Severe focal myelopathy secondary to chronic compression by an arachnoid pseudocyst in a Rottweiler

Z. S. POLIZOPOULOU (Ζ.Σ. ΠΟΛΥΖΟΠΟΥΛΟΥ), V. D. SOUFTAS (Β.Δ. ΣΟΥΦΤΑΣ), G. BRELLOU (Γ. ΜΠΡΕΛΛΟΥ), M. N. PATSIKAS (Μ.Ν. ΠΑΤΣΙΚΑΣ), N. SOUBASIS (Ν. ΣΟΥΜΠΑΣΗΣ), A. F. KOUTINAS (Α.Φ. ΚΟΥΤΙΝΑΣ)

■ Severe focal myelopathy secondary to chronic compression by an arachnoid pseudocyst in a Rottweiler

Polizopoulou Z. S.[1], DVM, PhD, DipECVCP, **Souftas V. D.**[2], MD, PhD, **Brellou G.**[3], DVM, PhD,

Patsikas M. N.[4], DVM, PhD, DipECVDI, **Soubasis N.**[4], DVM, PhD,

Koutinas A. F.[4], DVM, PhD, DipECVD

[1] *Diagnostic Laboratory, Faculty of Veterinary Medicine, Aristotle University of Thessaloniki*
[2] *Radiology – Medical Imaging Department of Medical School, Democritus University of Thrace*
[3] *Laboratory of Pathology, Faculty of Veterinary Medicine, Aristotle University of Thessaloniki*
[4] *Clinic of Companion Animals, Faculty of Veterinary Medicine, Aristotle University of Thessaloniki*

■ Βαριάς μορφής εστιακή συμπιεστική μυελοπάθεια από αραχνοειδή ψευδοκύστη σε σκύλο φυλής Rottweiler

Ζ. Σ. Πολυζοπούλου[1], DVM, PhD, DipECVCP,

Β. Δ. Σουφτάς[2], MD, PhD, **Γ. Μπρέλλου**[3], DVM, PhD,

Μ. Ν. Πατσίκας[4], DVM, PhD, DipECVDI, **Ν. Σούμπασης**[4], DVM, PhD,

Α. Φ. Κουτίνας[4], DVM, PhD, DipECVD

[1] *Διαγνωστικό Εργαστήριο, Κτηνιατρική Σχολή ΑΠΘ*
[2] *Εργαστήριο Ακτινολογίας - Ιατρικής Απεικόνισης, Τμήμα Ιατρικής, Δημοκρίτειο Πανεπιστήμιο Θράκης*
[3] *Εργαστήριο Παθολογικής Ανατομικής, Κτηνιατρική Σχολή ΑΠΘ*
[4] *Κλινική Ζώων Συντροφιάς, Κτηνιατρική Σχολή ΑΠΘ*

ABSTRACT. A four-year old Rottweiler was presented with tetraplegia, established progressively over a 4-month period. Initially the dog developed paresis of the posterior limbs that subsequently evolved to tetraparesis and finally tetraplegia. Upon neurological examination the dog exhibited spastic tetraplegia with exaggerated spinal reflexes in all four limbs. The neuroanatomical lesion localization indicated a focal or diffuse cervical spinal cord disease. Cisternal myelography revealed obstruction of the contrast medium flow at the level of C5 vertebral body. Magnetic resonance imaging disclosed intradural-extramedullary compression of the spinal cord at the level of C5-C6 intervertebral disc by a spinal arachnoid pseudocyst, syrinx formation and myelopathy expressed as abnormally higher signal on T2-weighted images at the C5 segment level. Severe demyelination, involving exclusively the white matter of the grossly affected segments and extending rostrally into the brainstem and caudally into the thoracic spinal cord segments, was noticed on histopathology. The unusually severe secondary degenerative change in the cervical spinal cord white matter, inflicted by focal SAP compression, was the most interesting finding.

