Severity of spinal cord dysfunction and pain associated with hydrated nucleus pulposus extrusion in dogs

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Keywords
Cervical, IVDD, intervertebral disc disease, HNPE, hydrated nucleus pulposus extrusion, discal, cyst

Summary
Objective: To identify the severity of neurological deficits, presence of signs of cervical pain, and the site of intervertebral disc space extrusion in 21 dogs diagnosed via magnetic resonance imaging (MRI) with a hydrated nucleus pulposus extrusion (HNPE) and compare those findings to dogs with other compressive cervical myelopathies.

Methods: Medical records and MRI findings were reviewed in dogs that were presented to two veterinary hospitals between 2006 and 2012 and subsequently diagnosed by MRI to have a HNPE (n = 21) or other compressive cervical myelopathies originating from the intervertebral disc (n = 174). Information obtained included signalment, severity of neurological deficits, presence of signs of neck pain, and site of HNPE. The severity of clinical neurological spinal cord dysfunction was determined for each dog in both groups using the Frankel scoring system (0–4). The MRI were reviewed for confirmation of diagnosis and site of HNPE. An ANOVA was used to compare age between groups and a Mann-Whitney test for pairwise comparisons of the Frankel score between groups. Values of p < 0.05 were considered statistically significant.

Results: Significantly more severe Frankel scores and less severe signs of cervical pain detected on palpation were observed in dogs with a HNPE as compared to dogs with other compressive myelopathies. The sites of HNPE were C3-C4 (8/21), C4-C5 (12/21), and C5-C6 (1/21).

Clinical significance: Dogs affected with HNPE have more severe clinical neurological deficits and less severe signs of cervical pain as compared to dogs with other compressive cervical myelopathies.

Introduction

In the dog, spinal cord diseases of the cervical region have numerous possible aetiologies, with intervertebral disc (IVD) disease being the most commonly reported cause (1–3). Intervertebral disc herniation occurring in the cervical spine has been reported to occur in 12.9 to 28% of all dogs affected with IVD herniation (1, 2).
have a decreased prevalence of cervical pain, more severe neurological deficits, and increased prevalence of respiratory compromise as a result of the lesion (6). Although debate exists as to the origin of this condition and what to formally name these lesions, for simplification this condition will be referred to as HNPE throughout this report.

The objectives of this study were to identify the severity of neurological deficits, presence of signs of cervical pain, and the site of IVD space extrusion in 21 dogs diagnosed via MRI with a HNPE and compare those findings to dogs with other cervical myelopathies originating from IVD. By expanding the number of reported cases of this rare myelopathy, we hope to refine diagnosis of the condition as it is often mistaken for other types of intraspinal ‘cystic’ lesions on MRI. We hypothesized that dogs suffering from HNPE would have more severe neurological deficits, but less overt cervical pain, and the site of spinal cord compression would be located in the cervical IVD locations.

Materials and methods

Inclusion criteria

Magnetic resonance imaging records of all cervical spinal studies performed at two veterinary referral hospitals (Ryan Veterinary Hospital at the University of Pennsylvania, Red Bank Veterinary Hospital) between June 2006 and January 2012 were reviewed to identify dogs with lesions associated with the IVD affecting the cervical spinal cord. Dogs with lesions consistent with a HNPE as well as dogs with spinal cord compression caused by an IVD on MRI examination were included in this study. The MRI inclusion criteria for the HNPE group were defined as a hyperintense ventral midline lesion on T2-weighted sequences, hypointensity on T1-weighted sequences, close association with the intervertebral disc, and a bi-lobed appearance (4, 6–8). Dogs for the comparison groups were identified as suffering from Hansen Type I IVD herniation if there was degenerated disc material extruded into the spinal canal, and suffering from Hansen Type II IVD herniation if the annulus fibrosis was bulging or protruding into the spinal canal. Dogs with IVD herniation in conjunction with other components of cervical spondylomyelopathy (hypertrophied articular facets, vertebral canal malformation, vertebral instability, ligamentous hypertrophy, joint capsule proliferation, osteophyte production) were assigned to the cervical spondylomyelopathy (CSM) group (9, 10). The latter three groups constituted the non-HPNE group. Clinical neuro-anatomical localization to the cervical spinal cord was also necessary in all groups for inclusion in this study.

