CARAMELLI, M., CASALONE, C., ELENI, C., DI GUARDO, G., PETRELLA, A., TROIANO, P., AGRIMI, U., BUSANI, L. & POCCHIARI, M. (1998) Comparison of neuropathological findings and PrP^{res} immunolocalization in sheep and goat scrapie. Proceedings of the 16th Meeting of the European Society of Veterinary Pathology, Lillehammer, Norway, September 23 to 26, 1998

CRAVERO, G. C., GUARDA, F., DOTTA, U. & GUGLIELMINO, R. (1977) La scrapie in pecore di razza biellese. Prima segnalazione in Italia. *Clinica Veterinaria* **100**, 1-5

DEAN, A. G., DEAN, J. A., COULOMBIER, D., BRENDEL, K. A., SMITH, D. C., BURTON, A. H., DICKER, R. C., SULLIVAN, K., FAGAN, R. F. & ARNER, T. G. (1995) Epi Info, Version 6: A Word-Processing, Database, and Statistics Program for Public Health on IBM-compatible Microcomputers. Atlanta, Centers for Disease Control and Prevention

DETWILER, L. A. (1992) Scrapie. *Revue Scientifique et Technique – Office International des Epizooties* **11**, 491-537

FOSTER, J. D., HOPE, J. & FRASER, H. (1993) Transmission of bovine spongiform encephalopathy to sheep and goats. *Veterinary Record* **133**, 339-341

FRASER, H. (1976) The pathology of natural and experimental scapie. In Slow Virus Disease of Animals and Man. Ed R. H. Kimberlin. Amsterdam, North Holland Publishing Co. pp 267-305

FRASER, H. & DICKINSON, A. G. (1973) Agent-strain differences in the distribution and intensity of grey matter vacuolation. *Journal of Comparative Pathology* **83**, 29-40

GOLDMANN, W., HUNTER, N., FOSTER, J. D., SALBAUM, J. M., BEYREUTHER, K. & HOPE, J. (1990) Two alleles of a neural protein gene linked to scrapie in sheep. *Proceedings of the National Academy of Sciences of the USA* **87**, 2476-2480

GREIG, J. R. (1950) Scrapie in sheep. *Journal of Comparative Pathology* **60**, 263-266

HARITANI, M., SPENCER, Y. I. & WELLS, G. A. H. (1994) Hydrated autoclave pretreatment enhancement of prion protein immunoreactivity in formalin-fixed bovine spongiform encephalopathy-affected brain. *Acta Neuropathologica* **87**, 86-90

HILL, A. F., DESBRUSLAIS, M., JOINER, S., SIDLE, K. C. L., GOWLAND, I., COLLINGE, J., DOEY, L. J. & LANTOS, P. (1997) The same prion strain causes vCJD and BSE. *Nature* **389**, 448-450

HOINVILLE, L. (1996) A review of the epidemiology of scrapie in sheep. *Revue Scientifique et Technique – Office International des Epizooties* **15**, 827-852

HUNTER, N., GOLDMANN, W., BENSON, G., FOSTER, J. D. & HOPE, J. (1993) Swaledale sheep affected by natural scrapie differ significantly in PrP genotype frequencies from healthy sheep and those selected for reduced incidence of scrapie. *Journal of General Virology* **74**, 1025-1031

HUNTER, N., MOORE, L., HOSIE, B. D., DINGWALL, W. S. & GREIG, A. (1997) Association between natural scrapie and PrP genotype in a flock of Suffolk sheep in Scotland. *Veterinary Record* **140**, 59-63

POCCHIARI, M., XI, Y. G., INGROSSO, L., LADOGANA, A., CARDONE, F., MASULLO, C., RIGHETTO, Z., BIGON, E., DI MARTINO, A. & CALLEGARO, L. (1994) Immunodiagnosis of bovine spongiform encephalopathy. *Livestock Production Science* **38**, 41-46

SIGURDARSON, S. (1991) Epidemiology of scrapie in Iceland and experience with control measures. In Sub-acute Spongiform Encephalopathies. Eds R. Bradley, M. Savey, B. Marchant. Dordrecht, Kluwer Academic Publishers. pp 233-242

SIMMONS, M. M., HARRIS, P., JEFFREY, M., MECK, S. C., BLAMIRE, I. W. H. & WELLS, G. A. H. (1996) BSE in Great Britain: consistency of the neurohistopathological findings in two random annual samples of clinically suspect cases. *Veterinary Record* **138**, 175-177

