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1	Acute non-compressive nucleus pulposus extrusion in cats: clinical features, diagnostic
2	imaging findings, treatment and outcome
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15	Keywords:
16	Cat; disc; extrusion; non-compressive; nucleus pulposus; outcome
17	Abstract
18	Objectives: The aim of the study was to describe the clinical features, diagnostic imaging
19	findings, treatment and outcome in cats diagnosed with presumptive acute non-compressive
20	nucleus pulposus extrusion.

21 Methods: Medical records and imaging studies of cats diagnosed with presumptive acute non-22 compressive nucleus pulposus extrusion were retrospectively reviewed. Long-term follow-up information was acquired from patient records and from either owners or referring veterinary 23 surgeons via a telephone questionnaire. 24 Results: Eleven cats met the inclusion criteria. All cats had a peracute onset of clinical signs, 25 with eight cats experiencing witnessed (n = 6) or suspected (n = 2) external trauma. 26 27 Neurological examination findings ranged from ambulatory paresis to plegia with loss of deep nociception. Neuroanatomical localisation included C1-C5 (n = 1), T3-L3 (n = 7) and L4-S3 28 29 (n = 3) spinal cord segments. Ten cats were discharged with a median hospitalisation time of 10 days (range 3 days to 26 days). One cat was euthanised during hospitalisation due to 30 complications unrelated to neurological disease. Cats that presented with paraplegia regained 31 32 voluntary movement within a median of 4 days (range 2 to 7 days). For those cats that presented non-ambulatory, all cats regained an ambulatory status with the median time to ambulation of 33 17 days (range 6 to 21 days). Five cats had absent voluntary urination at presentation; this 34 resolved in all but one cat that had long-term urinary incontinence. Overall the outcome for 35 cats diagnosed with acute non-compressive nucleus pulposus extrusion was good with almost 36 37 90% returning to ambulation with urinary and faecal continence. Conclusions and relevance: The majority of cats diagnosed with acute non-compressive 38 nucleus pulposus extrusion had characteristic clinical presentations and good outcomes. Acute 39 non-compressive nucleus pulposus extrusion should be considered as a differential diagnosis 40 for cats presenting with peracute onset of spinal cord dysfunction, particularly if there is a 41

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clinical history or evidence of trauma.

Introduction

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Acute non-compressive nucleus pulposus extrusion (ANNPE), previously referred to as a 45 traumatic intervertebral disc extrusion (IVDE), high-velocity/low-volume IVDE and type III 46 intervertebral disc extrusion occurs when a healthy and hydrated IVDE is exposed to sudden 47 and excessive force and is typically seen following vigorous exercise or trauma¹⁻⁴. This type of 48 intervertebral disc extrusion results in spinal cord contusion with minimal or no spinal cord 49 compression¹⁻³. 50 ANNPE has been frequently reported in dogs¹⁻³, however there are only single case reports 51 describing ANNPE in cats^{4,5}. Dogs with ANNPE typically present with a peracute onset of 52 spinal cord dysfunction that is non-progressive after 24 hours ^{1,2}. Clinical signs are often 53 strongly lateralised and mild to moderate spinal hyperaesthesia may be seen in approximately 54 half of affected cases^{2,6}. 55 Definitive diagnosis of ANNPE can only be confirmed by histopathology¹. However, magnetic 56 resonance imaging (MRI) can be used to make a presumptive diagnosis with with specific 57 characteristics identified to reach a presumptive ante-mortem diagnosis of ANNPE.^{2,3}. 58 59 Typical treatment involves physiotherapy and supportive care with the use of analgesics as required⁶. The outcome is considered good in dogs with only a minority failing to regain normal 60 neurological function². 61 Despite this disorder being well characterised in dogs, little is known about the clinical 62 presentation, imaging findings and outcome in cats. The aims of this study were therefore to 63 64 describe the clinical features, diagnostic imaging findings, treatment and outcome in a larger number of cats diagnosed with presumptive ANNPE. We hypothesised that cats diagnosed with 65 presumptive ANNPE would have a characteristic presentation and a good long-term outcome. 66

