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Nonsuppurative Meningoencephalomyelitis of Unknown Etiology in Mink

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Abstract. A central nervous system disease of mink occurred in three unrelated fur farms in Oregon in September, 1981. Only kits four to five months old were affected. Clinical signs consisted of posterior ataxia progressing to complete posterior paralysis with loss of motor control and sensation. Complete or partial recovery occurred in approximately 1.5 months in most mink. Microscopic lesions consisted of severe nonsuppurative meningoencephalitis and meningomyelitis with vacuolation of the white matter of the brain and spinal cord. Canine distemper virus infection and other recognized causes were ruled out on the basis of clinical signs, history, lesions, or laboratory findings. Experimental inoculations of mink with brain and spinal cord specimens from affected mink failed to reproduce the disease.

Mink from three farms were submitted to Oregon State University Veterinary Diagnostic Laboratory because of central nervous system disease. Mink on the unrelated farms had similar signs, and the onset occurred during the last two weeks of September, 1981 on all three premises. Similar histologic lesions were prominent in the brains and spinal cords of mink from the three sources. The cause of the disease was not determined, but laboratory and clinical findings discounted known central nervous system diseases of mink. This article will describe this previously unreported central nervous system disease of mink.

Clinical History

The disease occurred in the Willamette Valley of Western Oregon on three unrelated farms which were geographically separated by 15 to 60 miles. Interestingly a mink farm situated about 20 feet across a guard fence from farm B, and which shared mixed feed with it, reported no affected mink.

The first clinical cases were noticed on each of the farms during the last two weeks of September 1981. On each farm new cases occurred for approximately two weeks. Morbidities and mortalities on the farms are shown in table I. Management and housing conditions on the farms were similar, and diet on the farms consisted of fresh frozen turkey, chicken, fish by-products, cereal, and vitamin E and vegetable supplements. Kits on all farms, born in May, were vaccinated parenterally with botulism toxoid and killed mink virus enteritis vaccine (United-Invenex Veterinary Laboratory, Middleton, WI). Canine distemper vaccination was by spray administration of a modified live virus product (Spray Vac, American Laboratory, Madison, WI). All vaccinations took place in late July.

The disease affected only four- to five-month-old kits. On two of the farms a greater portion of males were affected, while the third owner had no information regarding sex distribution. On all three farms the disease incidence was higher in the mutation color phases than in the standard dark mink. Likewise, the incidence was higher in mink of the Aleutian genotype than in non-Aleutian color phases.

The initial clinical signs exhibited by the affected kits were ataxia and loss of coordination in the pelvic limbs. These signs progressed within a few days to complete paralysis of the pelvic limbs to the degree that the mink could no longer hold themselves upright to reach the feed placed on the top of the pen. If feed was placed in the bottom of the pen for them, the mink continued to eat. Intramuscular injections in the rear legs elicited no pain response by the mink. Thus, it appeared that there was a loss of both muscle control and sensation in the rear legs. Noticeable atrophy of muscles occurred. In mink that did not die, motor control of rear limbs returned in about 1.5 months, but some did not recover fully and were still somewhat ataxic and spastic in the

Table I. Morbidity and mortality of central nervous system disease in mink kits on three farms

Farm	Number of kits		
	Total on farm	Central nervous system disease	
		Exhibited signs	Died
A	8000	200	10
B	4000	300	75
C	2600	40	0

movement of their rear legs when observed by one of the authors (WW) in late November, 1981. Pelts of the affected mink were of acceptable quality when harvested in November or December. The affected mink appeared to be evenly distributed throughout the barns on each ranch. There has been no recurrence of the disease on any of the farms during the 1982, 1983, or 1984 production cycles.

Results

Necropsy of nine mink, including eight males, from farm A disclosed two with pneumonia and one with myocardiopathy and myopathy. Histology confirmed these lesions, and *Pseudomonas aeruginosa* was isolated from both mink with pneumonia while the myopathy and myocardiopathy was attributed to vitamin E deficiency. One of two male mink necropsied from farm B had mild enteritis and a group C *Salmonella* sp was isolated from a mesenteric lymph node. A male kit from farm C had severe urinary cystitis, and a female from this farm had no macroscopic lesions. None of the mink had macroscopic lesions in the central nervous system.

The significant microscopic findings in mink from all farms were nonsuppurative meningoencephalitis and meningomyelitis. In farm A, one kit with pneumonia and the one with myopathy and myocardiopathy had no central nervous system lesions, but the remaining seven had lesions in both the brain and spinal cords. Both kits from farm B had lesions in the brains and one of these had lesions in the spinal cord. The spinal cord of the second was not examined. A male mink from farm C had brain but not spinal cord lesions, and a female from this farm had lesions in the spinal cord but not in the brain.

