Association of clinical and magnetic resonance imaging findings with outcome in dogs with presumptive acute noncompressive nucleus pulposus extrusion: 42 cases (2000–2007)

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Objective—To assess associations of severity of neurologic signs (neurologic score), involvement of an intumescence, and findings of magnetic resonance imaging (MRI) with interval to recovery and outcome in dogs with presumptive acute noncompressive nucleus pulposus extrusions.

Design—Retrospective case series.

Animals—42 dogs with presumptive acute noncompressive nucleus pulposus extrusions.

Procedures—Medical records and magnetic resonance (MR) images of dogs evaluated from 2000 through 2007 were reviewed. Inclusion criteria were acute onset of nonprogressive myelopathy following trauma or strenuous exercise, MRI of the spine performed within 7 days after onset, MRI findings consistent with acute noncompressive nucleus pulposus extrusions, and complete medical records and follow-up.

Results—Clinical neuroanatomic localization of lesions was to the C1-C5 (n = 6), C6-T2 (6), T3-L3 (28), and L4-S3 (2) spinal cord segments. Median neurologic score was 3.5. Median duration of follow-up was 804 days (range, 3 to 2,134 days) after onset of neurologic signs. Outcome was successful in 28 (67%) dogs and unsuccessful in 14 (33%) dogs. Severity of neurologic signs, extent of the intramedullary hyperintensity on sagittal and transverse T2-weighted MR images, and detection of intramedullary hypointensity on GRE images were all associated with outcome on univariate analysis. Results of multivariate analysis suggested that maximal cross-sectional area of the intramedullary hyperintensity on transverse T2-weighted MR images was the best predictor of outcome.

Conclusions and Clinical Importance—Clinical and MRI findings can help predict outcome in dogs with acute noncompressive nucleus pulposus extrusions. (*J Am Vet Med Assoc* 2009;234:495–504)

Acute noncompressive nucleus pulposus extrusions most often occur when an otherwise healthy intervertebral disk is subjected to a brief excessive force. Such extrusions typically occur in dogs during performance of strenuous exercise or following trauma.[1–4] The force placed on the intervertebral disk may result in the nucleus pulposus being rapidly projected toward the spinal cord through a rent in the annulus fibrosus. The extruded nucleus pulposus strikes the spinal cord, causing contusion, and dissipates within the epidural space without resulting in a compressive mass.[1–4]

Acute noncompressive nucleus pulposus extrusions in dogs and cats have been reported.[1–7] Several other terms have been used to describe this condition, including traumatic disk prolapse,[5] dorsolateral intervertebral disk "explosion,"[1] high-velocity–low-volume disk extrusion,[6] Hansen type III intervertebral disk disease,[2–4] and traumatic disk extrusion.[7] The term ANNPE is used here because it describes the main features of the disease and helps differentiate it from the more common type of disk extrusion that occurs following intervertebral disk degeneration (Hansen type I intervertebral disk disease) and that typically results in spinal cord contusion and compression.

In dogs with ANNPE, the neurologic signs that develop depend on the site and severity of the lesion and

Abbreviations

ANNPE	Acute noncompressive nucleus pulposus extrusion
CI	Confidence interval
FSE	Fast spin-echo
GRE	T2* gradient echo
LL:VL	Lesion length-to-vertebral length ratio
MPSS	Methylprednisolone sodium succinate
MR	Magnetic resonance
MRI	Magnetic resonance imaging
PCSAL	Percentage cross-sectional area of the lesion

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are characterized by an acute, often asymmetric myelopathy that is nonprogressive after the first 24 hours.[1–4,a] Clinical signs, course of disease, and CSF and myelographic findings of dogs with ANNPE may be similar to those reported for dogs with ischemic myelopathy.[2–4] High-field MRI and experience in neuroimaging help in differentiating between these 2 diseases.[2–4,7–9,a] The MRI features of ANNPE include focal hyperintensity within the spinal cord overlying an intervertebral disk, with reduction in volume and signal intensity of the nucleus pulposus on T2-weighted images, narrowed intervertebral disk space, and extraneous material or signal change within the epidural space dorsal to the affected disk with absent or minimal spinal cord compression.[2–4,6,7,a] The region of spinal cord that corresponds to the focal hyperintensity on T2-weighted images is most commonly isointense on T1-weighted FSE images and does not have evidence of enhancement on T1-weighted FSE images obtained after administration of contrast agent. However, hypointensity on T1-weighted FSE images and mild enhancement on T1-weighted FSE images obtained after administration of contrast agent have also been described.[7]

A definitive diagnosis of ANNPE is only possible at postmortem examination by visual detection and histologic examination of the gelatinous nucleus pulposus extruded into the vertebral canal, the ruptured annulus fibrosus, and the contused spinal cord.[1] The improved availability of MRI has resulted in an increase in the number of dogs in which a diagnosis of ANNPE is made while alive[2–4]; however, limited information is available on outcome, and the prognostic role of MRI has not been reported to our knowledge.

In human medicine, MRI is considered the imaging modality of choice for evaluation of spinal cords after traumatic injury.[10] A distinct association between MRI signal intensity and histologic characteristics of acutely injured spinal cords has been identified in human patients with spinal cord injury[11] and in animals in experimental studies.[12–14] In those species, intramedullary hyperintensity on T2-weighted MR images has been associated with edema and necrosis of the spinal cord.[11–14] The signal intensity of hemorrhage on T1- and T2-weighted FSE MR images varies depending on the specific form of hemoglobin present (ie, oxyhemoglobin, deoxyhemoglobin, or methemoglobin), whether the RBCs are intact or lysed, and the strength of the MRI operating field.[15] Gradient echo sequences are the most sensitive means of detecting hemorrhage within the CNS because with this type of MRI sequences, hemorrhage appears hypointense at all stages.[16] The degree of parenchymal spinal cord injury detected via MRI is reportedly associated with the degree of neurologic deficits and has prognostic value for predicting neurologic recovery in humans with traumatic spinal cord injury.[17–23]

In veterinary medicine, researchers in only 3 studies have investigated the prognostic role of MRI in the diagnosis of traumatic[24] or ischemic[25,b,c] spinal cord injury in dogs. To the best of our knowledge, the prognostic role of MRI and clinical findings in dogs with ANNPE has not been investigated. The purpose of the study reported here was to assess associations of severity of neurologic signs, involvement of an intumescence, and MRI findings with interval to recovery and outcome in dogs with ANNPE.

