Vacuum phenomenon associated with triple cervical vertebral arch and ligamentum flavum anomaly resulting in severe stenotic myelopathy in a dog

Vacuümfenomeen geassocieerd met een drievoudige cervicale wervelboog- en ligamentum flavum-anomalie resulterend in erge stenotische myelopathie bij een hond

[1]S. Vermeire, [2]V. Rondahl, [3]H. Schmökel, [1]M. Rapp

[1]Department of Diagnostic Imaging, Evidensia Small Animal Referral Hospital Strömsholm, Djursjukhusvägen 11, 734 94 Strömsholm, Sweden
[2]Department of Pathology and Wildlife Disease, National Veterinary Institute, Ulls väg 2B, 751 89 Uppsala, Sweden
[3]Evidensia Spine Center, Evidensia Small Animal Referral Hospital Strömsholm, Djursjukhusvägen 11, 734 94 Strömsholm, Sweden

simon.vermeire@evidensia.se

ABSTRACT

A six-year-old American Staffordshire terrier with proprioceptive deficits of the right thoracic and pelvic limb was referred for further work-up. Cervical computed tomography (CT) and magnetic resonance imaging (MRI) revealed a triple cervical canal stenosis with dorsal spinal cord compression and concomitant compressive myelopathy caused by vertebral arch and ligamentum flavum proliferation and hypertrophy. Vacuum phenomena were noticed within the ligamentum flavum tissue, a previously unreported location for vacuum phenomena, which are primarily reported within degenerative joints and intervertebral discs. Decompressive surgery and rehabilitation resulted in a complete clinical recovery.

SAMENVATTING

Een zes jaar oude Amerikaanse staffordshireterriër met verminderde proprioceptie van de rechter voor- en achterpoot werd doorgestuurd voor verder onderzoek. Een drievoudige, cervicale stenose met dorsale ruggenmergcompressie en bijhorende myelopathie werden vastgesteld aan de hand van een computertomografisch en magneetcamera-onderzoek. Deze bevindingen waren secundair aan een proliferatie en hypertrofie van het ligamentum flavum en van de wervelboog. Vacuümfenomenen werden vastgesteld in de ligamentaire hypertrofie, een tot nu toe onbeschreven locatie. Chirurgische decompressie en revalidatie leidden tot volledig herstel.

INTRODUCTION

The vacuum phenomenon, a radiological sign used to describe the abnormal accumulation of gas lucencies (Magnusson, 1937), has become a frequently identified entity in veterinary diagnostic imaging due to the widespread use of computed tomography, a modality more sensitive for detecting gas than conventional radiology (Hathcock, 1994). Most often seen in dogs with degenerative intervertebral disc and joint diseases (Weber et al., 1995; Shwarz et al., 2000; Müller et al., 2014), vacuum phenomena are mentioned in the human literature in additional locations, such as the vertebral body, e.g. Schmorl node or secondary to vertebral collapse, and within the vertebral canal (Kumpan et al., 1986; Yoshida et al., 1997).

Although the gas accumulation itself is often considered benign, the distribution pattern or location may have clinical relevance. Research in human medicine has indicated that a linear intravertebral vacuum phenomenon most likely occurs secondary to a benign vertebral collapse, whereas a bubble-like intravertebral vacuum phenomenon is more suggestive of an infectious etiology (Gohil et al., 2014). While a vacuum phenomenon located in the intervertebral disc space in dogs is considered unreliable to presurgically identify herniated discs causing acute neurological signs (Müller et al., 2013), a human intraspinal