The microscopic central nervous system lesions in the mink from all farms were similar. Cerebral, cerebellar, and spinal cord meninges contained mild to marked lymphocytic and mild plasmocytic infiltrates with occasional dense foci and many perivascular lymphocytic cuffs. Microscopic lesions in the brain and spinal cord were predominantly lymphocytic and lymphoplasmocytic perivascular cuffs, and multiple inflammatory foci that consisted of microglia and lymphocytes with occasional swollen astrocytes (fig. 1). The inflammatory foci were predominately small, discrete, and dense but occasionally were rather large, sparsely cellular, and poorly demarcated. Perivascular cuffs and inflammatory foci were scattered throughout the cerebrum but were less numerous in the cortex, corona radiata, and internal capsule than in the hippocampus. These lesions generally were progressively more numerous and severe caudally in the diencephalon, brainstem and cerebellum where the molecular layer of the cortex (fig. 2) and the medulla were involved. In all but one of the mink with brain lesions, similar perivascular cuffs and inflammatory foci were scattered through the cervical, thoracic, and lumbar segments of the spinal cord involving both the gray and white matter (fig. 3).

Vacuolation of the white columns of the spinal cord occurred with variable intensity and distribution. Swollen degenerative axons were in these foci of vacuolation, occasionally in areas of white matter of spinal cord or brainstem without distinctive vacuolation (fig. 4), and associated with a few inflammatory foci in the gray matter of the spinal cord. Small numbers of microglia or lymphocytes infiltrated areas of vacuolation and occasional swollen myelin sheaths contained unidentifiable degenerating cells, probably leukocytes. Several mink had small subcortical foci of vacuolation in the cerebrum and some had mild focal vacuolation in the cerebellar medulla and peduncles. In the brainstem, vacuolation was most distinctive and consistent in the ventrolateral aspect of the pons in the area of the trigeminal nerve (fig. 5). In two mink brains fortuitously sectioned through the trigeminal nerve, vacuolation extended into the trigeminal nerve and in the one section that included the junction of the central and peripheral nervous systems, the vacuolation stopped at this site (fig. 6). Less distinctive and consistent vacuolation was in the pyramidal and medial longitudinal fascicular region of the pons. Occasional foci of vacuolation were scattered through other areas of the brainstem.

In addition to the brains and spinal cords, the lungs, livers, kidneys, stomachs, urinary bladders, small and large intestines, heart, and skeletal muscles were examined without significant findings except as described above. Lungs, livers, and kidneys from four mink of farm A and two mink each of farms B and C were