WILL, R. G., IRONSIDE, J. W., ZEIDLER, M., COUSENS, S. N., ESTIBEIRO, K., ALPEROVITCH, A., POSER, S., POCCHIARI, M., HOFMAN, A. & SMITH, P. G. (1996) A new variant of Creutzfeldt-Jakob disease in UK. *Lancet* **347**, 921-925

XI, Y. G., CARDONE, F. & POCCHIARI, M. (1994) Detection of proteinase resistant protein (PrP) in small brain tissue samples from Creutzfeldt-Jakob disease patients. *Journal of Neurological Sciences* **124**, 171-173

Electromyography under caudal epidural anaesthesia as an aid to the diagnosis of equine motor neuron disease

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Electromyography was used as an aid to the diagnosis of equine motor neuron disease in a conscious horse while it was under caudal epidural anaesthesia. A muscle biopsy was taken to confirm the diagnosis which was then supported by a postmortem examination.

ELECTROMYOGRAPHY is a well-established method of assessing the electrical activity of muscle. It is useful as an aid to the clinical diagnosis of many peripheral nerve diseases which result in the functional denervation of muscle fibres and myopathies (Daube 1991, Podell and others 1995). However, its value in the conscious horse is limited by the presence of movement artefacts or volitional activity, and although they can be overcome by performing the technique under general anaesthesia, there are risks associated with general anaesthesia in horses (Johnston and others 1995).

Equine motor neuron disease (EMND) is a neuromuscular disease which was first reported by Cummings and others (1990). It is associated with degenerative changes in lower motor neurons in the brainstem and spinal cord with no involvement of upper motor neurons (Polack and others 1998). The disease is similar to amyotrophic lateral sclerosis (motor neuron disease) in man. It is suspected that the disease has occurred in the UK since 1993 (Hahn and Mayhew 1993, Proudman and others 1993), but there have been no published cases that have been confirmed histopathologically. One case reported in Ireland was confirmed by examining a biopsy of a spinal accessory nerve taken under general anaesthesia (Prendergast and others 1994). This paper describes the use of electromyography under caudal epidural anaesthesia as an aid to the diagnosis of the disease in a conscious horse.

CASE HISTORY

A nine-year-old Irish draught thoroughbred cross showjumping mare from east-central Scotland had been observed constantly shifting its weight on its pelvic limbs for a month. It was also observed to lift its tailhead, be sweating and trembling, be losing weight, particularly over its hind quarters, and

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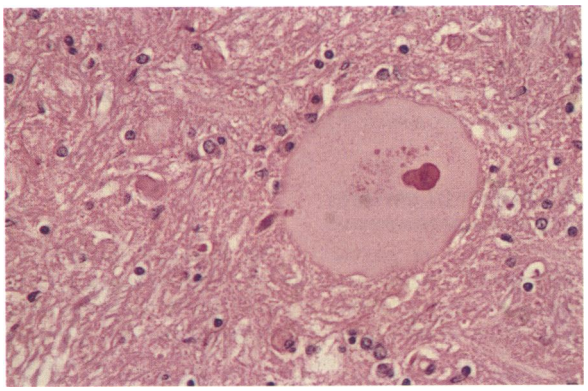

FIG 1: Chromatolytic motor neuron with cytoplasmic inclusions in the nucleus of cranial nerve VII, next to an accumulation of glial cells removing the remainder of a necrotic neuron. Haematoxylin and eosin. x 400

to be lying down for longer than normal. The horse had access to poor pasture for a few hours daily.

The clinical signs of profound sweating and trembling during periods of standing were most marked on its arrival at the hospital after it had been standing for several hours during the journey. Muscle tremors were observed over its hindquarters, forelimbs and neck. The horse adopted a base-narrow stance at rest and constantly shifted its weight between the pelvic limbs. Its cervical, forelimb and hindquarter muscle masses were atrophied. The tailhead was raised, and the tail and palpebral musculature appeared to be weak. Its pupils were more dilated and responded more slowly to light than the pupils of control horses in the same environment, but a fundoscopic examination did not reveal any lesions. No significant abnormalities were detected by an orthopaedic evaluation and no gait, proprioceptive, cranial nerve or cerebral deficits were observed. The horse appeared to be more comfortable when moving than when standing, and its pelvic limb gait had a slapping motion at the end of protraction.

Its serum creatinine kinase (CK) activity (877 iu/litre, normal range 150 to 385 iu/litre) and its aspartate aminotransferase (AST) activity (700 iu/litre, normal range 258 to 554 iu/litre) were mildly raised; and its serum α-tocopherol concentration, an indicator of vitamin E status, was low (0·8 μmol/litre, normal range 3 to 20 μmol/litre).