MRI procedure

All patients were anaesthetized and placed in dorsal recumbency for the MRI studies. Minimum sequences required to be included in this study were sagittal and transverse T2-WI, and T1-WI (transverse or sagittal) sequences. Magnetic resonance imaging studies were evaluated by either a board certified veterinary radiologist or a neurologist (RG).

Data collection

Medical records of all dogs were reviewed for details about the signalment (sex, age, neuter status, breed, body weight), severity of neurological deficits, presence of neck pain, and site of the lesion. The entire cervical spine, from the cervical (C) IVD 2–3 through C7– thoracic (T) 1, was examined in this study. Signs of neck pain that were detectable on palpation of the cervical spine were recorded in the medical record as either present, absent, or the dog resisted manipulation. A Frankel score was assigned to each patient in both groups for assessment of severity of spinal cord dysfunction. The Frankel score used in this study was a five-point system (0–4) where a score of 0 was tetraplegia with absent nociception, a score of 1 indicated tetraplegia with nociception present, a score of 2 indicated general proprioceptive ataxia and non-ambulatory tetraparesis, a score of 3 was general proprioceptive ataxia and ambulatory tetraparesis, and dogs with a score of 4 only had signs of spinal hyperaesthesia. For more clarification, dogs with a Frankel score of 3 showed signs of ataxia and weakness in the thoracic limbs, pelvic limbs, or both, but were still able to ambulate without assistance from the examiner. Dogs assigned a Frankel score of 2 were not able to ambulate without the assistance of the examiner but retained the ability to move the limbs.

Statistical analysis

Signalment data and Frankel score were assessed for differences between the HNPE

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Figure 1 Sagittal and transverse T2-weighted magnetic resonance imaging (MRI) showing a hydrated nucleus pulposus extrusion (HNPE) lesion affecting the spinal cord dorsal to the C4-C5 intervertebral disc space. Characteristic MRI findings observed with HNPE include a hyperintense, ventral midline extradural lesion on T2-weighted sequences typified by the symmetrical, bi-lobed ventral location, and loss of volume in the associated intervertebral disc.
group, the Hansen Type I and Type II IVD herniation groups, and the CSM group. Signs of cervical pain at the time of examination were compared between the HNPE group and the non-HNPE group. The Shapiro-Wilks test was used to assess normality for continuous variables (age, body weight). Mean ± SD was used to describe normally distributed continuous variables (age) while median (range) was used to describe not-normally distributed continuous variables (body weight). Categorical variables were described using proportions and percentages. One-way ANOVA was used to compare age between groups. The Kruskal-Wallis test was used initially to compare weights and Frankel score between the groups. The Mann-Whitney test was used to perform pairwise comparisons of the Frankel score between groups after the Kruskal-Wallis test and a Bonferroni p-value correction was used to adjust the p-values for these multiple comparisons. Categorical variables were compared using the Chi square test (male versus female) or Fisher’s exact test (if the expected cell count was less than 5 in any cell; neuter and sex status, presence of neck pain, multiple sites versus single site lesions). A p-value of <0.05 was considered significant for all comparisons. All statistical evaluations were performed using a statistical software packageb.

Results

Signalment

In the HNPE group, 21 dogs met the inclusion criteria; there were 16 males (15 neutered, 1 entire) and five neutered females. The mean age was 9.7 years (± 2.2 years SD). Body weight ranged from 4.4 kg to 30.5 kg with a median of 9.7 kg. The most common breed was the Miniature Pinscher (n = 5) followed by the Beagle (n = 3) and the Cocker Spaniel (n = 3). There were no significant differences in sex, age, and neuter status between the groups (HNPE, Hansen Type I IVD herniation, Hansen Type II IVD herniation, and CSM).

Table 1 Age, weight, and sex data of the four groups in the study population.