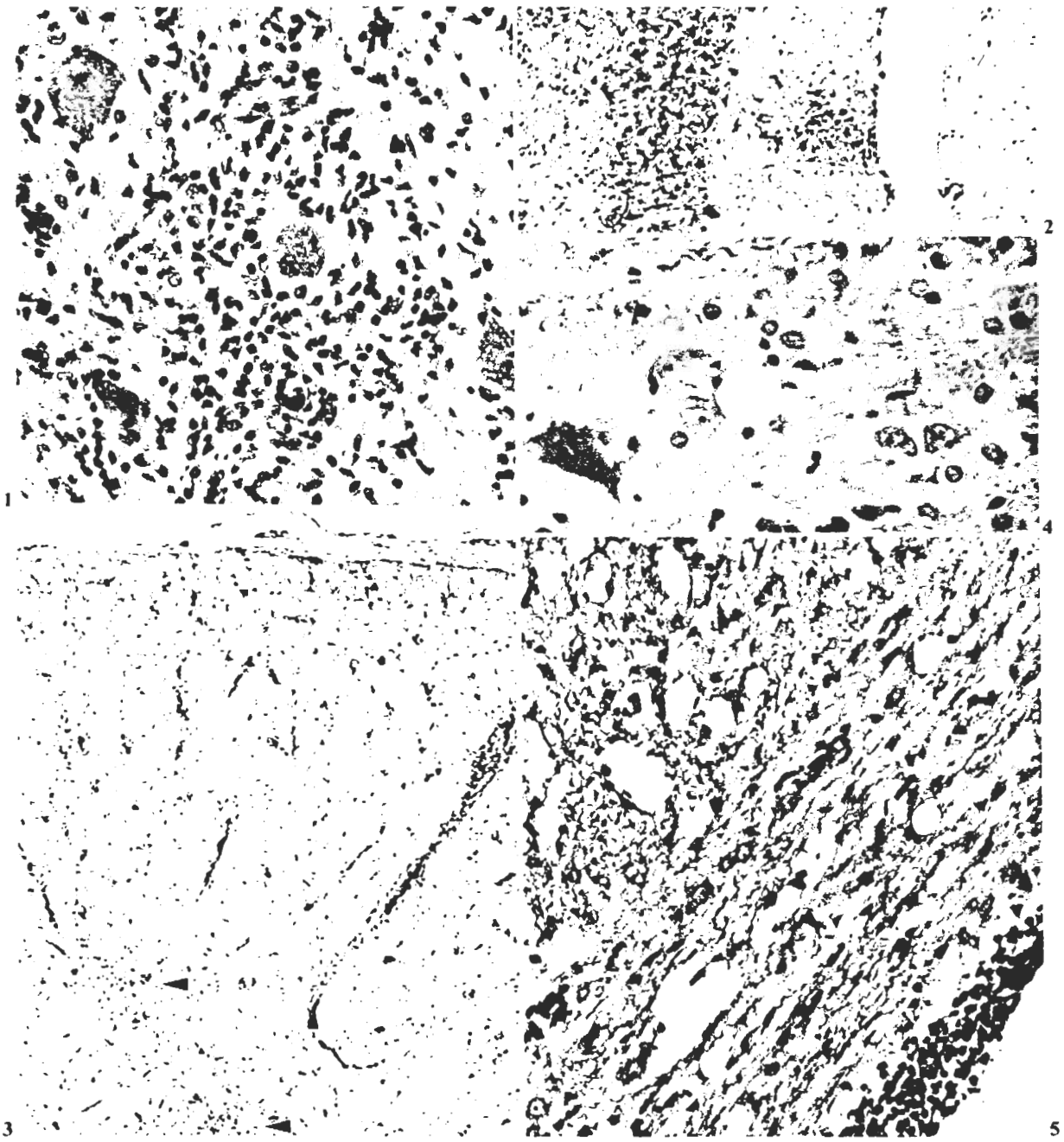

Fig. 1: Inflammatory focus in gray matter of spinal cord containing microglia, lymphocytes and several swollen astrocytes. Hematoxylin and eosin (HE).

Fig. 2: Cerebellum with dense, large inflammatory focus in molecular layer. HE.

Fig. 3: Cervical spinal cord with slight lymphoid meningeal infiltrate, mild vacuolation of white columns, perivascular lymphoid cuffs, and several mild inflammatory foci in ventral gray horn (arrowheads). HE.

Fig. 4: Swollen degenerative axon in an area of pons with several microglia and swollen astrocytes. HE.

Fig. 5: Vacuolation in ventrolateral portion of pons at base of trigeminal nerve. Dense meningeal lymphocytic infiltrate, marked vacuolation, mild microglial infiltrate, swollen myelin sheath contains several necrotic cells, and occasional swollen astrocytes. HE.

cultured on 5% sheep blood agar, MacConkey's agar, and thioglycolate broth with negative results. Refrigerated brain and spinal cord specimens of two mink from each farm were cultured four times at weekly intervals for *Listeria* sp.,[2] all with negative results. Brain and spinal cord specimens from three mink of farm A and two each of farms B and C, cultured for viruses on Crandell feline kidney, Madin-Darby canine kidney

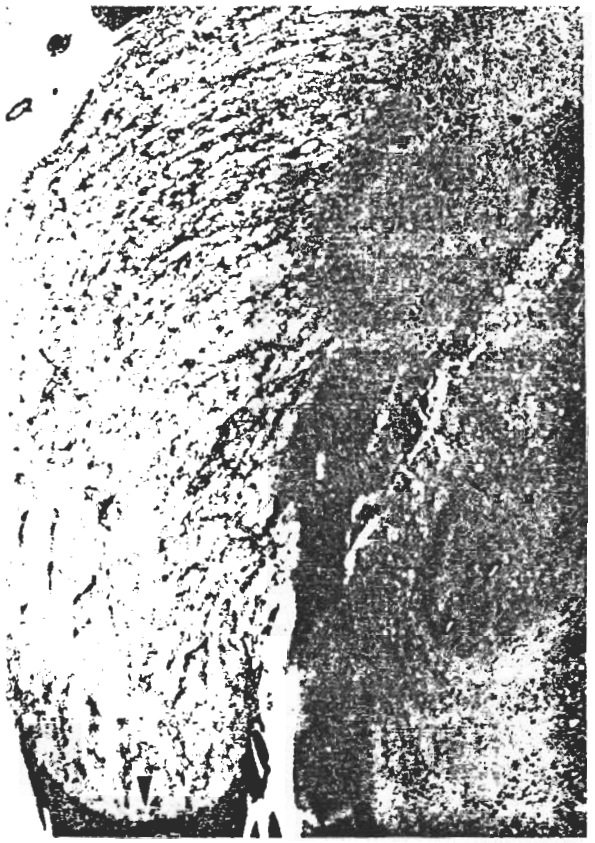

Fig. 6: Trigeminal nerve at site of origin in pons. Marked vacuolation extends to junction of the central and peripheral nervous systems (arrowhead). Focal vacuolation in subjacent pons. HE.

