Lesions of Spinal Cord Parelaphostrongylosis in Sheep. Sequential Changes Following Intramedullary Larval Migration

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Abstract. Spinal cord nematodiasis epidemiologically, clinically, and histologically consistent with Parelaphostrongylus tenuis infection was noted in two flocks of sheep. Spinal cords from two sheep with active infection and one from a partially recovered animal were studied in an effort to determine the sequence of lesions following larval invasion of the central nervous system. In the former two sheep, migration of larvae within the spinal cord induced asymmetrically irregular tracks of disrupted and necrotic tissue, primarily in white matter. Subsequently, macrophages infiltrated these regions and phagocytized the necrotic tissue, which led to cavity formation. Swelling and loss of axons, diminished myelin staining, mononuclear cell infiltration and increase in astrocytic fibers were often seen in adjacent tissue. Only occasional coiled larvae were found in these actively infected animals. Late stage lesions in the white matter in the partially recovered sheep included multiple small astrogliotic regions with diminished myelin and axonal content, and a single large multicavitary, atrophic, gliotic zone.

Neurologic disease has followed invasion of the central nervous system by third stage larval of the nematode Parelaphostrongylus tenuis, the “meningeal worm” of the white-tailed deer (Odocoileus virginianus), in a number of aberrant hosts. Involvement of domestic sheep has been reported in enzootic regions where they have been on pastures frequented by white-tailed deer. The cases which are the subject of this report originated in such a region, the Appalachian ridges and valleys of western Virginia, an area in which a high prevalence of infection of deer by P. tenuis has been reported.

Sheep become infected by accidental ingestion during grazing of gastropod intermediate hosts that contain infective third-stage larvae of P. tenuis. As part of their life-cycle in white-tailed deer, and presumably in sheep, these larvae penetrate the gastrointestinal wall, migrate intraperitoneally, enter the spinal cord along spinal nerves and have a subsequent intramedullary developmental phase. The latter generally induces relatively minor damage in the deer, while in sheep and other aberrant hosts it may lead to significant spinal cord injury. Lesions related to the latter, particularly those associated with the active phase of intramedullary larval migration in aberrant hosts, have been described. However, a likely sequence of neuropathological changes, following this migratory parasitic injury and extending to the late stage of the reaction, has not been delineated. To help address this deficiency we report the spinal cord lesions from three affected sheep—emphasizing the evolution of intramedullary lesions of ovine parelaphostrongylosis.

Case Histories

In the fall of 1982, two widely separated flocks of Suffolk sheep developed neurologic signs which involved 59% and between 3 and 10% of the animals, respectively. The signs included unilateral or bilateral rear-leg paresis, ataxia and recumbency. While the disease led to death or necessitated slaughter of some sheep, others had various degrees of recovery. White-tailed deer had previously been observed on pastures occupied by the affected sheep.

Materials and Methods

Formalin-fixed spinal cords from two actively infected sheep (one from each flock), a three-year-old ram and a two-year-old ewe, necropsied during the height of the outbreaks (Fall, 1982), were submitted to our laboratory. In addition, a year-old ram which had been clinically affected in October, 1982 and subsequently had partially recovered, was killed and necropsied in May, 1983. Five to seven cross sections of each spinal cord (including cervical, thoracic, lumbar and sacral levels) were examined grossly, embedded in paraffin and sectioned at 7 μm. These were stained by the hematoxylin and eosin, Holmes’ silver nitrate, luxol fast blue-periodic acid-Schiff (PAS), Masson’s trichrome, and phosphotungstic acid-hematoxylin techniques. Attempts were made to extract intact larvae from segments of formalin-fixed spinal cord in the actively infected sheep for parasitological identification; these
were unsuccessful, (W. R. Davidson, personal communication).

Results

Both actively infected sheep had multifocal asymmetric microscopic lesions of the spinal cord white matter. Lesions in various stages of development involved all levels of the cord in the three-year-old ram, and the thoraco-lumbar regions in the two-year-old ewe. In each of these sheep a single extensively coiled, apparently viable nematode larva, consistent in histological appearance with *P. tenuis*, was seen in tissue sections (R. C. Anderson, W. R. Davidson, J. R. Lichtenfels, personal communication) (fig. 1).2 In the three-year-old ram this parasite was in the ventrolateral white matter of the cervical enlargement, while in the two-year-old ewe it was in the dorsolateral white matter of the thoracic region of the spinal cord. Interspersed between coils of the larvae, the white matter appeared compressed, disrupted and necrotic (fig. 1). Similarly altered tissue was seen elsewhere, in regions without larvae; this suggested that passage of these parasites through spinal cord white matter produced necrotic tracks. Adjacent viable tissue, even in proximity to the larvae, contained swollen (ballooned) axons, foci of mononuclear macrophages and perivascular and leptomeningeal lymphocytic and occasionally eosinophilic infiltrates (fig. 1).