Materials and Methods

Case selection—Medical records and MR images were reviewed to identify dogs with a presumptive diagnosis of ANNPE that were referred to and evaluated at the Animal Health Trust from January 2000 through January 2007. Inclusion criteria consisted of the following: acute onset of nonprogressive (after 24 hours) myelopathy following trauma or strenuous exercise, MRI of the spine performed with a 1.5-Tesla unit within 7 days of onset, MRI findings consistent with a presumptive diagnosis of ANNPE, and complete postreferral medical records and follow-up. Magnetic resonance imaging findings of ANNPE were defined as focal hyperintensity within the spinal cord overlying an intervertebral disk, with reduction in volume and signal intensity of the nucleus pulposus on T2-weighted images; narrowed intervertebral disk space; and extraneous material or signal change within the epidural space dorsal to the affected disk with absent or minimal (< 10%) spinal cord compression.[2–4,6,7,a]

Medical records review—The following information was retrieved from the postreferral medical records: age; sex; breed; body weight; type of trauma or type of physical activity at onset of neurologic signs; treatment administered before referral; interval between onset of neurologic signs and performance of MRI; general physical and neurologic examination findings; results of hematologic, serum biochemical, and CSF analyses (when performed); treatment administered after diagnosis; duration of hospitalization; neurologic status during hospitalization and at reevaluations; and, when available or applicable, dates of recovery of nociception, voluntary motor activity, and unassisted ambulatory status, and date and cause of euthanasia (when performed by staff at the Animal Health Trust). On the basis of the severity of neurologic findings at the time dogs were first evaluated at the referral hospital, dogs were assigned a neurologic score from 1 (clinically normal) to 5 (most severe degree of neurologic dysfunction; **Appendix**).

Evaluation via MRI was performed by use of a 1.5-Tesla scanner[d] with the dog anesthetized in dorsal recumbency. T2-weighted FSE images were acquired in the dorsal, sagittal, and transverse planes for all dogs. T1-weighted FSE images, obtained before and after administration of contrast agent,[e] and GRE images were obtained in ≥ 1 plane in most dogs at the discretion of the radiologist. Slice thickness was 2 to 3 mm for dorsal and sagittal scans and 2.5 to 4 mm for transverse scans, depending on size of the dog. The MRI evaluations were performed to include vertebrae C1 through T2 in dogs with a clinical neuroanatomic localization to C1-C5 or C6-T2 spinal cord segments and vertebrae T1 through S3 in dogs with a clinical neuroanatomic localization to T3-L3 or L4-S3 spinal cord segments.

All MR images were reviewed to obtain a consensus on the diagnosis of ANNPE by 2 board-certified radiologists (RD and FJM), who were unaware of the

clinical findings and outcome for each dog. Images were evaluated on a workstation[f] or computer with proprietary software.[g] The surface area of the affected nucleus pulposus was measured[f] on mid-sagittal T2-weighted images and compared with the mean surface area of the 2 adjacent, apparently normal nuclei pulposi. The presence and the degree of spinal cord compression were assessed by comparing the cross-sectional area of the spinal cord at the site of nucleus pulposus extrusion to the cross-sectional area of the spinal cord immediately cranial to it on transverse T2-weighted images.[f] The ratio between the length of the intramedullary hyperintensity on mid-sagittal T2-weighted images and the length of either the C6 (for a cervical lesion) or L2 (for a thoracolumbar lesion) vertebral body (LL:VL) was calculated (**Figure 1**). The maximal cross-sectional area of the lesion (largest region of intramedullary hyperintensity on transverse T2-weighted images) was expressed as a percentage of the cross-sectional area of the spinal cord at the same level (PCSAL; **Figure 2**). The GRE images were examined for intramedullary hypointensity in the area above the affected intervertebral disk space. In addition, signal characteristics of the lesion on T1-weighted FSE images obtained before and after administration of contrast agent were reviewed.