A provisional diagnosis of EMND was made. Differential diagnoses included exertional rhabdomyolysis on the basis of the muscle atrophy and tremors and the mildly raised activities of muscle enzymes. Grass sickness was considered on the basis of the clinical signs of weight loss, base-narrow stance, muscle tremors and the area from which it came; however the horse maintained a good appetite and during periods of recumbency the tremors resolved. Botulism was discounted because the horse prehended, masticated and swallowed well, had no access to silage and had no clinical findings suggestive of flaccid paralysis.

The mare was sedated with 60 μg/kg romifine (Sedivet; Boehringer Ingelheim) and 0·12 mg/kg morphine (Morphine sulphate; Evans Pharmaceuticals) administered intravenously. It was anaesthetised with a sacrococcygeal epidural injection of 0·2 mg/kg lignocaine hydrochloride (2 per cent Lignavet Injection; C-Vet Veterinary Products) so that it could be examined electromyographically and a biopsy of the sacrocaudalis dorsalis medialis muscle could be taken. The electromyography was carried out with an electrodiagnostic unit (Neurostar MS92B; Medelec) by inserting a reference and ground electrode subcutaneously just cranial to the tailhead. The recording electrode was inserted into the sacrocaudalis dorsalis medialis muscle on the side which it was not intended to biopsy. The electromyogram revealed spontaneous fibrillation potentials and trains of positive sharp waves consistent with lower motor neuron disease.

A muscle biopsy was taken as described by Valentine and others (1998) and a histopathological examination revealed small groups of angular atrophied fibres and numerous fibres containing single and multiple internal nuclei. A few fibres were markedly hypertrophic. These changes were consistent with a relatively recent onset of denervation and were similar to the changes observed in other cases of EMND (Valentine and others 1998).

To determine whether the horse's glucose metabolism was abnormal, as had been reported in previous cases (Divers and others 1994), it was given an oral glucose absorption test. After being starved for 12 hours, 1 g glucose/kg bodyweight was administered as a 20 per cent solution by nasogastric tube (Mair and others 1991). The horse's blood glucose concentration had increased by only 63 per cent two hours after administration, compared with a normal response of a 100 per cent increase (Mair and others 1991). To investigate whether this low hyperglycaemic response was due to intestinal malabsorption or to a change in its peripheral glucose metabolism, the horse's serum insulin concentration was measured two days later and it was given an intravenous glucose tolerance test. After being starved for 12 hours, 0·5 g/kg of 40 per cent glucose solution (Arnolds Veterinary Products) was injected rapidly, in approximately one minute. The horse's serum insulin concentration (4·6 μU/ml, normal range 5·4 to 36 μU/ml) and its response to the intravenous glucose tolerance test were considered normal; its blood glucose concentration had increased by 328 per cent over baseline after 15 minutes, and had returned to below the baseline value by two hours (Garcia and Beech 1986).

The horse was euthanased after the diagnosis of EMND had been confirmed by the histopathology of the muscle biopsy.

Pathology

There was diffuse muscle atrophy and pale discoloration of the medial head of the triceps. The brain, spinal cord, trigeminal ganglion, cranial cervical ganglion and a section of the ventral branch of the spinal accessory nerve (Jackson and others 1996) were removed and fixed in 4 per cent buffered neutral formaldehyde. Sections of brain were taken at the level of the basal nuclei, thalamus, midbrain, rostral pons, and rostral and caudal medulla oblongata. Segments from the cranial cervical spinal cord, cervicothoracic intumescence, thoracic spinal cord and lumbosacral intumescence were examined. Haematoxylin and eosin-stained tissue sections revealed neuronal degeneration in the motor nucleus of the trigeminal nerve, the nucleus of the facial nerve and in every segment of the spinal cord examined, with the exception of a section from the fifth thoracic spinal cord segment. A few neurons in affected nuclei were swollen and chromatolytic with a variable loss of Nissl substance. Some neurons contained multiple eosinophilic cytoplasmic inclusions (Fig 1). Focal aggregates of glial cells with prominent astrocytes and a few macrophages marked the site of earlier neuronal cell death. There were a few spheroids (swollen axons) in the ventral horns of the spinal cord, and there was evidence of very mild Wallerian-like degeneration in the ventral funiculi. There was marked, multifocal, active Wallerian degeneration in the spinal accessory nerve. No pathological changes were evident in the preganglionic parasympathetic neurons in the brainstem, or in the pre- and postganglionic neurons in the spinal cord and cranial cervical ganglion, ruling out a diagnosis of grass sickness. Sections of the retina were stained with haematoxylin and eosin, periodic acid-Schiff (PAS) and Schmorls and examined under fluorescent microscopy (Riis and others 1999) for the presence of lipofuscin. There was a moderate amount of granular, PAS-positive material in the cells of the retinal pigment epithelium, some of which were distended with this material. The sections and a positive control autofluoresced intensely, consistent with a moderate accumulation of ceroid lipofuscin-like material.