Keywords: Arachnoid pseudocyst, dog, MRI, myelography, myelopathy

Correspondence: Polizopoulou Z. S.
Diagnostic Laboratory, Aristotle University of Thessaloniki,
11, S. Voutyra str., 546 27 Thessaloniki, Greece

Αλληλογραφία: Ζ. Σ. Πολυζοπούλου
Κτηνιατρική Σχολή ΑΠΘ, Διαγνωστικό Εργαστήριο, Στ. Βουτυρά 11, 546 27 Θεσσαλονίκη

ΠΕΡΙΛΗΨΗ. Το περιστατικό που περιγράφεται αφορούσε σε σκύλο φυλής Rottweiler, ηλικίας τεσσάρων ετών, ο οποίος προσκομίστηκε στην Κλινική των Ζώων Συντροφιάς, επειδή εμφάνιζε για διάστημα 4 μηνών μυελική αταξία και τετραπάρεση που επιδεινώνονταν προοδευτικά (αυχενικό σύνδρομο). Στη νευρολογική εξέταση ο σκύλος εμφάνιζε σπαστική τετραπληγία, χωρίς άλλα ευρήματα από τη γενική κλινική εξέταση και τις αρχικές εργαστηριακές εξετάσεις (αιματολογική, βιοχημική του ορού και ακτινολογική εξέταση της αυχενικής μοίρας της σπονδυλικής στήλης). Στη μυελογραφία διαπιστώθηκε αδυναμία προώθησης του σκιαγραφικού μέσου μετά από το επίπεδο του 5ου αυχενικού σπονδύλου και στη μαγνητική τομογραφία παρατηρήθηκε ενδοσκληρίδια-εξωμυελική συμπίεση και διόγκωση του νωτιαίου μυελού στο επίπεδο του 5ου και 6ου μεσοσπονδύλιου διαστήματος από αραχνοειδή ψευδοκύστη και εστιακή μυελοπάθεια που αφορούσε στα νευροτόμια A_5-A_6. Στην ιστοπαθολογική εξέταση διαπιστώθηκε διάχυτη απομυελίνωση της αυχενικής μοίρας του νωτιαίου μυελού, η οποία ήταν ιδιαιτέρως έντονου βαθμού στα νευροτόμια A_5-A_6, αλλά επεκτεινόταν και σε απομακρυσμένα από την αλλοίωση σημεία, όπως ο προμήκης μυελός και η θωρακική μοίρα του νωτιαίου μυελού, γεγονός το οποίο ήταν και το πλέον ενδιαφέρον εύρημα.

Λέξεις ευρετηρίασης: Αραχνοειδής ψευδοκύστη, σκύλος, μυελοπάθεια, μυελογραφία, μαγνητική τομογραφία

INTRODUCTION

Spinal arachnoid pseudocysts (SAP) are cerebrospinal fluid-filled, intradural-extramedullary cavitary lesions that have been reported with increasing frequency as causes of spinal cord compression in dogs and are similar to human type III meningeal cysts (Hardie et al. 1996, Bagley 2005). In most of the reports there is a relative overrepresentation of Rottweilers developing single or multiple SAP in the cervical spinal cord (Rylander et al. 2002, Gnirs et al. 2003, Jurina and Grevel 2004). The etiology of SAP remains controversial though congenital defects or developmental malformations and secondary changes following inflammatory or repeated traumatic insults have been suggested (Rylander et al. 2002, Gnirs et al. 2003, Jurina and Grevel 2004). The latter could be associated with the excessive mobility and conformational peculiarities of cranial cervical region in Rottweilers (Gnirs et al. 2003). Neurological signs are usually of mild to moderate severity, being indicative of a progressive transverse myelopathy secondary to focal spinal cord compression. Most of the clinical studies describe the diagnostic approach, surgical management and outcome of the cases, but information regarding the secondary changes within the spinal cord is very limited, probably because most animals recover after surgery (Frykman 1999, Rylander et al. 2002, Skeen et al. 2003, Jurina and Grevel 2004). This report presents the clinical and histopathological findings in a Rottweiler with a cervical SAP and secondary focal myelopathy.

CASE HISTORY

A four-year old intact female Rottweiler was admitted to Companion Animal Clinic, Faculty of Veterinary Medicine, Aristotle University of Thessaloniki, due to progressive spinal ataxia and tetraparesis. Mild to moderate pelvic limb ataxia had been observed 4 months before the admission, progressing eventually to tetraparesis and tetraplegia.

Upon neurological examination the dog exhibited spastic tetraplegia with exaggerated (+3) spinal reflexes in all four limbs. The other neurological functions and tests were within normal limits. Neuroanatomical localization of the lesion was indicative of a focal to diffuse cervical (C1-C5) spinal cord disease.