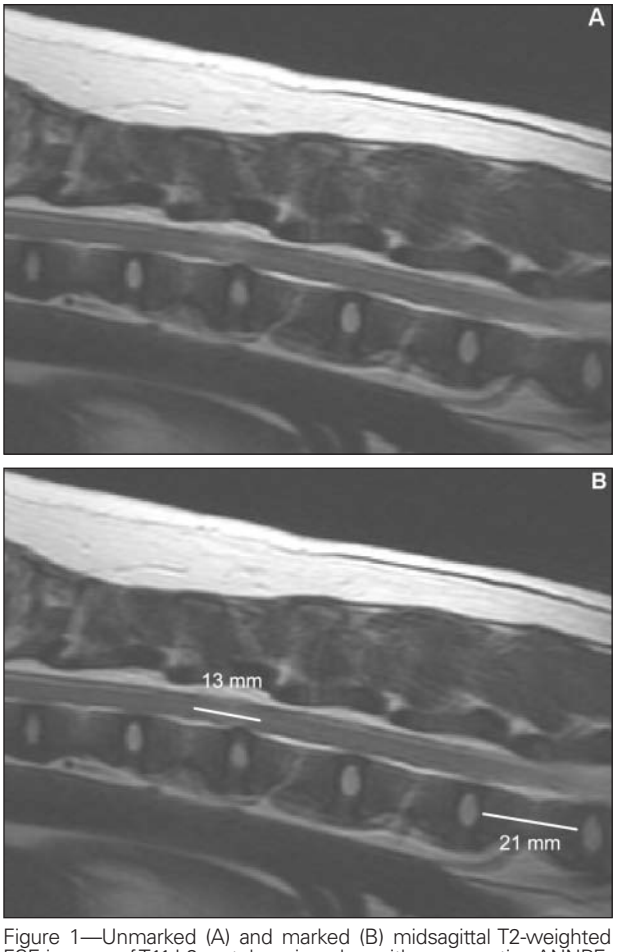

Figure 1—Unmarked (A) and marked (B) midsagittal T2-weighted FSE images of T11-L2 vertebrae in a dog with presumptive ANNPE. The length of the intramedullary hyperintense region above the T12-T13 disk and the length of L2 vertebral body were outlined as indicated (B). Computer software[f,g] was used to calculate these lengths in millimeters, and the LL:VL was calculated (0.62).

Dates upon which dogs recovered nociception, voluntary motor activity, and unassisted ambulation were retrieved from medical records when applicable and available. Nociception was defined as the conscious response of a dog (eg, crying, trying to bite, turning toward the examiner, or consistent change in respiratory pattern) to the application of heavy pressure to the hind limb digits and tail with forceps. Interval to recovery of voluntary motor activity was defined as the number of days from onset of neurologic signs until a dog recovered visible voluntary motor activity in the involved limb or limbs. Interval to unassisted ambulation was defined as the number of days from onset of neurologic signs until a nonambulatory dog regained the ability to stand and could take a series of steps without assistance and without falling.

Outcome was determined by means of a detailed questionnaire administered to the owner and the referring veterinarian at the time of the study and based on

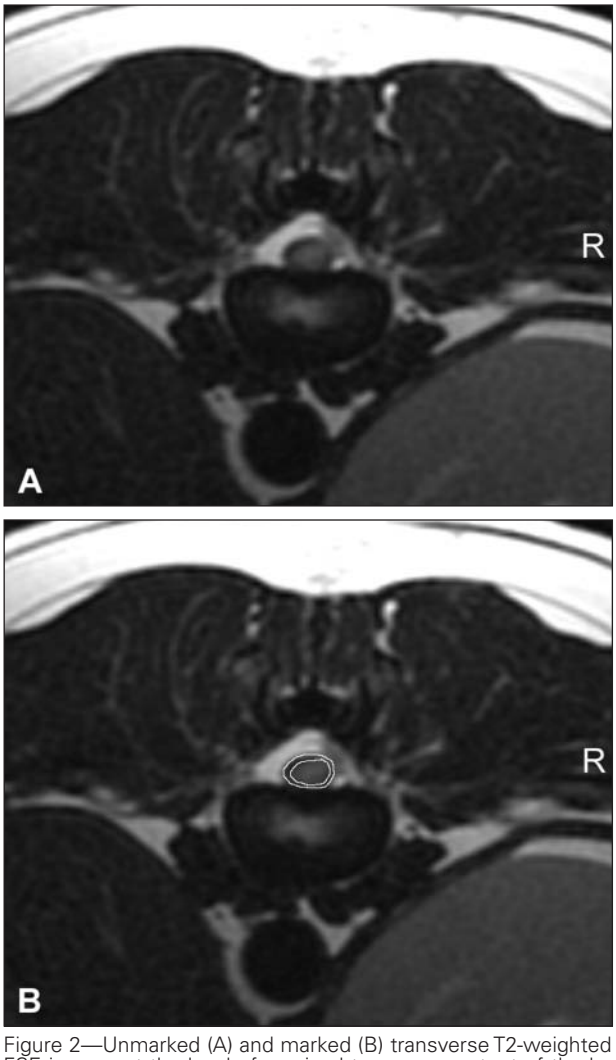

Figure 2—Unmarked (A) and marked (B) transverse T2-weighted FSE images at the level of maximal transverse extent of the lesion in Figure 1. The cross-sectional area of the hyperintense region and the cross-sectional area of the spinal cord were outlined manually as indicated (B). Computer software[f,g] was used to calculate the areas of the outlined regions (PCSAL, 90%). Notice the signal change within the epidural space on the right side (R) and the lack of spinal cord compression.

the information retrieved from the medical record. The questionnaire included questions about the timing and degree of recovery following diagnosis of ANNPE and the current health status or the cause and date of death. In addition, reexamination was offered for all dogs that were alive at the time of the study. Outcome was defined as successful when the dog was clinically normal or had mild to moderate residual proprioceptive or motor deficits but was able to perform daily activities (eg, rising and walking unassisted, moving around the house, eating, drinking, going outside for walks, and playing) without extra care from the owner and was completely urinary and fecally continent. Outcome was defined as unsuccessful when the dog had severe proprioceptive and motor deficits, with or without episodic or persistent urinary or fecal incontinence, or was euthanatized because of a lack of recovery.

Statistical analysis—All statistical analysis was performed with standard statistical software.[h,i] Continuous variables were summarized as median and range; categoric variables were summarized by frequency. Analysis with receiver-operating characteristic curves was used to identify cutoff values for LL:VL and PCSAL that would maximize sensitivity when used to predict an unsuccessful outcome. Sensitivity and specificity for each cutoff value as well as predictive values for test results were determined with standard equations. Optimal cutoff values for LL:VL and PCSAL that were identified in these calculations were used to establish binary variables for these measurements in all additional analyses.