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years) (Mean ± SD)</th>
<th>Weight (kg) Median (range)</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>HNPE (n = 21)</td>
<td>9.7 ± 2.2</td>
<td>9.7 (4.4 – 30.5)*</td>
<td>16 (15 neutered)</td>
<td>5 (5 neutered)</td>
</tr>
<tr>
<td>Hansen Type I IVDD</td>
<td>8.2 ± 3.1</td>
<td>8.5 (2.6 – 60)</td>
<td>67 (53 neutered)</td>
<td>37 (36 neutered)</td>
</tr>
<tr>
<td>Hansen Type II IVDD</td>
<td>8.9 ± 3.06</td>
<td>29.1 (5.9 – 68.2)</td>
<td>31 (26 neutered)</td>
<td>18 (17 neutered)</td>
</tr>
<tr>
<td>CSM (n = 21)</td>
<td>7.7 ± 3.4</td>
<td>45.8 (17.5 – 75)</td>
<td>13 (10 neutered)</td>
<td>8 (7 neutered)</td>
</tr>
</tbody>
</table>

HNPE = hydrated nucleus pulposus extrusion; IVDD = intervertebral disc disease; CSM = cervical spondylomyelopathy; n = number. *Indicates statistically significant difference in weight in the HNPE group versus Hansen Type II group (p <0.0001), and the HNPE group versus cervical spondylomyelopathy group (p <0.0001).

Hansen Type II (median weight 29.1 kg) and CSM (median weight 45.8 kg) groups were significantly heavier when compared to the HNPE group (median weight 9.7 kg) (p <0.0001). Difference in weight between the HNPE group and the Hansen Type I group (median weight 8.5 kg) was not significant (p = 0.53). Table 1 summarizes the signalment data for all groups.

Clinical signs and Frankel score

Seventeen of the 21 dogs in the HNPE group and 65 of the 174 dogs in the non-HNPE group were presented with clinical signs of non-ambulatory tetraparesis or tetraplegia. Dogs diagnosed with a HNPE were more likely to be presented with signs of severe tetraparesis or tetraplegia than were all other groups (HNPE versus Type I, p <0.0004; HNPE versus Type II, p = 0.006; HNPE versus CSM, p = 0.0004). The median Frankel score for the HNPE group was 2. Table 2 summarizes the distribution of Frankel scores between the groups evaluated.

Signs of cervical pain

Nineteen of the 21 dogs in the HNPE group had an assessment of cervical hyperesthesia recorded in the medical record. Ten of those dogs had no evidence of pain on palpation or manipulation of the cervical spine. In comparison, five of the 101 dogs assessed in the Hansen Type I group, nine of the 44 dogs in the Hansen Type II group, and four of the 21 dogs in the CSM group were non-painful on palpation or manipulation of the cervical spine. Overall the dogs in the HNPE group displayed less severe signs of discomfort on manipulation of the cervical spine than dogs in the non-HNPE group (p <0.001). Table 3 summarizes the frequency of signs of cervical pain in each group.

Table 2 Severity and distribution of neurological deficits as assessed through the Frankel Score.

<table>
<thead>
<tr>
<th>Group</th>
<th>Distribution of Frankel Scores</th>
<th>Median Frankel Score (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>HNPE (n = 21)</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Hansen Type I IVDD</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Hansen Type II IVDD</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>CSM (n = 21)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

HNPE = hydrated nucleus pulposus extrusion; IVDD = intervertebral disc disease; CSM = cervical spondylomyelopathy. *Indicates statistically significant difference between the HNPE group and all other groups (versus Type I p <0.0004; versus Type II p = 0.006; versus CSM p = 0.0004).

b Stata for Mac 12: Stata Corporation, College Station, TX

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Intervertebral disc site

The IVD sites affected in the HNPE group were C3-C4 (8/21), C4-C5 (12/21), and C5-C6 (1/21). No dogs in the HNPE group were affected at a site other than C3-C4, C4-C5, or C5-C6. Dogs suffering from a HNPE had a larger proportion of extrusions at the C3-C4 and C4-C5 disc spaces than did the non-HNPE group. These intervertebral disc spaces were the least commonly affected sites in all other groups (Figure 2).

Discussion

This study found that dogs suffering from a HNPE had more severe neurological dysfunction at the time of presentation and displayed less severe signs of cervical pain on spinal palpation as compared to dogs in the non-HNPE group. In previous studies, tetraparesis or tetraplegia secondary to cervical IVD herniation only occurred in 9.1–17.6% of the population and cervical hyperpathia was the most common clinical sign in dogs suffering from IVD herniation (1, 3, 11). Ten of the 21 dogs in the HNPE group reported here were presented with signs of tetraplegia and another seven were presented with signs of non-ambulatory tetraparesis. In one other study, all 10 of the dogs in the study population were either tetraparetic or tetraplegic (6). With the information collected thus far, there appears to be an increased severity of neurological deficits in dogs diagnosed with a HNPE. However, we might not have captured in our study another population of dogs that were suffering from a HNPE which did not exhibit neurological deficits severe enough to warrant advanced imaging.