Material and Methods

69 Ethics Statement

- 70 Ethics approval was granted by the Royal Veterinary College (RVC) Ethics and Welfare
- 71 Committee (reference number 2015 1324).
- 72 Criteria for inclusion
- 73 Medical records of cats that had presumptively been diagnosed with ANNPE at the RVC
- between 2008 and 2014 were reviewed. In order to be included, cats needed to have had an
- 75 MRI of the affected spinal cord segments within 48 h of the onset of clinical signs, MRI
- 76 findings consistent with the diagnosis of presumptive ANNPE and have follow-up information
- for a minimum of 3 months. Recorded information included immediate history preceding onset
- of clinical signs, treatment prior to referral, signalment, general physical examination findings,
- 79 neurological examination findings, duration of time from detecting neurological signs to MRI,
- 80 treatment administered following diagnosis, duration of hospitalisation and presence of
- 81 complications. In relevant cases the time to recover nociception, voluntary motor activity and
- 82 unassisted ambulation was also recorded.
- 83 Diagnostic imaging
- MRI was performed using a 1.5 Tesla scanner (Intera, Philips Medical Systems) and included
- a minimum of T2- and T1-weighted sagittal and transverse images. All imaging studies were
- reviewed for diagnostic accuracy by a board certified neurologist (SDD) blinded to the clinical
- signs and neuroanatomical localisation, and only those cases with imaging features consistent
- 88 with presumptive ANNPE diagnosis were included in the study. MRI findings compatible with
- 89 ANNPE included (1) a reduction in volume of the T2- weighted hyperintensity of the nucleus
- 90 pulposus signal, (2) a focal T2-weighted hyperintensity within the spinal cord overlying an
- 91 intervertebral disc space, (3) mild narrowing of the intervertebral disc space, and (4) extraneous

material or signal change within the vertebral canal with absent or minimal spinal cord compression^{2,3,5} (Figure 1 a, b).

Assessment of outcome

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Short-term outcome was defined as the period between the onset of clinical signs up to 6 weeks following presumptive diagnosis of ANNPE, and information was retrieved from medical records. Long-term outcome was defined as a minimum follow-up period of 3 months⁷. This information was initially obtained via telephone interview with the referring veterinary surgeons. For cats that were deceased, date and cause of death as well as the last documented neurologic status were recorded. Conforming to local ethics and welfare committee guidelines, only owners of cats that were still alive at the time of data collection were subsequently contacted. Owners were mailed a letter with study details and a standardized questionnaire that had been reviewed and approved by a local ethics and welfare committee. Telephone interviews were conducted using the questionnaire, which included questions covering specific aspects of the disease, such as amount of activity, lameness, paresis and incontinence, type of medical and supportive treatment received, response to treatment and quality of life (supplementary material). A successful outcome was defined as resolution or improvement of clinical signs with the cat being able to ambulate independently with control of urination and defaecation, while an unsuccessful outcome was defined as a cat that required support to ambulate or had persistent urinary or faecal incontinence.

Results

Of 14 potential cats identified, 11 were included in the study (Table 1). The cats had a median age of 7 years (range 2 years 9 months to 13 years) at presentation. Eight of the cats were male

- neutered and three were female neutered. Breeds comprised the domestic shorthair (n = 6),
- domestic longhair (n = 3), Egyptian Mau (n = 1) and British Shorthair (n = 1).
- 117 Historical findings
- All cats had an acute or peracute onset of clinical signs. The median time to presentation was
- 119 14 h (range 2–48 h) following the onset of neurological signs. Prior to presentation six of the
- cats had been involved in a witnessed traumatic event (road traffic accident [n = 3] or fall from
- a height [n = 3]). The remaining five cats were found either in the home or nearby the house
- and the onset of clinical signs was not witnessed.
- 123 Clinical findings
- The majority of cats (n = 10) had clinical signs referable to the paraparesis or paraplegia (Table
- 1). Neuroanatomical localisation included the C1–C5 (n = 1), T3–L3 (n = 7) and L4–S3 (n =
- 126 3) spinal cord segments. The clinical signs were non-progressive in all cats following
- presentation. Five of the cats had signs consistent with external trauma, including head trauma,
- pulmonary contusions and scuffed nails.
- 129 MRI findings
- 130 MRI revealed ANNPE located at C3–C4 (n = 1), T12–T13 (n = 1), T13–L1 (n = 1), L1–L2 (n
- = 1), L3–L4 (n = 3), L4–L5 (n = 1) and L5–L6 intervertebral disc spaces (n = 3). One cat had
- a dorsal spinous process fracture of the L7 vertebra, which was not associated with the
- neuroanatomical localisation nor the anatomical localisation of the ANNPE and was therefore
- 134 considered incidental. There was evidence of ill-defined T2-weighted hyperintensity within the
- epaxial musculature compared with surrounding muscle suggestive of contusion, haemorrhage
- or oedema in five cats (Figure 1c). Of these five cats, two cats had no history or examination
- findings consistent with trauma, while the other three cats were involved in a witnessed trauma.