DISCUSSION

Equine motor neuron disease was reported as a new neurological disorder in 1990 (Cummings and others 1990), although a retrospective study of stored muscle biopsies identified a case in 1985 (Valentine and others 1998). It has been suspected in the UK since 1993 but no cases have been confirmed histopathologically. The similarities and differences between this disease and grass sickness make it an important differential diagnosis, especially in central Scotland (Divers 1999).

The disease is an acquired neurodegenerative disorder which affects adult horses that have little or no access to fresh grass or are fed poor quality hay. The clinical syndrome can be explained by profound extensor weakness in the weight-bearing muscle masses and includes neurogenic muscular atrophy, increased periods of recumbency and trembling of the postural musculature. Other signs have included shifting weight, base-narrow stance, low neck posture, high tailhead carriage, normal to ravenous appetite, coprophagia, and deposits of lipofuscin on the tapetal-non-tapetal junction of the fundus (Cummings and others 1990, Divers and others 1992, Riis and others 1999). An absence of gross changes in the fundus has been reported, although the cells of the retinal pigment epithelium usually appear to be congested with ceroid-lipofuscin when the retina is examined histopathologically (Riis and others 1999).

Electromyography evaluates the electrical activity within the motor unit. A motor unit is defined as a lower motor neuron and a finite number of muscle fibres. Electromyograms are often recorded in anaesthetised horses to eliminate the artefacts generated by volitional activity and movement, but general anaesthesia in horses is not without risk (Johnston 1995) and is expensive. Weak horses have particular difficulty in recovering from general anaesthesia, and electromyography under sedation and caudal epidural anaesthesia can corroborate a clinical diagnosis of EMND without putting the horse at any extra risk. Skeletal muscle is electrically quiescent if no volitional or reflex activity occurs, and spontaneous activity is classically associated with neuromuscular abnormalities. In this case, trains of positive sharp waves and fibrillation potentials were recorded which were consistent with partial or complete denervation. Positive sharp waves are often observed first in the process of denervation. The electromyographic results were similar to those observed in other horses with EMND (Cummings and others 1990) but they are not specific for EMND and can also be observed in other myopathic disorders. The electromyography provided evidence of neuromuscular disease which was subsequently confirmed by the muscle biopsy. The constant shifting of weight by the horse during the recording caused some difficulty, but with patience, a satisfactory result was obtained.

The mild increases in serum CK, AST and the low level of vitamin E were consistent with previous findings (Divers and others 1994). As in this case, many horses with EMND have low hyperglycaemic responses to an oral glucose tolerance test (Divers and others 1994) which may be due either to intestinal malabsorption or to the increased peripheral utilisation of absorbed glucose (Divers and others 1994). However, the horse's normal response to the intravenous glucose tolerance test and its normal blood insulin concentrations were consistent with findings in other horses with EMND (T. Divers, personal communication), and suggested that its low response to the oral test was due to intestinal malabsorption. As in other cases (Divers and others 1994), no gross or histological abnormalities of the small intestine or pancreas were detected. It is possible that the malabsorption may be associated with the abnormal ultrastructure identified in the mitochondria of intestinal epithelial cells (T. Divers, personal communication). Abnormal glucose metabolism, including a reduction in the number of insulin receptors and the associated reduction in insulin sensitivity (Perurena and Festoff 1987) is also a characteristic of human motor neuron disease (Karim and others 1993). It is uncertain whether this is a primary dysfunction or a secondary effect due to the decreased utilisation of glucose by atrophic muscles (Reyes and others 1984).