and Vero cell lines, were negative (personal communication, J. F. Everman, Washington Animal Disease Diagnostic Laboratory, Pullman, WA). Hemagglutination inhibition tests for Newcastle disease virus done on sera of four mink from farm A and two each from farms B and C, all of which had central nervous system lesions, were also negative. Negative results were also obtained from indirect immunofluorescence and avidin-biotin peroxidase tests for canine distemper virus, done on formalin-fixed, paraffin-embedded brain sections of one mink with severe lesions from each farm (personal communication, M. K. Axthelm, Department of Veterinary Pathobiology, The Ohio State University, Columbus, OH).

Experimental inoculations: Brain and spinal cord specimens from three mink on farm A and one from farm B, all of which had lesions, were stored at −60°C until prepared for animal inoculation. A 10^{-1} dilution was prepared from each inoculum in phosphate buffered saline without added antibiotics. Aliquots (0.2 ml) of these homogenates were inoculated into eight-month-old nonimmunized Aleutian and non-Aleutian stock mink at Washington State University. Seventy-three mink were inoculated by intracerebral, intraperitoneal, or subcutaneous routes. Two mink died within three days due to trauma related to intracerebral inoculations, as indicated by necropsy findings. The remaining mink were kept 11 months until the next pelting season and none developed clinical signs of central nervous system disease. Two mink that died during this period had no macroscopic or microscopic central nervous system lesions.

Discussion

The clinical signs and histologic lesions in mink from the three farms described herein were similar; this suggests that the same disease was involved. The high mortality on farm B relative to farms A and C could have been caused by poor care during the recumbent period or possibly related to a *Salmonella* sp infection also identified on the farm. While no etiologic diagnosis was confirmed, the clinical signs, lesions, and laboratory findings in these mink were not consistent with any of the encephalopathies previously reported in mink. These conditions include canine distemper virus,[1,4] Newcastle disease virus,[5] transmissible mink encephalopathy,[6,7] Aujeszky's disease,[3] lead toxicity,[4] mercury toxicity,[12,13] *Listeria* sp,[5] toxoplasmosis,[10] and thiamine deficiency.[9,11]

Initially, canine distemper virus was considered the most likely diagnosis despite the atypical clinical signs[1,4] but was ruled out on the basis of lack of cytoplasmic or intranuclear inclusion bodies or other characteristic extra-central nervous system lesions. Additionally, the immunoperoxidase/fluorescent antibody tests were negative for canine distemper virus. Aujeszky's disease virus, like canine distemper virus, should have been isolated by the cell culture procedures that were done, or at least been transmissible to experimental mink. Unlike the syndrome reported here, high mortality was a feature of an outbreak of Aujeszky's disease in mink.[3] In addition, Aujeszky's disease virus does not appear to be present in the Pacific Northwest. (J. A. Schmitz and J. F. Everman, unpublished data).

Sera from all three farms was negative for Newcastle disease virus antibodies, thus this possible diagnosis was discounted. Clinical signs and lesions reported in outbreaks of toxoplasmosis in mink[10] differ from those of our mink. In addition, no *Toxoplasma* sp tachyzoites were detected in any of our mink. Negative bacterial cultures together with the nature and distribution of the central nervous system lesions were interpreted to

indicate that the etiology was not *Listeria monocytogenes*. The central nervous system lesions in our mink were not compatible with thiamine deficiency[11] nor for lead[8] or mercury toxicosis.[12,13] Additionally, these are usually diet-related problems and though the adults on all three ranches received the same food as the kits, only the kits were affected with the disease. Similarly, the young age of the affected kits as well as the nature of the lesions rules out transmissible mink encephalopathy as a diagnosis.[6,7]

For the reasons described above, the central nervous system disease that occurred in the young mink on these farms does not appear to represent any of the central nervous system diseases previously described in mink. A similar disease problem, with identical clinical signs and histologic lesions, was seen by one of the authors (JAS) in mink from another (fourth) Oregon farm in 1974. Immunofluorescence and avidin-biotin peroxidase tests for canine distemper virus on paraffin-embedded brain sections of a mink from this farm were also negative (personal communication, M. K. Axthelm). There has been no recurrence of the disease on that farm. Similar disease signs and histologic lesions were also seen in mink from an Ohio fur farm in the autumn of 1981 (personal communication, G. G. Long, Purdue University, Animal Disease Diagnostic Laboratory, West LaFayette, IN). Despite our failure to transmit the disease by experimental inoculation of mink, the histologic lesions in the central nervous system are suggestive of a viral etiology. This disease apparently has not been reported previously.

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