Cross-tabulation with a Fisher exact test was used to examine associations between outcome (successful vs unsuccessful) and treatment administered before referral (MPSS alone or corticosteroids in general vs other types of treatment), neurologic score, involvement of an intumescence (involvement of C6-T2 or L4-S3 vs C1-C5 or T3-L3 spinal cord segments), interval between onset of neurologic signs and performance of MRI (< 24 hours vs 25 to 72 hours vs 73 to 168 hours), detection of intramedullary hypointensity in GRE (present vs absent), LL:VL (> 1.28 vs ≤ 1.28), and PCSAL (≥ 90% vs < 90%).

Multivariate logistic regression was used to identify associations between outcome and the aforementioned clinical and MRI predictor variables that achieved a value of $P < 0.25$ during univariate analyses. Values of the Akaike information criterion were used to compare nonnested logistic regression models.[26] Cross-tabulation with a Fisher exact test was also used to examine associations between treatment administered before referral and neurologic score, detection of intramedullary hypointensity in GRE images, LL:VL, and PCSAL as well as associations between interval to onset of neurologic signs and performance of MRI and detection of intramedullary hypointensity in GRE images, LL:VL, and PCSAL.

Kruskall-Wallis ANOVA with a post hoc pairwise Wilcoxon rank sum test was used to identify associations between interval to unassisted ambulation and neurologic score, involvement of an intumescence, detection of intramedullary hypointensity in GRE images, LL:VL, and PCSAL. All statistical analyses regarding outcome were repeated after excluding dogs that underwent an MRI evaluation 73 to 168 hours after onset of neurologic signs and dogs that were euthanatized before 2 weeks after onset of neurologic signs. Results of these additional statistical analyses are reported only when they differed from the result of the original analysis that included all 42 dogs. The level of significance was set at $P < 0.05$ for all hypothesis tests and final regression models. Results are presented as Fisher exact *P* values unless indicated otherwise, with 95% CIs when applicable.

Results

Forty-two dogs met the inclusion criteria and were used in the study. Median age at diagnosis of ANNPE was 6.7 years (range, 2.1 to 10.7 years), and median body weight was 19.6 kg (43.1 lb; range, 3.3 to 37.0 kg [7.3 to 81.4 lb]). Sixteen dogs were female (9 spayed and 7 sexually intact), and 26 were male (13 neutered and 13 sexually intact). Breeds included Labrador Retriever (n = 8), mixed breed (6), Border Collie (5), Staffordshire Bull Terrier (4), Whippet (4), Cavalier King Charles Spaniel (2), Jack Russell Terrier (2), Miniature Schnauzer (2), and 1 each of Australian Silky Terrier, Basenji, Border Terrier, English Bull Terrier, Fox Terrier, Golden Retriever, Greyhound, Japanese Spitz, and Yorkshire Terrier.

Types of physical activities at onset of neurologic signs, intervals between onset of neurologic signs and performance of MRI, and treatments administered prior to referral were summarized (**Table 1**). Of the 19 dogs

Table 1—Type of physical activity at onset of neurologic signs, interval between onset of neurologic signs and performance of MRI, and treatment prior to referral in 42 dogs with ANNPE.

Characteristic	No. of dogs	Percentage of dogs
Physical activity at onset of neurologic signs		
Running, playing, or jumping	25	60
Traumatic event* that was witnessed	14	33
Traumatic event* that was suspected	3	7
Interval between onset of neurologic signs and performance of MRI (h)		
> 24	26	62
25–72	11	26
73–168	5	12
Treatment administered prior to referral		
Corticosteroid	19	45
Carprofen or meloxicam	9	22
No medication	14	33

*Traumatic events included being hit by a car and running into another dog or into a solid object.

that had been treated with corticosteroids, 15 received MPSS, 2 received dexamethasone, and 2 received prednisolone. All 15 dogs treated with MPSS received an IV injection (30 mg/kg [13.6 mg/lb]) within 8 hours after onset of neurologic signs, and 4 dogs received an additional 1 or 2 injections of 15 mg of MPSS/kg (6.8 mg/lb) or 30 mg of MPSS/kg.

Results of general physical examination were unremarkable other than a finding of superficial soft tissue injury in 8 of the dogs that sustained a witnessed or suspected trauma. Neurologic scores for each dog were summarized (**Table 2**). Fourteen of the 28 dogs with neurologic signs of a lesion localized to the T3-L3 spinal cord segment had a transient decrease in magnitude of the withdrawal reflex in the pelvic limbs. These 14 dogs were evaluated within 24 hours after onset of neurologic signs and had a neurologic score of 4 (n = 9 dogs) or 5 (5). In these 14 dogs, at the time of evaluation, patellar and perineal reflexes were normal and the site of the lesion based on the cutaneous trunci reflex was consistent with the site of the intramedullary lesion on MRI images. Neurologic signs of ANNPE were symmetric in 16 dogs and asymmetric in 26 dogs (10 dogs had signs lateralized on the right side, and 16 dogs had signs lateralized on the left side). Discomfort or hyperalgesia was detected during palpation of the affected spinal segments in 24 (57%) dogs. Results of hematologic and serum biochemical analyses did not reveal any specific physiologic abnormalities.