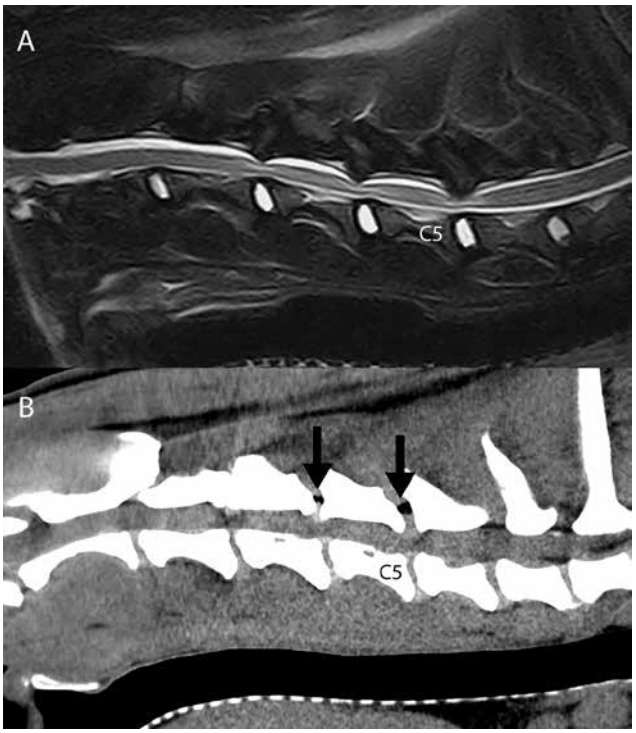

Figure 1. A. FSE T2 sagittal 0.25T MR image and B. soft tissue algorithm sagittal reconstructed CT images of the cervical spine. A. Intramedullary spinal cord T2 hyperintensities are seen at the level of C3-4, C4-5 and C5-6 associated with mild (C3-4) and moderate (C4-5, C5-6) dorsal, midline spinal cord compression. B. Multiple vacuum phenomena can be detected dorsally to the spinal cord at the level of C4-5 and C5-6 (arrows).

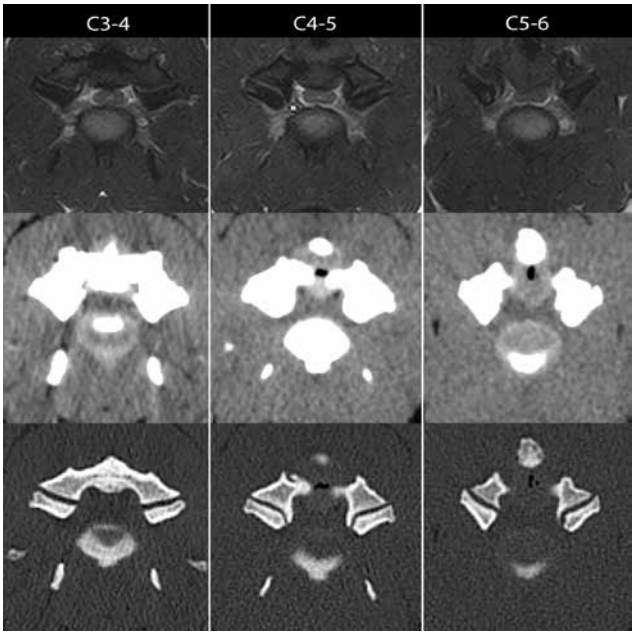

Figure 2. Transverse MR and CT images at the level of C3-4, C4-5 and C5-6 with the upper row representing the HYCE sequence, the middle row the CT soft tissue algorithm and the bottom row the CT bone algorithm acquisition. Dorsal midline spinal cord compression is present at the level of at all three sites, successively worsening caudally.

vacuum phenomenon may have a large clinical relevance by causing nerve root compression and subsequent radicular symptoms (Yoshida et al., 1997).

In the present case report, vacuum phenomena in the degenerative and hypertrophic ligamentum flavum of a dog with cervical stenotic myelopathy is described and a tentative theory of the origin of this phenomenon is proposed.

CASE PRESENTATION

Signalment, history and clinical findings

A six-year-old, intact, male American Staffordshire terrier with a six-week history of mild right thoracic and severe right pelvic limb proprioceptive deficits was presented for further examination. The neurological symptoms were acutely initiated during an incident involving another dog that tried to attack him. The owner pulled his dog back by the leash. The owner had not noticed any abnormalities prior to this event. Six weeks of strict rest and non-steroidal anti-inflammatory drug treatment revealed no clinical improvement.