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All cats received physiotherapy performed by a veterinary physiotherapist and/or qualified veterinary nurse consisting of massage, passive range of motion exercises, assisted standing and exercises to develop strength and coordination, as appropriate and tolerated by each cat. Five cats that demonstrated signs of spinal hyperaesthesia received analgesic medication that included opioids (ie, methadone and buprenorphine; n = 3), non-steroidal anti-inflammatory drugs (n = 1) and gabapentin (n = 1). The median time for cats with absent deep nociception (n = 3) to regain sensation was 2 days (range 1–3 days). Of the cats that presented with paraplegia, including those with absent deep nociception (n = 5) the median time for them to regain voluntary movement (non-ambulatory) was 4 days (range 2–7 days). For those cats that presented non-ambulatory (including paraplegic cats; n = 9) the median time to ambulation was 17 days (range 6–21 days). Five cats required bladder management during hospitalisation, including indwelling catheter placement (n = 1), intermittent catheterisation (n = 1) and manual bladder expression (n = 3). Two cats received a sympatholytic medication (prazosin) to aid in bladder management. Three cats were discharged with improved motor function but continued to require manual bladder expression. The cats had a median hospitalisation time of 10 days (range 3–26 days). Four of the 10 cats that survived to discharge were ambulatory at that time. One cat did not survive until discharge, and was euthanased owing to respiratory deterioration as a result of pulmonary contusions. Short-term outcome (4–6 weeks following diagnosis of presumptive ANNPE) in six cats revealed all cats were ambulatory and had improved neurological function compared with the

time of discharge; however, none of the cats were considered to be neurologically normal.

Long-term outcome

Long-term outcome in eight cats (four cats were also included in the assessment of short-term outcome) was obtained from the referring veterinary surgeons (n=2) or veterinary surgeons and owners (n=6). The median duration of time between the onset of clinical signs and assessment of outcome was 44 months (range 4–68 months). None of the cats displayed signs of further improvement 6 months after reaching a presumptive diagnosis of ANNPE. Although all cats were ambulatory and did not demonstrate any signs of spinal hyperaesthesia, none were reported to have become neurologically normal. Owners or veterinary surgeons assessed all cats to have regained a good quality of life; however, quality of life was considered decreased compared with before the onset of clinical signs in all of the cats with 3/8 cats now indoor-only cats.

- One cat (cat 2) had ongoing urinary incontinence requiring twice daily manual bladder expression, and the same cat had intermittent faecal incontinence (Table 1).
- Overall, 7/8 cats (88%) were considered to have a successful long-term outcome, and one cat was considered to have an unsuccessful outcome.

Discussion

The differential diagnosis for cats presenting with an acute or peracute onset of paresis or plegia includes aortic thrombo-embolism, ischemic myelopathy, fibrocartilaginous embolism, intervertebral disk disease, and vertebral fractures and luxations^{8,9}. It has previously been reported that trauma accounts for 14% of cases of feline spinal cord injury,¹⁰ and the occurrence of a vertebral fracture or luxation is generally considered the most important differential diagnosis for cats presenting with a peracute onset of spinal cord dysfunction after a witnessed or suspected traumatic event. Of the cats included in this study nearly three-quarters of the cats had experienced a witnessed traumatic event or there was evidence of trauma based on their clinical exam or imaging findings. This highlights the need to include ANNPE as a possible

differential diagnosis for any cat presenting with an acute or peracute onset of spinal cord dysfunction, particularly if there is any history or evidence of trauma.

When considering the location of the ANNPE the most frequent sites were the L3-L4 and L5-6 intervertebral discs. There was also one patient with a cervical ANNPE. This is consistent with the previous case reports that describe a lumbar and cervical ANNPE^{4,5}. Whilst this contrasts to the findings in dogs, which predominantly have T12-T13 and T13/L1 ANNPE², it is more consistent with data looking at the location of IVDE, with previous studies suggesting that the mid to caudal lumbar region is more commonly affected in cats¹¹⁻¹³.

When considering the outcome for patients diagnosed with ANNPE it is overall very good with almost 90% of the cats being ambulatory with full urinary and faecal continence. None of the cats were described as returning to 'normal' following the onset of clinical signs, and this is consistent with one of the previous case reports that suggested there was ataxia present six months following diagnosis⁴. However, 50% of cats had returned to former behaviours including outside activity and climbing on to furniture. It is currently unclear for those cats that were no longer allowed outside, if this reflected a concern on part of the owners or an actual inability to perform activities as before the onset of clinical signs. From the results of this study, it is difficult to draw any conclusions on potential prognostic indicators for cats with a presumptive ANNPE.

The incidence of ANNPE in cats is not known, although it appears to be infrequent, however it is possible that this reflects a decreased awareness of the condition and therefore an under-diagnosis. The treatment involved in caring for cats following the diagnosis of ANNPE is primarily supportive, involving the use of analgesics as appropriate, bladder management where required and intensive physiotherapy. The cost of treatment compared to cats diagnosed with vertebral fracture/luxation or IVDD is often reduced owing to the fact that there is no need

for surgery. In addition it is often possible for caregivers to be trained to provide physiotherapy and bladder management at home. This combined with the evidence presented in this study that suggests cats with ANNPE appear to have a favourable prognosis highlights the need for ANNPE to be considered as an important differential diagnosis in cats with a peracute onset of spinal cord dysfunction.