Magnetic resonance imaging was performed in all dogs on the day of initial evaluation at the referral hospital. The affected intervertebral disk was located at C2-C3 in 4 dogs, C3-C4 in 2 dogs, C6-C7 in 6 dogs, T7-T8 in 1 dog, T11-T12 in 1 dog, T12-T13 in 12 dogs, T13-L1 in 10 dogs, L1-L2 in 3 dogs, L2-L3 in 1 dog, L3-L4 in 1 dog, and L4-L5 in 1 dog. Each dog had only 1 intervertebral disk affected. The surface area of the affected nucleus pulposus ranged from 54% to 66% (median, 60%) smaller than the mean surface area of the 2 adjacent, apparently normal nuclei pulposi. Mild spinal cord compression (1% to 7% compression; median, 3%) was evident in 13 dogs. The median PCSAL was 69% (range, 25% to 100%) in all 42 dogs. The median LL:VL was 0.62 (range, 0.19 to 6.53) in all 42 dogs, 0.63 (range, 0.19 to 6.53) in the 12 dogs with a cervical lesion, and 0.60 (range, 0.25 to 3.76) in the 30 dogs with a thoracolumbar lesion.

Gradient echo imaging was performed in 35 dogs and revealed an intramedullary hypointense region in the area above the affected intervertebral disk space in 8 dogs. Of these 8 dogs, 1 had a neurologic score of 3, 4 had a score of 4, and 3 had a score of 5. Evaluation of T1-weighted images of the spinal cord region corresponding to the focal hyperintense region detected in T2-weighted images revealed isointensity in images of all but 2 dogs with mild hypointensity. Mild heterogenous contrast agent enhancement was detected only in 4 of the 5 dogs that were evaluated 73 to 168 hours (3 to 7 days) after onset of neurologic signs.

Cerebrospinal fluid analysis was performed in 10 (24%) dogs. Samples of CSF were collected from the cerebellomedullary cistern in 2 dogs and the lumbar subarachnoid space in 8 dogs. Total protein content in CSF was higher than the upper reference limit in 6 dogs (0.39 to 0.89 g/L; median, 0.73; reference range, 0.00 to 0.35 g/L). Three of the 6 dogs with a high CSF protein concentration also had mild (12 to 36 WBC/μL), mixed (n = 2), or neutrophilic (1) pleocytosis.

Treatment after diagnosis of ANNPE included restricted exercise for 4 to 6 weeks in all dogs and physiotherapy in 35 dogs. In addition, analgesia (opioids) and anti-inflammatory drugs (carprofen or meloxicam) were administered for a few (1 to 5) days in dogs that had signs of pain at the initial evaluation or during hospitalization at the referral hospital. In dogs with loss of voluntary control of micturition, diazepam and phenoxybenzamine were used to ease manual expression of the bladder.

Median duration of hospitalization; intervals to recovery of nociception, voluntary motor activity, and unassisted ambulation; and duration of follow-up were summarized (**Table 3**). Fourteen of the 32 dogs that were still alive when the study was conducted were reevaluated at the Animal Health Trust. All owners responded to the follow-up questionnaire. The referring veterinarians of all 10 nonsurviving dogs and of 9 dogs whose owners reported persistent neurologic dysfunction were contacted to obtain additional follow-up information.

Outcome was considered successful in 28 dogs and unsuccessful in 14 dogs (**Table 4**). Of the 14 dogs with an unsuccessful outcome, 3 were euthanized because of lack of recovery of nociception at 3, 6, and 7 days

Table 2—Neurologic scores of 42 dogs evaluated for ANNPE at a veterinary referral hospital, stratified by clinical neuroanatomic localization.

	Clinical neuroanatomic localization			
Neurologic score	**C1-C5**	**C6-T2**	**T3-L3**	**L4-S3**
2	1	0	3	0
3	3	4	9	1
4	2	2	9	0
5	0	0	7	1

Values indicate number of dogs.
See Appendix for definitions of scores.

Table 3—Duration of hospitalization, interval to recovery, and duration of follow-up after onset of neurologic signs of ANNPE in dogs.

Variable	No. of dogs	Median (d)	Range (d)
Duration of hospitalization	42	4.5	0–29
Interval to recovery of nociception	5	6	4–7
Interval to recovery of voluntary motor activity	10	6	3–26
Interval to recovery of unassisted ambulation	30	16.5	2–93
Duration of follow-up	42	804	3–2,134

Table 4—Neurologic scores and outcome of 42 dogs evaluated for ANNPE at a referral veterinary hospital, stratified by clinical neuroanatomic localization.

Neurologic score by clinical neuroanatomic localization	Successful outcome*	Unsuccessful outcome*
2		
C1-C5	1	0
T3-L3	3	0
3		
C1-C5	3	0
C6-T2	4	0
T3-L3	9	0
L4-S3	1	0
4		
C1-C5	2	0
C6-T2	2	0
T3-L3	3	6
5		
T3-L3	0	7
L4-S3	0	1

Values indicate number of dogs.
*Outcome at follow-up was deemed successful when a dog was clinically normal or had mild to moderate residual proprioceptive or motor deficits but was able to perform daily activities without extra care from the owner and was completely urinary and fecally continent. Outcome was deemed unsuccessful when a dog had severe proprioceptive and motor deficits, with or without episodic or persistent urinary or fecal incontinence, or was euthanatized because of a lack of recovery.

after onset of neurologic signs and 1 was euthanatized because of lack of recovery of voluntary motor activity at 12 days after onset. Because outcome in these 4 dogs might have been different if they were allowed more time to recover, statistical analyses were repeated after excluding data from these dogs. A fifth dog was euthanatized 287 days after onset of neurologic signs because of persistent fecal incontinence and severe proprioceptive and motor dysfunction. The remaining 9 dogs were all ambulatory with moderate to severe proprioceptive and motor deficits; 6 had episodic fecal incontinence, 1 had persistent fecal incontinence, 1 had partial urinary incontinence, and 1 had partial urinary and fecal incontinence.