On arrival at the referral hospital, the dog was alert with a normal posture but still mildly atactic on his pelvic limbs with mild to severe proprioceptive deficits of the right thoracic and right pelvic limb, respectively. The right thoracic limb also showed mild muscle atrophy, a missing radial reflex and worn claws. The cranial nerves and the other spinal reflexes were normal, as were the left thoracic and pelvic limbs. Except for a tense neck, no pain was observed on palpation or mobilization of the spine. Results of the neurological examination were mostly consistent with a disorder of the C1-C5 spinal cord segments. Complete blood count and biochemistry profile showed only mild leucopenia (3,6 x 10.9/l; reference 6-17). The most likely diagnosis was thought to be fibrocartilaginous embolism with secondary ischemic myelopathy. The absence of clear pain or forebrain signs made intervertebral disc disease, inflammatory central nervous system disease, such as meningomyelitis, or neoplasia less likely.

IMAGING, DIAGNOSIS AND OUTCOME

A native cervical CT (Philips Brilliance 40, Philips Medical Systems, the Netherlands) and MRI (Vet-MR Grande, 0.25 Tesla, Esaote, Italy) were performed under general anesthesia (Figures 1 and 2). The CT examination revealed cervical canal stenosis at the C3-4, C4-5, and C5-6 intervertebral levels with mild, moderate and severe dorsal midline spinal cord compression, respectively (Figures 1B and 2). This multifocal stenosis was caused by (1) a well-defined and smooth, bony proliferation of the cranial and caudal aspects of the dorsal laminae and spinous processes and (2) the

adjacent presence of a moderate amount of soft tissue between the vertebral arches. Changes were visible from the caudal aspect of the spinous process of C3 to the cranial aspect of the dorsal spinous process of C6. Vacuum phenomena, seen as round to oval areas of hypoattenuation (-450 to -580 Hounsfield units), were noticed within the soft tissue changes or adjacent to the bony proliferations of C3-4, C4-5 and C5-6. No signs of ventral or lateral spondylosis were observed. Small osteophytes were seen at both the C4-5 and right-sided C5-6 articular process joints.

The subsequently performed MRI provided evidence of myelopathy at the stenotic areas with thin and elongated intramedullary T2 hyperintense lesions (Figures 1A and 2). The proliferative tissues between the vertebral arches were T1 and T2 isointense to the surrounding musculature and caused the ventral displacement of the spinal cord and effacement of the T2 signal dorsal to the spinal cord, indicating dorsal spinal cord compression. The T2 signal on the ventral and lateral aspects of the spinal cord was maintained over the entire spinal cord. The intervertebral discs at all three stenotic areas showed no signs of degenerative diseases. The ligamentum flavum connecting the vertebral laminae of the adjacent vertebrae could not be identified or differentiated from the proliferative tissue.

To alleviate the neurological signs, decompressive surgery was performed at C3-4, C4-5 and C5-6 by means of a triple dorsal laminectomy and removal of the soft tissue proliferations. The dog was hospitalized for eleven days due to an initial deterioration of his neurological condition after surgery (nonambulatory tetraparesis). He regained an ambulatory state 28 days post surgery. During the follow-up consultations, the dog was considered fully recovered without any neurological deficit six months after surgery.

The extirpated tissue was fixed in 4 % buffered formalin, processed by standard procedures and embedded in paraffin blocks. Tissue sections (5 µm thick) were stained with Mayer's hematoxylin/eosin for routine examination and with special stains to identify acid mucins (Alcian blue-PAS), calcium deposits (Von Kossa), proteoglycans (Safranin O), and elastin (Van Gieson). The tissue consisted of thickened, dense, fibrous connective tissue with abundant intracellular collagen, mild fibroplasia and foci of loose vascular connective tissue along the dorsal edge (Figure 3A). In the dorsal parts, there were sparse multifocal fibroplasia and hemosiderophagocytosis, and small numbers of intact and fragmented elastin fibers (Figure 3B) with a mixture of neutral and acid mucins (Figure 3C). In the ventrally oriented projections, the stroma was basophilic with multifocal cartilage differentiation and a dominance of acid mucins (Figure 3D). The ventral proliferations and cartilaginous tissue contained moderate to high amounts of proteoglycans, and the dorsal as well as the more fibrous parts contained no or minimal amounts of proteoglycans (Figure 3E). Small, focal mineralizations were seen in a few ventral proliferations, and a few dispersed individual cell mineralizations were seen in the cartilaginous tissue (not shown). The histopathological diagnosis was chronic degeneration, proliferation and hypertrophy of the fibrocartilaginous tissue consistent with ligamentum flavum.