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References

CUMMINGS, J., DE LAHUNTA, A., GEORGE, C., FUHRER, L., VALENTINE, B. A., COOPER, B. J., SUMMERS, B. A., HUXTABLE, C. R. & MOHAMMED, H. O. (1990) Equine motor neuron disease: a preliminary report. *Cornell Veterinarian* **80,** 357-379

DAUBE, J. R. (1991) AAEM Minimonograph #11: Needle examination in clinical electromyography. *Muscle and Nerve* **14,** 685-700

DIVERS, T. (1999) Comparing equine motor neuron disease (EMND) with equine grass sickness (EGS). *Equine Veterinary Journal* **31,** 90-91

DIVERS, T., MOHAMMED, H. O., CUMMINGS, J., DE LAHUNTA, A., VALENTINE, B. A., SUMMERS, B. A. & COOPER, B. J. (1992) Equine motor neuron disease: a new cause of weakness, trembling and weight loss. *Compendium on Continuing Education for the Practicing Veterinarian* **14,** 1222-1226

DIVERS, T., MOHAMMED, H. O., CUMMINGS, J. F., VALENTINE, B. A., DE LAHUNTA, A., JACKSON, C. A. & SUMMERS, B. A. (1994) Equine motor neuron disease: findings in 28 horses and proposal of a pathophysiological mechanism for the disease. *Equine Veterinary Journal* **26,** 409-415

GARCIA, M. C. & BEECH, J. (1986) Equine intravenous glucose tolerance test: glucose and insulin responses of healthy horses fed grain or hay and of horses with pituitary adenoma. *American Journal of Veterinary Research* **47,** 570-572

HAHN, C. N. & MAYHEW, I. G. (1993) Does equine motor neuron disease exist in the United Kingdom? *Veterinary Record* **132,** 133-134

JACKSON, C. A., DE LAHUNTA, A., CUMMINGS, J. F., DIVERS, T. J., MOHAMMED, H. O., VALENTINE, B. A. & HACKETT, R. P. (1996) Spinal accessory nerve biopsy as an ante mortem diagnostic test for equine motor neuron disease. *Equine Veterinary Journal* **28,** 215-219

JOHNSTON, G. M., TAYLOR, P. M., HOLMES, M. A. & WOOD, J. L. (1995) Confidential enquiry of perioperative equine fatalities (CEPEF-1): preliminary results. *Equine Veterinary Journal* **27,** 193-200

KARIM, A. R., VIRK, P. K., ROSSI, M. L., WILLIAMS, A. C. & STURMAN, S. G. (1993) Interaction of motor neurone disease plasma with glucose transport. *Functional Neurology* **8,** 89-94

MAIR, T. S., HILLYER, M. H., TAYLOR, F. G. R. & PEARSON, G. R. (1991) Small intestinal malabsorption in the horse: an assessment of the specificity of the oral glucose tolerance test. *Equine Veterinary Journal* **23,** 344-346

PERURENA, O. H. & FESTOFF, B. W. (1987) Reduction in insulin receptors in amyotrophic lateral sclerosis correlates with reduced insulin sensitivity. *Neurology* **37,** 1375-1379

PODELL, M., VALENTINE, B. A., CUMMINGS, J. F., MOHAMMED, H. O., COOPER, B. J., REED, S., DIVERS, T. J., JACKSON, C. A. & DE LAHUNTA, A. (1995) Electromyography in acquired equine motor neuron disease. *Progress in Veterinary Neurology* **6,** 128-134

POLACK, E. W., KING, J. M., CUMMINGS, J. F., DE LAHUNTA, A., DIVERS, T. J. & MOHAMMED, H. O. (1998) Quantitative assessment of motor neuron loss in equine motor neuron disease (EMND). *Equine Veterinary Journal* **30,** 256-259

PRENDERGAST, M., BASSETT, H. F. & CUMMINGS, J. F. (1994) Equine motor neuron disease. *Veterinary Record* **135,** 416

PROUDMAN, C. J., KNOTTENBELT, D. C. & EDWARDS, G. B. (1993) Equine motor neuron disease. *Veterinary Record* **132,** 198-199

REYES, E. T., PERURENA, O. H., FESTOFF, B. W., JORGENSEN, R. & MOORE, W. V. (1984) Insulin resistance in amyotrophic lateral sclerosis. *Journal of Neurological Science* **63,** 317-324

RIIS, R. C., JACKSON, C., REBHUN, W., KATZ, M. L., LOEW, E., SUMMERS, B., CUMMINGS, J., DE LAHUNTA, A., DIVERS, T. & MOHAMMED, H. (1999) Ocular manifestations of equine motor neuron disease. *Equine Veterinary Journal* **31,** 99-110

VALENTINE, B. A., DIVERS, T. J., MURPHY, D. J. & TODHUNTER, P. G. (1998) Muscle biopsy diagnosis of equine motor neuron disease and equine polysaccharide storage myopathy. *Equine Veterinary Education* **10,** 42-50

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