All owners of dogs with episodic fecal incontinence reported that their dogs appeared aware of the need to defecate but were not able to control the urge to defecate for as long as they could before the spinal cord injury occurred. Episodes of incontinence were more likely to occur when dogs were excited or were kept indoors for ≥ 6 hours. The 2 dogs with persistent fecal incontinence defecated in the house every day, and owners did not believe their dog was aware of the need to defecate. In 1 dog, urinary incontinence resulted in recurrent urinary tract infections and eventual pyelonephritis, septicemia, and death 1,081 days after onset of neurologic signs. Of the 9 incontinent dogs that were still alive at the time of the study, 3 were reevaluated and all had intact nociception and a normal perineal reflex.

The median interval between onset of neurologic signs and follow-up in the 10 dogs with an unsuccessful outcome attributable to incontinence and moderate to severe proprioceptive and motor dysfunction was 1,166.5 days (range, 120 to 1,517 days). All 10 dogs had a clinical neuroanatomic localization to the T3-L3 spinal cord segment during initial evaluation at the referral hospital. Permission for postmortem examination was not granted by the owners of the dogs that were euthanatized. According to the owners and referring veterinarians, none of the dogs in the study had recurrence of neurologic signs.

Statistical analysis—High neurologic score was significantly ($P < 0.001$) associated with an unsuccessful outcome. All dogs with a neurologic score of 2 or 3 had a successful outcome, 7 of 13 dogs with a score of 4 had a successful outcome, and all dogs with a score of 5 had an unsuccessful outcome (Table 4).

Analysis of receiver-operating characteristic curves revealed that a cutoff value of 90% for the PCSAL and a value of 1.28 for the LL:VL would maximize sensitivity when used to predict an unsuccessful outcome. A high PCSAL was significantly ($P < 0.001$) associated with an unsuccessful outcome. A high LL:VL was also significantly ($P = 0.02$) associated with an unsuccessful outcome when all 42 cases were included in the analysis, although this association became nonsignificant ($P = 0.09$) when data from the 4 dogs that were euthanatized before 2 weeks after onset of neurologic signs were excluded. Detection of intramedullary hypointensity on GRE images of 35 dogs was also significantly ($P = 0.007$) associated with an unsuccessful outcome.

When a PCSAL cutoff value of 90% was used to predict an unsuccessful outcome, the resulting sensitivity and specificity were 86% (95% CI, 67% to 100%) and 96% (95% CI, 90% to 100%), respectively; the corresponding area under the curve was 0.91 (95% CI, 0.79 to 1.00). With the same cutoff value, the predictive value of a positive test result was 92% (95% CI, 78% to 100%) and the predictive value of a negative test result was 93% (95% CI, 84% to 100%). These predictive values meant that a dog with a PCSAL ≥ 90% had a 92% chance of having an unsuccessful outcome, whereas a dog with a PCSAL < 90% had a 93% chance of having a successful outcome. With exclusion of data from the 4 dogs that were euthanatized before 2 weeks after onset of neurologic signs, the cutoff value did not change but the sensitivity of PCSAL for predicting an unsuccessful outcome decreased slightly to 80%.

When an LL:VL cutoff value of 1.28 was used to predict an unsuccessful outcome, the resulting sensitivity and specificity were 57% and 82%, respectively; the corresponding area under the curve was 0.74 (95% CI, 0.59 to 0.90). With the same cutoff value, the predictive value of a positive test result was 62% and the predictive value of a negative test result was 79%. With exclusion of the data from the 4 dogs that were euthanatized before 2 weeks after onset of neurologic signs, the cutoff value did not change but the sensitivity of LL:VL for predicting an unsuccessful outcome decreased to 50%.

Outcome was not associated with treatment with corticosteroids in general or MPSS alone versus other types of treatment administered before referral ($P = 0.34$ and $P = 0.08$, respectively) or involvement of an intumescence ($P = 0.23$). The latter 2 variables were considered for inclusion in the multivariate logistic regression models, along with neurologic score, detection of intramedullary hypointensity in GRE images,

LL:VL, and PCSAL. Multivariate logistic regression analysis resulted in 2 models for prediction of outcome. The first included only the PCSAL ($P < 0.001$) as a predictor of outcome, and the second included LL:VL ($P = 0.01$) and hypointensity in GRE images ($P = 0.02$) as independent predictors of outcome. When data from the 4 dogs that were euthanatized before 2 weeks after onset of neurologic signs were excluded, LL:VL was no longer significant. Because the value for the Akaike information criterion was lower for the model that included PCSAL (18.9) than it was for the model that included LL:VL and hypointensity in GRE images (30.7), the model that included PCSAL was deemed superior and the variable LL:VL was removed from the sensitivity analysis.

Severity of neurologic signs (as a categoric variable with 4 levels or as a binary variable with only 2 levels) at the time of initial evaluation at the referral hospital could not be included in any of the logistic regression models because of quasi-complete data separation (a value of 0 in any one of the cells of a 2 × 2 or 2 × 4 contingency table). Once the MRI variables were taken into account and included in either of the possible final models, the variables involvement of an intumescence and treatment with MPSS before evaluation at the referral hospital were not significantly ($P > 0.06$) associated with outcome. For the 13 dogs with a neurologic score of 4, a high PCSAL was significantly ($P = 0.005$) associated with an unsuccessful outcome, whereas the variables LL:VL and detection of a hypointense region on GRE images were not significantly ($P = 0.10$ and $P = 0.09$, respectively) associated with an unsuccessful outcome. Treatment with corticosteroids in general or MPSS alone versus other types of treatment administered before referral was not associated with neurologic score ($P > 0.30$), detection of intramedullary hypointensity on GRE images ($P > 0.20$), LL:VL ($P > 0.30$), or PCSAL ($P > 0.15$). Interval between onset of neurologic signs and performance of MRI (< 24 hours vs 25 to 72 hours vs 73 to 168 hours) was not associated with detection of intramedullary hypointensity on GRE images ($P = 0.70$), LL:VL ($P = 0.60$), PCSAL ($P = 0.70$), or outcome ($P = 0.20$).