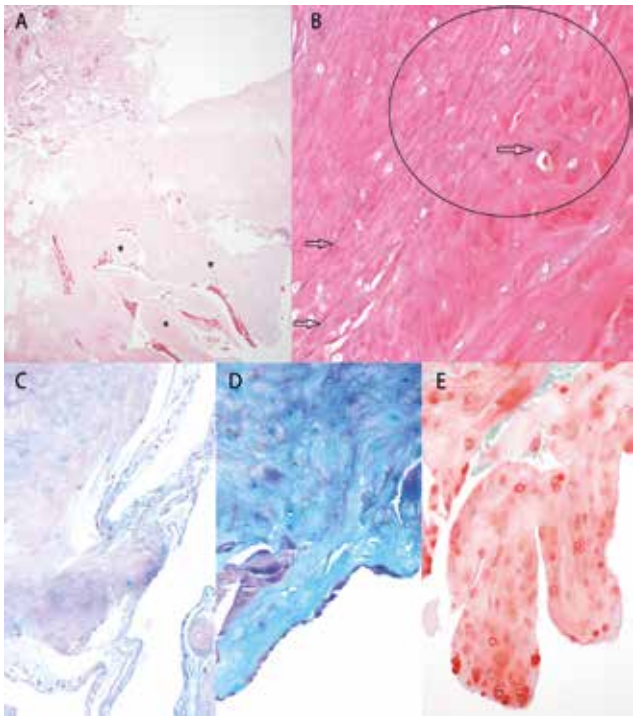

Figure 3. Histopathology results. A. Overview with dorsal fibrovascular tissue in upper part of image and ventral fibrocartilaginous proliferations indicated by *(HE, original magnification 40x). B. VG-Elastin stain showing elastin fibers (arrows) and fractured fibers in the circled area (original magnification 100x). C. Alcian blue-PAS showing a mixture of neutral and acid mucin (purple) staining (original magnification 100x). D. Alcian blue-PAS showing dominant acid (blue) staining (original magnification 100x). E. Safranin O staining showing moderate to strong (orange to red) proteoglycan staining in the ventral fibrocartilaginous proliferations (original magnification 100x).

DISCUSSION

A multifocal ligamentum flavum degeneration and hypertrophy associated with proliferation of the vertebral arch of the four adjacent cervical vertebrae with concomitant vacuum phenomena were seen causing moderate-to-severe dorsal vertebral canal stenosis and associated compressive myelopathy in a middle-aged American Staffordshire terrier. To the best of the authors' knowledge, there are no published data describing this phenomenon within the ligamentum flavum tissue.

The vacuum phenomenon is a radiographic sign describing the abnormal accumulations of gas lucencies. Initially described within the intervertebral disc

by Magnusson (1937), vacuum phenomena have also been occasionally observed in other joint spaces as well as within vertebrae (Libicher et al., 2007; Ito et al., 2008). Intervertebral disc vacuum phenomena and those located within synovial joint spaces are often associated with degenerative joint disease or excessive distractive forces, e.g. in case of stress radiography, joint luxation (Knutsson, 1942; Weber et al., 1995; Gottschalk et al., 1999, Schwarz et al., 2000), whereas intravertebral vacuum phenomena may be associated with both benign, e.g., traumatic fracture, osteomyelitis, and malignant (neoplasia) processes (Knutson, 1942; Resnick et al., 1981; Gohil et al., 2014). These gas lucencies should be differentiated from the venous air embolisms routinely seen on computed tomography studies in both humans and small animals secondary to vessel catheterization and contrast administration (Heng et al., 2014).