Conclusions

This study is obviously limited by its retrospective nature and the small number of included cases. However, the majority of cats diagnosed with presumptive ANNPE presented with paraparesis or paraplegia and had neuroanatomical localisation of T3–L3 and L4–S3 spinal cord segments. Nearly 75% of the cats were involved in a witnessed trauma or had evidence of trauma based on clinical examination or imaging findings. The majority of cats diagnosed with ANNPE had good outcomes. ANNPE should be considered as a differential diagnosis for cats presenting with peracute onset of spinal cord dysfunction, particularly if there is a clinical history or evidence of trauma.

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Conflict of Interest

The authors do not have any potential conflicts of interest to declare.

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Signalment, clinical presentation and outcome of 11 cats diagnosed with presumptive ANNPE

Table 1

			<u> </u>	Neurological	Deep			Time to	Duration of	Follow-up
Cat	Age	Sex	Breed	Examination	nociception	Neuro-	Site of	Ambulation	hospitalisation	time and
	8-			Findings	present	localisation	ANNPE	(days)	(days)	outcome
	12 y			1 manigs	present			(ditys)	(days)	4 mo
1	12 y 5	MN	DSH	Donomlopio	Vac	T2 I 2	L3-L4	15	11	Now indoor
1		MIN	DSH	Paraplegic	Yes	T3-L3	L3-L4	15	11	
	mo									cat
										11 mo
				Non-						Urinary
	2 y		Egyptian	ambulatory	Absent					incontinence
2	9	MN	Mau	paraparetic;	right pelvic	L4-S3	L5-L6	9	23	and
	mo		Mau	right pelvic	limb					occasional
				limb plegic						faecal
										incontinence
										Euthanised
	10 y			Non-						due to
3	6	FN	DLH	ambulatory	Yes	T3-L3	L3-L4	n/a	n/a	pulmonary
	mo			paraparetic						contusions
										20 mo
				Non-						Now indoor
4	6 y	MN	DSH	ambulatory	Yes	T3-L3	T12-T13	16	20	cat
				paraparetic						cat
				NY.						LEE
				Non-			~~ ~.			LTF
5	4 y	MN	BSH	ambulatory	Yes	C1-C5	C3-C4	18	9	
				tetraparetic						
										41 mo
	4 y	y FN	DSH	Ambulatory paraparetic	Yes	T3-L3	L4-L5	n/a	3	Only
										allowed
6										outside in
										daylight
										hours
										46 mo
				Non-						Returned to
	13 Y	MN	DLH	ambulatory	Absent					previous
7				paraparetic;	right pelvic	T3-L3	L3-L4	21	7	lifestyle;
				right pelvic	limb					now
				limb plegic						deceased
				mno piegie						
										due to

										unrelated
										causes
8	5 y	FN	DSH	Ambulatory paraparetic	Yes	L4-S3	L5-L6	n/a	3	67 mo Now indoor cat
9	8 y	MN	DSH	Non- ambulatory paraparetic	Yes	L4-S3	L5-L6	6	7	68m Returned to previous lifestyle;
10	7 у	MN	DSH	Paraplegic	Yes	T3-L3	L1-L2	18	13	LTF
11	8 y 6 mo	MN	DLH	Paraplegic	Absent bilaterally in pelvic limbs	T3-L3	T13-L1	21	26	46 mo Returned to previous lifestyle; now deceased due to unrelated causes

ANNPE = acute non-compressive nucleus pulposus extrusion; y = years; mo = months; MN =

male neutered; FN = female neutered; DSH = domestic shorthair; DLH = domestic longhair;

BSH = British Shorthair; LTF = lost to follow up

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Figure 1. (a) Sagittal T2-weighted and (b) transverse T2-weighted images at the level of the L5–L6 intervertebral disc space, and (c) L4 vertebral body of an Egyptian Mau aged 2 years and 9 months (cat 2). (a) A focal intraparenchymal hyperintensity is present at the level of the L5–L6 intervertebral disc space (long arrow). Although the nucleus pulposus has a reduced volume compared with the adjacent discs, it has remained a homogeneous hyperintense signal. (b) A small amount of extraneous material present in the epidural space (arrow). (a,c) A poorly demarcated hyperintensity within the epaxial musculature at the level of the L4 vertebral body, suggestive of epaxial muscle contusion, oedema or haemorrhage, was considered indicative for external trauma (short arrow [a] and arrow [c])