Results of Kruskal-Wallis ANOVA indicated that interval to unassisted ambulation and neurologic score were significantly ($P = 0.01$) associated. Results of a pairwise post hoc Wilcoxon rank sum test suggested that interval to unassisted ambulation for dogs with a neurologic score of 5 was significantly longer, compared with that for dogs with a neurologic score of 3 ($P = 0.002$) and that for dogs with a neurologic score of 4 ($P = 0.04$). There was also a significant ($P = 0.02$) association between interval to unassisted ambulation and PCSAL, but there was no association between interval to unassisted ambulation and detection of a hypointensity in GRE images ($P = 0.3$), LL:VL ($P = 0.14$), or involvement of an intumescence ($P = 0.11$).

Discussion

Clinical, MRI, and histologic findings in dogs with presumptive ANNPE have been reported.[1–4,7,a] A definitive diagnosis of ANNPE is only possible at postmortem examination via visual and histologic detection of the extruded gelatinous nucleus pulposus within the vertebral canal, the ruptured annulus fibrosus, and the contused spinal cord.[1] An antemortem diagnosis of ANNPE can be reached on the basis of a combination of certain clinical (acute onset of nonprogressive myelopathy following trauma or strenuous exercise) and MRI features (focal area of hyperintensity within the spinal cord overlying an intervertebral disk, with reduction in volume and signal intensity of the nucleus pulposus in T2-weighted images; narrowed intervertebral space; and extraneous material or signal change within the epidural space dorsal to the affected disk with absent or minimal spinal cord compression).[7–9]

The amount of information on outcome in dogs with ANNPE is limited.[1,7,27,a] Univariate analysis in the present study identified a significant association between outcome (successful vs unsuccessful) and the severity of neurologic signs (neurologic score) at the initial evaluation at the referral hospital, the extent of the intramedullary hyperintensity on sagittal and transverse T2-weighted images, and the detection of intramedullary hypointensity on GRE images. In addition, a significant association was identified between neurologic score, the extent of the intramedullary hyperintensity in transverse T2-weighted images, and interval to recovery of unassisted ambulation.

Because findings from imaging should always be interpreted in conjunction with clinical findings, we attempted to investigate the association of outcome with the clinical and MRI variables combined by means of multivariate logistic regression. Although univariate analysis revealed that a high neurologic score was strongly associated with an unsuccessful outcome, that variable could not be included in the final logistic regression models because of quasi-complete data separation (all dogs with a neurologic score of 2 or 3 had a successful outcome, and all dogs with a score of 5 had an unsuccessful outcome).[28] When assessing the group of dogs with a neurologic score of 4 (paraplegia or tetraplegia with intact nociception), only PCSAL remained a significant predictor of outcome, although the lack of significance for the variables LL:VL and hypointense region in GRE images might have been attributable to the limited statistical power. In addition, PCSAL and LL:VL may have been collinear, which would have caused one of the variables to be dropped from the final model. Limited statistical power was also a likely reason for failure to detect a significant association between involvement of an intumescence and outcome in univariate and multivariate models. Indeed, only 8 of the 42 (19%) dogs included in this study had a lesion involving an intumescence and only 1 of them (with a neurologic score of 5) had a poor outcome.

Statistical analysis did not reveal any associations between treatment with MPSS alone or with corticosteroids in general and neurologic score from the initial evaluation at the referral hospital, detection of intramedullary hypointensity on GRE images, LL:VL, PCSAL, or outcome. These results should be interpreted cautiously because treatment protocols were not standardized, treatment was not randomized, and the neurologic score was assigned at the referral hospital

and was not based on the assessment of the referring veterinarian. Therefore, it is possible that dogs with more severe neurologic signs at onset of ANNPE were more likely to receive corticosteroids (particularly MPSS) prior to referral than were dogs with milder signs.

A study[29] in humans with traumatic spinal cord injury suggested that the interval between onset of neurologic signs and performance of MRI influenced the longitudinal extent of intramedullary edema detected. Results of the present study suggested that there was no effect of timing of MRI on the longitudinal and transverse extent of the lesion detected or prediction of outcome. However, additional studies are needed to investigate the speed at which changes in the MRI appearance of lesions evolve following various degrees of spinal cord injury and the impact of these changes on the prognostic value of MRI findings.

Several studies[17–23] of acute traumatic spinal cord injury in humans have identified an association between the severity of neurologic signs detected at initial evaluation, degree of spinal cord damage detected via MRI, and outcome. An association between outcome and the severity of neurologic signs (loss of nociception) and extent of the lesion on MR images (area of intramedullary hyperintensity on sagittal T2-weighted images greater than or equal to the length of the L2 vertebral body) was detected in a study[24] of 77 paraplegic dogs with Hansen type I intervertebral disk degeneration and extrusion. In a study[25,b] of 50 dogs with ischemic myelopathy that underwent MRI within 1 week after onset of neurologic signs, a significant association was identified between the severity of neurologic signs at initial evaluation, the sagittal and transverse extent of the spinal cord intramedullary hyperintensity on T2-weighted images, and the outcome. Results of the aforementioned studies[17–25] are comparable to those of the present study and suggest that MRI findings, along with clinical findings, should be used to help predict outcome in dogs with acute spinal cord injury.