Routine clinicopathological evaluation (complete blood count, serum biochemistry, urinalysis), cerebrospinal fluid analysis and plain survey radiographs of the cervical spine were unremarkable. Cisternal myelography revealed dorsal and ventral attenuation of the contrast material within the caudal part of the 5th cervical vertebra (Figure 1). Magnetic resonance imaging (MRI) disclosed intradural-extramedullary spinal compression by a subarachnoid pseudocyst at the level of C5-C6 intervertebral space and the formation of a syrinx (25 mm-long) in the spinal cord cranially to the 5th vertebral body level. In the same area, a mild distension of the central canal along with axonal myelopathy was visualized on T2-weighted images, expressed as an abnormally higher signal (Figure 2). Spinal cord widening was isointense on T1-weighted scans and did not enhance after the intravenous injection of 10 ml (10 mmol) gadolinium-DTPA (Magnevist®, Bayer Schering Pharma AG, Germany). Spinal cord myelopathy at C5 level, due to chronic spinal cord compression and impaired cerebrospinal fluid (CSF) flow caused by the SAP, were subsequently diagnosed. Demyelinating disease, either primary (neurodegenerative syndrome) or

Figure 1. Cervical myelogram showing attenuation of contrast material at the level of the C5-C6 vertebrae.
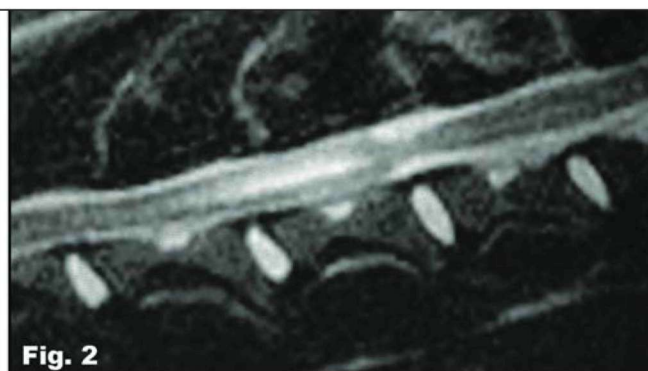

Figure 2. Saggital T2-weighted Fast Spin Echo image (TR, 3500 ms; TE, 120 ms) shows an elongated area of high signal intensity in C4-C5 spinal cord segments.

secondary (myelitis), was suspected due to the chronicity of the case. Since severe neurological dysfunction made functional recovery rather impossible, the owners elected euthanasia giving their consent for necropsy.

Necropsy revealed a 2 cm long enlargement of the spinal cord, occupying the 5th and 6th spinal segments (Figure 3) looking pale and dull upon transverse sectioning at the area of dorsal and lateral funiculi. Brain and spinal cord were fixed in 10% neutral buffered formalin and specimens were routinely processed, embedded in paraffin, cut at 4-5 μm and stained with haematoxylin and eosin (HE). Selected sections were stained with Luxol fast blue-cresyl Echt violet and Bielschowsky's silver stain. Glial fibrillary acidic protein (GFAP) was immunostained on deparaffinized sections by standard streptavidin-biotin peroxidase immunohistochemistry using a rabbit anti-GFAP antibody (DAKO, Glostrup, Denmark; 1:200) as primary and biotinylated goat anti-rabbit IgG (DAKO; 1:250) as secondary antibody. Diamino-benzidine was used as chromogen and tissues were counterstained with haematoxylin. HE stained sections from the area caudally to the spinal cord enlargement demonstrated a ruptured fibrotic cyst without epithelial lining (pseudocyst) and pronounced spinal cord compression at the level of C5 (Figure 3 inset).

In the affected areas the lesions were restricted exclusively to white matter and were most extensive and severe in the dorsal and lateral funiculi of the abnormally enlarged cervical cord segments (Figure 4A), where myelin was hardly stained and appeared spongiotic due to oedema, microcavitation and rare-faction (Figures 4 and 5A). Severe demyelination, swelling and splitting of myelin sheaths, gliosis, prominent gemistocytic astrocytosis (Figures 4, 5A and 6A) and macrophage infiltration with only a few gitter cells were also demonstrated (Figure 4B). In the cavitated areas there was some axonal depletion, although most of the axons were well preserved. Occasional axons showed mild to moderate degeneration and swelling with the presence of a few axonal spheroids (Figure 6B).