The mechanism of vacuum phenomenon formation is still equivocal, with theories assigning important roles to local pressure changes, compromised tissue vascularity, and the composition of the vacuum gas consisting of 90-92% nitrogen (Ford et al., 1977; Gohil et al., 2014). The histopathological finding of fibrocartilaginous changes in the ligamentum flavum is of special interest and suggests an explanation for the unique localization of the vacuum phenomena seen in this case. Fibrocartilaginous tissue is a connective tissue mainly seen in intervertebral discs, intra-articular discs, such as the temporomandibular joint disc, and menisci (Almarza et al., 2004). With increasing age and degeneration, these discs change significantly with alterations in both morphology, e.g. concentric tears or loss of height, and biochemical distribution. The main biochemical change in disc degeneration is the loss of proteoglycan leading to, among other changes, decreased osmotic pressure of the disc tissue (Urban and Roberts, 2003; Adams and Roughley, 2006). As the osmotic pressure decreases, the tissue nitrogen might precipitate out of solution and accumulate as dissolved gas, i.e. create vacuum phenomena (Gohil et al., 2014). Whereas tissues with extensive blood flow can clear nitrogen relatively easily (Hall, 2011), less perfused tissues, such as synovial joints, combined with a compromised vascularity due to degeneration, could further facilitate the creation of vacuum phenomena. In the present case, the authors hypothesize that the fibrocartilaginous transformation of the ligamentum flavum has resulted in a similar drop of pressure and compromised tissue vascularity with subsequent vacuum phenomena formation.

Whether the ligamentum flavum hypertrophy occurred first with secondary osseous proliferations or vice versa remains unknown. However, the histopathological changes of the ligamentum flavum with fibrosis, i.e. an increase in collagen fibers and a loss of elastic fibers, and calcifications are typically seen in post-inflammatory repair processes (Yoshiiwa et al., 2016). This suggests that a primary osseous proliferation has caused mechanical stress on the ligamentum flavum, and secondary repetitive inflammatory reactions and repair processes have resulted in chronic active ligamentum flavum hypertrophy and proliferation with minimal residual inflammation.

Osseous-associated cervical spondylomyelopathy (OA-CSM) is another condition of vertebral stenosis characterized by both osseous and ligamentum flavum hypertrophy, yet it differs both anatomically and demographically from the present case. First, the spinal cord compression in OA-CSM is most often secondary to osseous proliferation of the articular process joints causing lateralized compressions (da Costa et al., 2012), which is in contrast with the present case in which only mild osteoarthritis of these joints was observed, and the compressions were located dorsally. Secondly, OA-CSM has been reported in young dogs (median age: 2 years) of various large and giant breeds (Gasper et al., 2014). In a recent study by De Decker et al. (2012) in young Basset Hounds (median age: 1.4 years), a combined vertebral arch and ligamentum flavum hypertrophy was also noticed, yet limited to one or two sites of spinal cord compression. The authors suspect an underlying genetic defect based on the breed-specific characteristic of the observed changes, even though further investigation is warranted. Neither the last mentioned study nor studies investigating OA-CSM mention the presence of vacuum phenomena (da Costa et al., 2012; De Decker et al., 2012; Gasper et al., 2014).

In conclusion, this case presents a novel location for vacuum phenomena within the proliferative ligamentum flavum. A tentative theory of origin is proposed. Yet, further investigation is necessary to unravel the exact underlying formation process and to reveal its clinical relevance.

ACKNOWLEDGEMENTS

This case report was funded by Stiftelsen Strömsholm Djursjukvård.

REFERENCES

Adams MA, Roughley PJ. (2006). What is intervertebral disc degeneration, and what causes it? *Spine* (Phila Pa 1976) *31*, 2151–2161.

Almarza AJ, Athanasiou KA. (2004) Design characteristics for the tissue engineering of cartilaginous tissues. *Annals of Biomedical Engineering 32*, 2-17.

da Costa R, Echandi R, Beauchamp D. (2012). Computed tomography myelographic findings in dogs with cervical spondylomyelopathy. *Veterinary Radiology and Ultrasound 53*, 64-70.