Other interesting results of the present study included the distribution of lesions within the spinal cord, the transient decrease in magnitude of the withdrawal reflex in dogs with a severe T3-L3 myelopathy, and the detection of incontinence in a high proportion of the dogs with a poor outcome. The most commonly affected intervertebral disk spaces were T12-T13, T13-L1, and L1-L2, which accounted for 60% (25/42 dogs) of lesion locations. These intervertebral disk spaces were also the most commonly affected sites in 2 other studies of dogs with ANNPE, accounting for 85% (17/20 dogs)[a] and 55% (6/11 dogs)[7] of lesion locations. The higher incidence of ANNPE at the junction between the mobile lumbar segment of the vertebral column and the comparatively immobile thoracic segment of the vertebral column is likely attributable to the strong biomechanical forces that act at this junction, particularly during strenuous exercise or trauma.[30,31]

Fourteen of the 28 dogs with clinical neuroanatomic localization to the T3-L3 spinal cord segment had a transient decrease in magnitude of the withdrawal reflex in the pelvic limbs. This phenomenon reportedly occurs in dogs with acute thoracolumbar spinal cord injury[9,32] and is suggested to result from the sudden interruption of descending supraspinal input on motor neurons and interneurons, fusimotor depression, and additional segmental inhibition.[32–36] This phenomenon has important implications for the clinician because it may lead to erroneous neuroanatomic localization, site of diagnostic investigation, and prognosis.

A third (33%) of the dogs included in the present study had an unsuccessful outcome based on our definitions of successful and unsuccessful outcomes. This high percentage may be attributable to the fact that, in some situations, the owner requested euthanasia before the dog had enough time to improve. The 3 dogs with loss of nociception that were euthanized at 3, 6, and 7 days after onset of neurologic signs might have recovered nociception if allowed to live longer and therefore might have eventually had a successful outcome. However, the 5 dogs that recovered nociception did so with a median time of 6 days after onset of neurologic signs and ultimately had a poor outcome (moderate to severe proprioceptive and motor deficits and incontinence). The dog that was euthanized because of lack of recovery of voluntary motor activity at 12 days after onset of neurologic signs might also have had a better outcome if allowed more time to recover. However, again, median interval to recovery of voluntary motor activity was 6 days after onset of neurologic signs in the dogs included in this study. After excluding the 4 dogs that might have recovered if they were allowed more time, the association between outcome and neurologic score, PCSAL, and detection of intramedullary hypointensity in GRE images remained unchanged, whereas the association with LL:VL became nonsignificant.

Overall, 10 dogs had an unsuccessful outcome attributable to incontinence and moderate to severe proprioceptive and motor dysfunction. In these 10 dogs, the median interval between onset of neurologic signs and last follow-up was 1,166.5 days. Therefore, it is unlikely that a longer period of follow-up might have resulted in a different outcome in this group of dogs.

In the study reported here, 10 of 16 paraplegic dogs with clinical neuroanatomic localization to the T3-L3 spinal cord segment recovered nociception (when it had been lost) and ambulatory status but had residual incontinence (mainly intermittent fecal incontinence). Persistent incontinence for 27 months after ANNPE at the thoracolumbar junction reportedly developed in a dog that recovered ambulatory status after it had been paraplegic with intact nociception.[27] The prevalence of fecal incontinence with or without concurrent urinary incontinence is reportedly high in dogs that recovered nociception and the ability to walk following thoracolumbar intervertebral disk extrusion.[37] Interestingly, as was evident in dogs in the present study, the fecal incontinence in most of those dogs was intermittent and was characterized by the inability to control the urge to defecate for as long as the dogs could before spinal cord injury occurred. Humans with incomplete upper motor neuron spinal cord injuries also develop fecal incontinence.[38] Affected humans experience a reduction in sensation within the rectum that decreases the ability of the internal and external anal sphincters to respond appropriately to rectal distention, thereby resulting in

incontinence.[38–42] In addition, incontinence may result also from loss of upper motor neuron inhibitory influences on the reflex activity of the rectum and reduced voluntary control of the external anal sphincter.[38–42]

The main limitations of the present study involved its retrospective nature, the lack of postmortem examination in dogs that were euthanatized, the limited power in some statistical analyses, and the inability to assess initial neurologic deficits in dogs that were not referred immediately to our facility after the spinal cord injury. In addition, predictors of recovery of nociception or voluntary motor activity could not be evaluated because of the limited number of dogs in each group. A larger, prospective study would allow more information to be obtained on changes in the MRI appearance of spinal cord injury lesions with time and predictors of recovery times and outcome in dogs with ANNPE.

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d. 1.5-Tesla Signa Echospeed MRI, General Electric Medical Systems, Milwaukee, Wis.
e. Gadolinium: Omniscan (gadodiamide) Nycomed, Oslo, Norway or Multihance (gadobenate dimeglumine), Bracco, Milan, Italy.
f. GE Advantage Windows, version ADW3.1, General Electric, Milwaukee, Wis.
g. E-film, Merge Emed, Milwaukee, Wis.
h. Stata, version 10.0, StataCorp, College Station, Tex.
i. SAS, version 9.1.3, SAS Institute Inc, Cary, NC.

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Appendix

Scores for severity of neurologic signs according to clinical neuroanatomic localization in dogs with presumptive ANNPE.

	Clinical neuroanatomic localization	
Score	**C1-C5 or C6-T2**	**T3-L3 or L4-S3**
1	Clinically normal	Clinically normal
2	Ambulatory hemiparesis or tetraparesis	Ambulatory monoparesis or paraparesis
3	Nonambulatory tetraparesis with or without monoplegia or hemiplegia	Nonambulatory paraparesis with or without monoplegia
4	Tetraplegia with or without UI or FI	Paraplegia with or without UI or FI
5	Tetraplegia, loss of nociception, UI, and FI	Paraplegia, loss of nociception, UI, and FI

UI = Urinary incontinence. FI = Fecal incontinence.