Smaller foci of demyelination and myelin vacuolation of white matter tracts extended both rostrally and caudally from the affected cervical segments with progressively decreasing severity, while Wallerian axonal degeneration of axons was minimal. These foci were relatively symmetrical and extended cranially to the brainstem and cerebellum and caudally up to the T1 vertebra level. Most of the lesions were localized within the fasciculus gracilis and cuneatus of the dorsal funiculi, dorsal and ventral spinocerebellar, lateral corticospinal and rubrospinal fasciculi of the lateral funiculi and anterior corticospinal and vestibulospinal fasciculi of the ventral funiculi. In medulla oblongata, foci of mild demyelination were detected at the spinal tract of the trigeminal nerve, corpus restiforme, medial lemniscus, spinocerebellar and rubrospinal fasciculi. In the pons, lesions were similarly mild and involved the medial lemniscus, corticopontine, corticomedullary and corticospinal fasciculi. Foci of mild myelin vacuolation were also found in the cerebellar peduncles and deep cerebellar white matter.
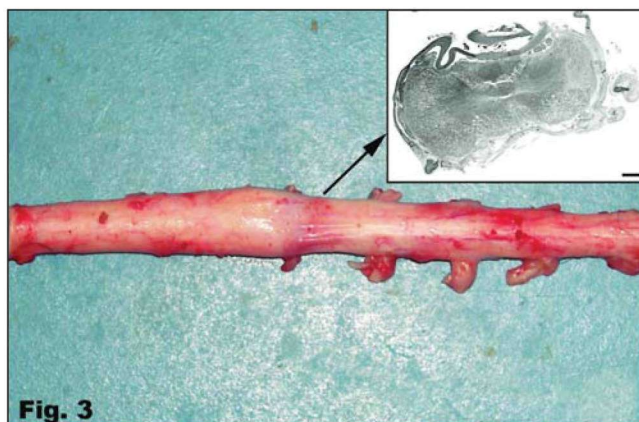
Figure 3. Gross appearance of the cervical spinal cord, showing a focal enlargement at the level of the 4th and 5th segments. Inset: Spinal cord, C5. Spinal cord dorsoventral narrowing is highly indicative of compressive myelopathy (arrow). Barr= 600 μm.
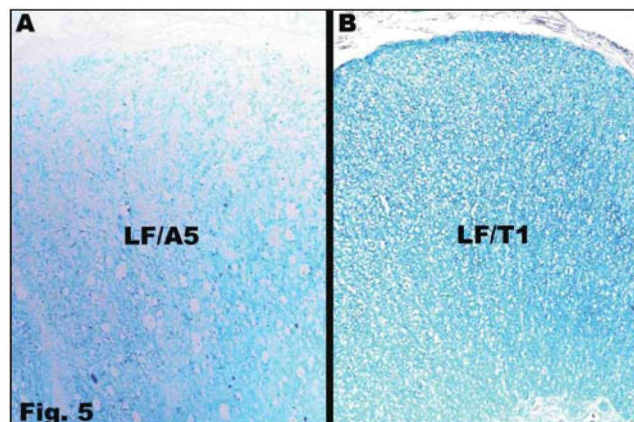

Figure 5. Spinal cord, C5 (5A) and T1 (5B). Side to side comparison of the lateral funiculi (LF) white matter myelin staining at two different levels of the spinal cord. Compare pallor due to demyelination (5A) with normal myelin staining (5B). Luxol fast blue-cresyl Echt violet, Barr= 250 μm.
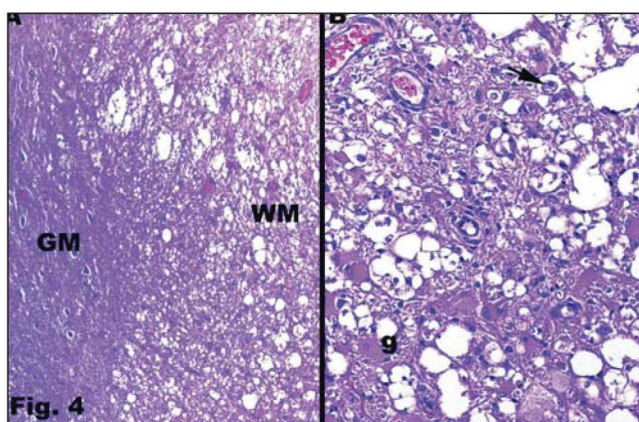