De Decker S, De Risio L, Lowrie M, Mauler D, Beltran E, Giedja A, Kenny PJ, Gielen I, Garosi L, Volk H. (2012). Cervical vertebral stenosis associated with a vertebral arch anomaly in the Basset hound. *Journal of Veterinary Internal Medicine 26*, 1374-1382.

Ford LT, Gilula LA, Murphy WA, Gado M. (1977). Analy-

sis of gas in vacuum lumbar disc. *American Journal of Roentgenology 128*, 1056-1057.

Gasper JA, Rylander H, Stenglein JL, Waller KR. (2014). Osseous-associated cervical spondylomyelopathy in dogs: 27 cases (2000-2012). *Journal of the American Veterinary Medical Association 244*, 1309-1318.

Gohil I, Vilensky J, Weber E. (2014). Vacuum phenomenon: clinical relevance. *Clinical Anatomy 27*, 455-462.

Gottschalk RD, Kirberger RM, Fourie SL. (1999). Vacuum phenomenon in equine carpal, metacarpophalangeal and metatarsophalangeal joints. *Journal of South African Veterinary Association 70*, 5-8.

Hall JE. (2011). Effect of high partial pressures of individual gases on the body. In: Hall JE. (editor). *Guyton and Hall Textbook of Medical Physiology*. Twelfth edition, Philadelphia, PA, Saunders Elsevier, 535-540.

Hathcock J. (1994). Vacuum phenomenon of the canine spine: CT findings in 3 patients. *Veterinary Radiology and Ultrasound 35*, 285-289.

Heng H, Ruth J, Lee K. (2014). Venous air embolism detected on computed tomography of small animals. *Journal of Small Animal Practice 55*, 420-423.

Ito H, Yoshikawa T, Hayashi N, Ohtomo K. (2008). MDCT demonstration of intraarticular gas in the glenohumeral joint and sternoclavicular joint with reference to arm position. *Radiation Medicine 26*, 422-426.

Knutsson F. (1942). The vacuum phenomenon in the intervertebral disc. *Acta Radiologica 23*, 173-179.

Kumpan W, Salomonowitz E, Seidl G, Wittich G. (1986). The intravertebral vacuum phenomenon. *Skeletal Radiology 15*, 444-447.

Libicher M, Appelt A, Berger I, Baier M, Meeder PJ, Grafe I, DaFonseca K, Nöldge G, Kasperk C. (2007). The intravertebral vacuum phenomenon as specific sign of osteonecrosis in vertebral compression fractures: results from a radiological and histological study. *European Radiology 17*, 2248-2252.

Magnusson W. (1937). Über die Bedingungen des Hervortretens der wirklichen Gelenkspalte auf dem Röntgenbilde. *Acta Radiologica 18*,733-741.

Müller M, Ludewig E, Oechtering G, Scholz M, Flegel T. (2013). The vacuum phenomenon in intervertebral disc disease of dogs based on computed tomography images. *Journal of Small Animal Practice 54*, 253-257.

Resnick D, Niwayama G, Guerra J Jr, Vint V, Usselman J. (1981). Spinal vacuum phenomena: anatomical study and review. *Radiology 139*, 341-348.

Schwarz T, Owen M, Long S, Sullivan M. (2000). Vacuum disk and facet phenomenon in a dog with cauda equine syndrome. *Journal of the American Veterinary Medical Association 217*, 862-864.

Urban J, Roberts S. (2003). Degeneration of the intervertebral disc. *Arthritis Research and Therapy 5*, 120-130.

Weber W, Berry C, Kramer R. (1995). Vacuum phenomenon in twelve dogs. *Veterinary Radiology and Ultrasound 3*6, 493-498.

Yoshida H, Shinomiya K, Nakai O, Kurosa Y, Yamaura I. (1997). Lumbar nerve root compression caused by lumbar intraspinal gas. Report of three cases. *Spine 22*, 348-351.

Yoshiiwa T, Miyazaki M, Notani N, Ishihara T, Kawano M, Tsumura H. (2016). Analysis of the relationship between ligamentum flavum thickening and lumbar segmental instability, disc degeneration, and facet joint osteoarthritis in lumbar spine stenosis. *Asian Spine Journal 10*, 1132-1140.