Lesions at a more advanced stage of development were characterized by larger numbers of macrophages that infiltrated and progressively removed the necrotic tissue (fig. 2). In larger lesions this led to linear cavities in the white matter (fig. 3). As this process proceeded, adjacent white matter had axonal swelling that increased in prominence and led to degeneration—leaving small unstained spaces (spongiform change), and diminished myelin staining (fig. 3). Reactive astrocytes and macrophages were also present around the necrotic tracks at this stage. Smaller regions of axonal swelling and loss and myelin degeneration, possibly sections through the margins of the evolving necrotic lesions, and mild perivascular and leptomeningeal infiltrates were also present.

Alterations in the gray matter of the two actively infected sheep consisted of rare swollen axons, occasional chromatolytic neurons and a single necrotic track with a robust macrophage response. In addition, one of these sheep had focal ventral spinal nerve radiculopathy, with loss of some myelinated nerve fibers.

Lesions in the one-year-old ram which had partially recovered were thought to reflect a late stage of development. These lesions were present in the spinal cord

![Fig. 1: Cross sections of coiled *P. tenuis* larva with adjacent dark staining necrotic tissue (large curved arrow) and pale staining mass of macrophages (arrowhead) in actively infected sheep. Surrounding tissue contains swollen axons (small arrows). This and all other photomicrographs are of spinal cord white matter. Luxol fast blue-PAS.](image-url)

![Fig. 2: Necrotic track contains a prominent macrophage infiltrate in an actively infected sheep. Luxol fast blue-PAS.](image-url)

![Fig. 3: Cross-sections of cavities with residual debris (arrows) in an actively infected sheep. Adjacent white matter has swollen axons, small unstained spaces (spongiform appearance) and diminished myelin staining. Luxol fast blue-PAS.](image-url)
white matter and were mainly of two types. Multiple small astrogliotic foci with diminished myelin staining contained central areas of axonal depletion, and at times, small residual cavities (figs. 4, 5). These foci were most evident in lateral funiculi at lower lumbar levels, although they were occasionally found in other regions. A second type of lesion occurred in the left ventral funiculus at the L1 level, and consisted of several cavities within an extensive zone of axonal loss with related diminished myelin staining and astrogliosis (figs. 6, 7). No larvae were found on microscopic study of sections of the spinal cord in this ram.

No lesions were noted in other organs in the partially recovered ram, except for focal fibrous pleural adhesions to the rostral aspect of the right lung. No data were available in this regard for the other two sheep.

Discussion

Diagnosis of neurologic disease caused by *P. tenuis* in aberrant hosts rests upon the presence of typical lesions together with the parasites in the central nervous system of animals exposed to presumably infected white-tailed deer. These features were present in our two actively infected sheep. Although no parasites were found in the spinal cord of the partially recovered animal, it was also considered to have had this disease. This animal developed clinical signs consistent with ovine parelaphostrongylosis along with others in its flock, and when necropsied some seven months later, had spinal cord lesions which could well have evolved from those seen in the actively infected sheep.

The spinal cord lesions in the two actively infected sheep resembled those associated with the intramedullary activity of viable larvae in other naturally and experimentally infected sheep.1,6,9,13 Such lesions included the presence of coiled larvae with related necrosis of tissue, swollen and degenerated axons, diminished myelin staining, perivascular infiltration and astrogliosis. Larvae and lesions in our sheep primarily involved spinal cord white matter, in contrast to the more...
frequent intramedullary gray matter location in white-tailed deer.

A major focus of our study was the evolution of spinal cord lesions in ovine parelaphostrongylosis. An important aspect of the tissue injury in this entity relates to the fact that ovine intramedullary larvae are larger and more highly coiled than those of the white-tailed deer; this is probably related to the fact that *P. tenuis* cannot complete its life cycle in sheep. These features (parasitic size, coiling) of the larvae in our sheep probably led to significant disruption and necrosis of white matter through which the parasite migrated. In addition, axonal swelling and breakdown, and inflammation were seen in tissue adjacent to these migratory tracks. Such effects appeared to be due to local trauma, along with the possibility that some soluble product of the nematode also played a role. The presence of axonal and inflammatory lesions adjacent to apparently viable parasites suggested that at least some intramedullary movements of the organism in sheep were sluggish.

As in other necrotic states in the central nervous system, we noted a macrophage reaction to necrotic spinal cord tissue that removed much of the latter. This eventually produced linear cavities (probably containing cerebrospinal fluid), along the parasite’s migratory pathway in the affected white matter. In addition loss of some swollen axons and myelin, and an astrocytic reaction occurred in adjacent tissue. These events likely produced the astrogliotic, sometimes cavitary, axon and myelin depleted regions seen in the partially recovered animal—representing late stage lesions. The large multicavitary, axon and myelin depleted region seen in L1 in this animal may have been a site of extensive parasitic activity. The finding of cavitation and nerve fiber loss as consequences of intramedullary migration of *P. tenuis* in a partially recovered sheep some seven months after clinical onset is a new observation, and indicates that permanent injury of spinal cord can be caused by these parasites in this aberrant host.

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References


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