Figure 4. Spinal cord, C5. (A) Spongiotic appearance of demyelinated areas in the white matter (WM). Gray matter (GM) is unaffected. (B) Higher magnification of the demyelinating lesion showing myelin sheath breakdown, polycavitation and gliosis with numerous gemistocytes (g). Gitter cell (arrow) infiltration is unremarkable. Haematoxylin and Eosin, (A) Barr=250 μm and (B) Barr= 50 μm.
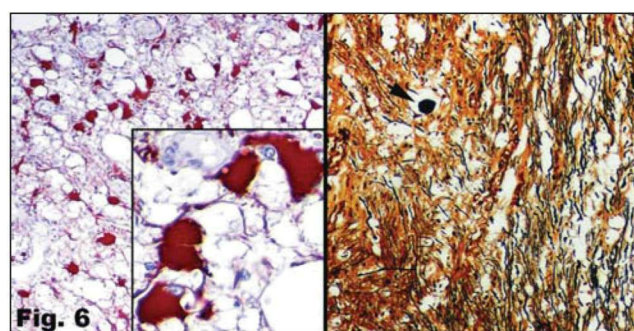

Figure 6. 6A. Spinal cord, C5. The intense positive cytoplasmic GFAP staining of astrocytes (brown color) makes it easier to appreciate the prominence of gemistocytic response. Inset: gemistocytes. GFAP immunohistochemical stain, Barr= 100 μm; inset Barr= 25 μm. **6B.** Spinal cord, C5. Relative preservation of the axons coursing through severely demyelinated area. There is moderate axonal loss with a single axonal spheroid (arrow). Bielschowsky's silver stain, Barr= 100 μm.

DISCUSSION

Cervical SAP are usually diagnosed with myelography showing a bulbous dilatation of the subarachnoid space (Gnirs et al. 2003, Skeen et al. 2003). However, both in humans and dogs, a complete block of contrast medium flow at the lesion site similar to what was seen in the present case has also been described, thus suggesting the presence of a SAP totally isolated from the subarachnoid space and mimicking an intradural lesion (Bassiouni et al. 2004, Jurina and Grevel 2004). This may cause minimal compliance of the fluid-filled cystic structure and persistent spinal cord compression that might explain the dilatation and severity of the lesions (Gnirs et al. 2003, Wang et al. 2003, Bassiouni et al. 2004).

In the present case the neurological deterioration was the result of compression-induced lesions, which are rather uncommon in SAP compared to other com-

pressive myelopathies. Even in those cases, in which a persistent spinal cord deformity was witnessed upon spinal surgery, subsequent clinical improvement, following the decompression, may indicate that lesions are usually mild to moderate and reversible (Frykman 1999, Gnirs et al. 2003). Histopathologic analysis on SAP tissue obtained at surgery has revealed chronic mesenchymal tissue proliferation, moderate fibrosis and adhesion of pia to arachnoid mater (Gnirs et al. 2003, Jurina and Grevel 2004). Degenerative changes observed in the spinal cord of affected dogs, in which a post-mortem examination was allowed, included axonal degeneration, myelin loss, multifocal white matter cystic cavitation and moderate to severe meningeal fibrosis (Rylander et al. 2002). Gray matter lesions have been minimal, in contrast to other types of compressive myelopathies in which they have been amply seen within the intermediate and ventral horn area (Al Mefty et al.1993).

In the experimental chronic compression of the spinal cord, changes such as myelin destruction, loss of white matter axons and gray matter neurons at the affected segments may lead to severe and irreversible motor paresis due to loss of neurons via apoptosis (Al Mefty et al. 1993, Yamaura et al. 2002). Loss of oligodendrocytes could be responsible for the demyelination of long tracts, because individual oligodendrocytes myelinate multiple axons in the CNS (Yamaura et al. 2002). It is speculated that this type of oligodendrocyte loss contributes to long-tract degeneration observed in chronic compressive myelopathies (Yamaura et al. 2002). In humans with longstanding myelopathies secondary to SAP, these changes may ultimately lead to fibrosis, atrophy and permanent neurological deficits, although a positive correlation between duration of preoperative disease and outcome is not always possible (Yamaura et al. 2002, Bassiouni et al. 2004).

In the Rottweiler of the present study the pseudocyst was completely isolated from the subarachnoid space, hence corresponding to category III of human SAP (Nabors et al. 1988). A functional one-way valve might have developed, allowing the inflow of cerebrospinal fluid, but blocking its outflow from the cavity and leading to progressive expansion and spinal cord compression (Summers et al. 1995, Jurina and Grevel 2004).