Table 3

<table>
<thead>
<tr>
<th>Group</th>
<th>Assessment of spinal hyperaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Painful</td>
</tr>
<tr>
<td>HNPE (19/21)</td>
<td>5</td>
</tr>
<tr>
<td>Hansen type I IVDD (101/104)</td>
<td>91</td>
</tr>
<tr>
<td>Hansen type II IVDD (44/49)</td>
<td>29</td>
</tr>
<tr>
<td>CSM (21/21)</td>
<td>14</td>
</tr>
</tbody>
</table>

HNPE = hydrated nucleus pulposus extrusion; IVDD = intervertebral disc disease; CSM = cervical spondylomyelopathy. *Clinical finding of absence of neck pain was significant in the HNPE group versus the non-HNPE group (p <0.001).

Dogs suffering from spinal cord dysfunction secondary to a HNPE displayed less severe signs of cervical pain associated with manipulation of the spine as compared to those dogs with cervical IVD herniation. A recent study found the prevalence of neck pain in dogs affected with cervical IVD herniation can be up to 85%, which is consistent with the findings of the current study (12). In our population, only five of the 19 dogs in the HNPE population showed signs of pain and another four dogs were resistant to manipulation of the neck but did not show any apparent signs of pain. A large proportion of neurologic examinations found resistance to manipulation as the assessment of response to spinal manipulation. Because of the interobserver variability in spinal pain assessment, it is impossible to know if the ‘resistant’ dog is experiencing pain and reluctant to exhibit overt signs of pain, or if these dogs resist manipulation in general. Due to the variability in this neurologic exam parameter, those patients that were resistant to manipulation were separated into a category different from those that did or did not show signs of pain.

The reason for the difference in cervical spinal pain observed between groups is unknown, however it may relate to the difference in the location of the lesion within the spinal canal and the composition of the lesion itself. In general, lesions affecting the spinal cord and associated structures cause pain by irritating the meninges, the dorsal root, or the dorsal root ganglia through inflammation, exposure of the nucleus pulposus within the spinal canal and subsequent activation of the immune system, or via spinal cord compression resulting in local ischemia and oedema (13). The location of the HNPE lesions may limit exposure of the herniated disc material in the epidural space. Remaining competent fibres of the annulus fibrosus, the dorsal longitudinal ligament, or another intraspinal structure may provide a barrier that contains and limits the exposure of the nucleus pulposus within the epidural space. An inflammatory response is observed when the nucleus pulposus is exposed within the epidural space and results in a local increase in the concentration of inflammatory cytokines (13, 14). Therefore,

![Figure 2](image-url) Frequency of affected cervical disc space in the four groups studied. HPNE = hydrated nucleus pulposus extrusion; IVDD = intervertebral disc disease; CSM = cervical spondylomyelopathy.
by limiting exposure of the herniated material in the epidural space, the inflammatory response is suspected to be less severe with HNPE as compared to that of Type I IVD herniation. Additionally, with the midline location of the HNPE lesions in canine patients, there is less risk of nerve root compression than with the lateralized location in humans. The contents of the lesions described here are suspected to be more pliant and malleable allowing a larger contact area with the spinal cord and less impingement on nerve roots and vasculature. Therefore a lesion that conforms to the spinal cord as the spine moves may induce a less noxious stimulus with greater neurological deficits than a calcified and lateralized IVD.

