degeneration of myelinated axons in the ventral roots and in peripheral nerves associated with the loss of parent motor neurons. Muscles with a predominance of type I fibers are more severely atrophied than are those with mostly type II fibers.[1,12] Overall, there is a change in myofibrillar metabolic features, including reduced oxidative capacity and increased glycolytic activity, corresponding to a shift from slow to fast fibers.[13] In fact, the only macroscopic visible lesion in the neuromuscular system of affected horses at necropsy examination is a paleness of the deeper muscles of the limbs, which normally have a large percentage of type I fibers.[12]

Lipopigment deposition is always observed in the endothelial cells of capillaries in the spinal cord and the retinal epithelium,[4,14] and abnormal lipopigment deposition is occasionally found in the liver and gut (brown bowel disorder) (Fig. 6).

Despite the abnormal oral glucose absorption curve in many horses with EMND, body fat stores at necropsy examination usually appear normal. Because of the abnormal glucose absorption curves in many horses, the small intestine of affected horses was studied retrospectively in more detail.