Reactive astrocytosis, observed in the demyelinated areas and assumed to be stimulated by myelin basic protein (Bologa 1985), minimal lymphoplasmacytic infiltration within the affected segments and symmetrical distribution of white matter involvement may exclude the inflammatory process as a cause of demyelination (Bologa 1985, Summers et al. 1995). Extensive white matter spongiosis and microcavitation may be held responsible for the focal enlargement of the C4-C5 spinal cord segments, which, by interfering with the caudal flow of contrast medium, gave the false impression of an intramedullary space-occupying lesion. Therefore, it is advisable to use MRI in all SAP-suspect cases, because it reveals the precise location and relationship of the lesion to the spinal cord, provides additional information on spinal cord integrity and the existence of other abnormalities, such as atrophy or syringomyelia (Rylander et al. 2002, Skeen et al. 2003, Jurina and Grevel 2004). Myelography may fail, as it was shown here, to diagnose non-communicating cysts or worse, to misdiagnose them as space-occupying lesions which bear poor prognosis and may lead to the wrong decisions (Skeen et al. 2003, Jurina and Grevel 2004). Despite the controversy regarding the efficacy of surgical treatment (Frykman 1999, Rylander et al. 2002, Skeen et al. 2003, Jurina and Grevel 2004) and the difficulty in predicting a favourable outcome, it has been suggested that factors like young age (<3 years), short duration of clinical signs (<4 months) and marsupialization of SAP are associated with a more favourable outcome (Skeen et al. 2003). The fact that none of the operated animals was tetraplegic probably justifies our decision not to pursue decompressive surgery in this Rottweiler (Frykman 1999, Rylander et al. 2002, Skeen et al. 2003, Jurina and Grevel 2004). ■

REFERENCES

Al-Mefty O, Harkey LH, Marawi I, Haines DE, Peeler DF, Wilner HI, Smith RR, Holaday HR, Haining JL, Russel WF, Harrison B, Middleton TH (1993) Experimental chronic compressive cervical myelopathy. Journal of Neurosurgery, 79: 550-561.

Bagley RS (2005) Clinical features of important and common diseases involving the spinal cord of dogs and cats. In: Fundamentals of Veterinary Clinical Neurology, Blackwell, Ames, pp. 166-167.

Bassiouni H, Hunold A, Asgari S, Hübschen U, König H-J (2004) Spinal intradural juxtamedullary cysts in the adult: surgical management and outcome. Neurosurgery, 55: 1352-1360.

Bologa L (1985) Oligodendrocytes, key cells in myelination and target in demyelinating disease. Journal of Neuroscience Research, 14: 1-20.

Frykman OF (1999) Spinal arachnoid cyst in four dogs: diagnosis, surgical treatment and follow-up results. Journal of Small Animal Practice, 40: 544-549.

Gnirs K, Ruel Y, Blot S, Begon D, Rault D, Delisle F, Boulouha L, Colle MA, Carozzo C, Moinsonierre P (2003) Spinal subarachnoid cysts in 13 dogs. Veterinary Radiology and Ultrasound, 44: 402-408.

Hardie RJ, Linn KA, Rendano VT (1996) Spinal meningeal cyst in a dog: a case report and literature review. Journal of the American Animal Hospital Association, 32: 477-480.

Jurina K, Grevel V (2004) Spinal arachnoid pseudocysts in 10 rottweilers. Journal of Small Animal Practice, 45: 9-15.

Nabors MW, Pait TG, Byrd EB, Karim NO, Davis DO, Kobrine AI, Rizzoli HV (1988) Updated assessment and current classification of spinal meningeal cysts. Journal of Neurosurgery, 68: 366–377.

Rylander H, Lipsitz D, Berry WL, Sturges BK, Vernau KM, Dickinson PJ, A_or SA, Higgins RJ, LeCouteur RA (2002) Retrospective analysis of spinal arachnoid cysts in 14 dogs. Journal of Veterinary Internal Medicine, 16: 690-696.

Skeen TM, Olby NJ, Mu_ana KR, Sharp NJ (2003) Spinal arachnoid cysts in 17 dogs. Journal of the American Animal Hospital Association, 39: 271-282.

Summers BA, Cummings JF, de Lahunta A (1995) Principles of neuropathology. In: Veterinary Neuropathology, Mosby, St. Louis: pp. 42-44.

Wang MJ, Levi AD, Green BA (2003) Intradural spinal arachnoid cysts in adults. Surgical Neurology, 60: 49–56.

Yamaura I, Yone K, Nakahara S, Nagamine T, Baba H, Uchida K, Komiya S (2002) Mechanism of destructive pathologic changes in the spinal cord under chronic mechanical compression. Spine, 27: 21-26.