Lesion localization in dogs affected with HNPE reported here differs from the commonly affected sites in dogs with compressive cervical myelopathies associated with the IVD as 12 of the 21 dogs with HNPE were affected at the C4-C5 disc space and another eight were affected at the C3-C4 disc space. As compared to the non-HNPE group where the C4-C5 and the C3-C4 disc spaces were the least commonly affected sites in all subgroups, respectively. Historically we consider the C2-C3 disc space the most commonly affected cervical site of IVD herniation in chondrodystrophic breeds with a decreasing frequency at sequential disc spaces moving caudally (1, 12, 15). The Type I IVD herniation comparator population presented here was most commonly affected at the C2-C3 IVD space in agreement with previous studies. The next most commonly affected site was C6-C7 IVD space followed by the C5-C6 IVD space. Similarly with the Type II IVD herniation and CSM groups, the C4-C5 and the C3-C4 IVD spaces were the least frequently affected sites (Figure 2). Further investigation is required to determine if an anatomical or functional inciting factor may predispose the C3-C4 and the C4-C5 IVD spaces to HNPE formation.

In the HNPE group, the findings of the MRI examination of a hyperintense ventral midline lesion on T2-weighted sequences that was hypointense on T1-weighted sequences, together with sustained enhancement on T2 FLAIR sequences, close association with the intervertebral disc, and bilobed appearance were noted in all cases. Konar and colleagues first described the ventral, symmetrical, and elongated shape of these ‘cysts’ dorsal to the IVD in dogs (4). Beltran and colleagues further characterized these lesions by describing a loss of volume in the nucleus pulposus of the adjacent IVD (6). Both of these findings were also identified in our study population (Figure 1).

The association of a HNPE with the IVD has been demonstrated in people by performing a positive contrast discogram, or injection of contrast media into the nucleus pulposus verifying a connection as contrast flows from the nucleus pulposus into the lesion (8, 16–18). People describe severe radiating pain in the affected leg upon injection of the contrast into the nucleus pulposus that is probably secondary to distention of the cyst (17). Performing this procedure with cervical lesions in dogs is both high risk and unnecessary. Further distention of the cervical lesion with discography can exacerbate already severe clinical signs quickly leading to respiratory compromise and death.

In veterinary medicine, only one report exists of biopsy of a HNPE lesion located in the thoracolumbar spine of a German Shepherd dog using a surgical approach that would preserve the integrity of the lesion (4). Biopsy revealed that the wall of the lesion was composed of irregular fibrous tissue consistent with fragments of the annulus fibrosus with some necrosis of the nucleus pulposus (4). The exact location of a HNPE within the spinal canal still remains to be determined. Further characterization of the location of these lesions at the current time would be speculative and biopsy of both the lesion and the associated intra-spinal structures is needed to better determine location within the spinal canal.

With the evidence presented thus far and the unknown location of the lesions within the spinal canal, the appropriate terminology and classification of these lesions has not yet been elucidated. Discal cysts are a well-recognized condition in human patients but given the lateralization observed, the anatomic location of the human discal cyst may not be the same as the lesions described in this paper. Therefore the most appropriate term at this time may be either discal cyst as proposed by Konar and colleagues or HPNE as proposed by Beltran and colleagues (4, 6).

The limitations of this study include its retrospective nature and the small case number in the HNPE group. The data presented here suggest that clinical signs and affected IVD sites differ between the HNPE group and other forms of cervical myelopathies. The majority of the patients suffering from HNPE reported here suffered more severe neurological deficits and did not show any apparent signs of pain or resisted manipulation as compared to the IVD herniation dogs that displayed signs of severe pain on manipulation of the cervical spine. Hydrated nucleus pulposus extrusion also appeared in the cervical spine most frequently at the C4-C5 disc space with the C3-C4 disc space being the second most commonly affected site. Although HPNE was rare in the overall population of dogs evaluated in this study, it should be considered as an aetiology in dogs with an absence of neck pain and clinical signs of a severe cervical myelopathy. Further studies need to be performed to determine the true cause of HNPE, the ideal treatment, and the long-term clinical outcome of canine HNPE patients.

Conflict of interest
None declared.

References
In the original article by R. Pettitt et al., “Radiographic and ultrasonographic changes of the patellar ligament following tibial tuberosity advancement in 25 dogs” (Vet Comp Orthop Traumatol 2014; 27: 216-221) two values were reported incorrectly in the text on page 219: 1st column, 2nd paragraph, last sentence. The last sentence in this paragraph should have read as follows:

“Following treatment, the mean width increased by between 0.32 and 0.60 mm (p <0.001).”

The values of 0.32 and 0.60 had been incorrectly reported as 0.31 and 0.58 in the original text. This has now been updated in the PDF file which is available online. The authors apologise for this oversight.

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