TRADITION AND MODERNITY IN VETERINARY MEDICINE, 2024, vol. 9, No 2(17): 83–92

HORNER'S SYNDROME IN DOGS – A REVIEW

Said Cafer, Bengü Bilgiç, Mehmet Erman Or

Institute of Internal Medicine, Faculty of Veterinary Medicine, Istanbul University – Cerrahpasa, Istanbul, Türkiye, 34320

E-mail: saidcafer@ogr.iuc.edu.tr, bengu.bilgic@iuc.edu.tr, ermanor@iuc.edu.tr

ORCID: 0009-0002-4470-9890 S.C.; 0000-0002-6952-2937 B.B.; 0000-0002-8764-1956 M.E.O.

(Submitted: 10 August 2024; Accepted: 10 October; 25 November 2024)

ABSTRACT

Horner's syndrome is characterized by the symptoms of miosis, anisocoria, ptosis, enophthalmos and protrusion of the third eyelid as a result of an interruption in the sympathetic nervous system extending from the hypothalamus of the brain to the eye. It has been identified in almost every mammal, including humans. The sympathetic nervous system consists of 3 main parts and these are the central, preganglionic and postganglionic neurons. In order to find the interruption on this system, diagnosis and differential diagnosis must be made and the underlying ethiology of the disease must be found. For this, an accurate examination and lesion localization is required. Topical application of cocaine to the eyes is considered the gold standard in the pharmacological method of lesion localization. Although there are many underlying etiologies, idiopathic Horner's syndrome in dogs is more common than other etiologies. Apart from the pharmacological methods, radiology, CT and MRI imaging techniques are also common tools used to determine the ethiology.

Key words: Horner's syndrome, dog, myosis, ptosis, enophthalmos, anisocoria.

Introduction

Horner's syndrome was first described by François Pourfour du Petit in 1727, with the findings observed after the transection of upper sympathetic nerves of a in a dog (Pearche, 2020). It was later named after Johann Friedrich Horner and was recorded with the symptoms that occur as a result of the interruption of the innervation of the eye's sympathetic system and additional tissues connected to the eye (Abbas *et al.*, 2015). These symptoms include protrusion of the upper eyelid called ptosis, protrusion of the third eyelid, sunken eyeball called enophthalmos, miosis and related anisocoria (Zwueste *et al.*, 2019). In addition to these symptoms, facial anhidrosis has also been reported in humans (Martin, 2007). It is thought that 45% of dogs with Horner's syndrome are idiopathic (Fitzmaurice, 2010). In a study conducted in the United Kingdom on Golden Retrievers with Horner's Syndrome, it was reported that the majority of these cases were seen in males and that they occurred due to idiopathic reasons (Boydell, 1995). Many studies have been conducted to determine the most affected race (Simpson *et al.*, 2013; Zwueste *et al.*, 2019). In a study conducted with dogs with Horner's Syndrome, it was reported that 110 of 155 dogs were of Golden Retriever breed and 100 of them were of idiopathic origin (Boydel P, 2000). Similarly, in another study, 10 of 21 dogs were determined to be Golden Retrievers (Simpson *et al.*, 2013). It has been reported that Golden Retrievers with idiopathic Horner's Syndrome are generally male (Gould, 2014).

Horner's Syndrome can occur due to lesions in any part of the sympathetic nervous system line. First, second and third order neuron lesions may develop secondarily due to brachial plexus lesions, injuries or middle ear disease such as otitis media (Gould, 2014). However, in most cases, the location of the lesion cannot be determined. This explains the idiopathic course of most of the disease (Van Den Broek, 1987). Despite its generally idiopathic course, it heals spontaneously and may not require treatment (Viscasillas *et al.*, 2013). This idiopathic course may often result from

failure to make a correct differential diagnosis or limited veterinary knowledge. However, the underlying ethiology of the disease may worsen the prognosis. For this reason, finding the underlying ethiology, using differential diagnoses and determining the prognosis are very important for the course of the disease. In this review article, it is aimed to explain the anatomy and ethiology of the disease as well as lesion localizations in order to better understand the disease.

Clinical Anatomy

Ocular sympathetic innervation is provided by the 3-neuron sympathetic system that reaches from the hypothalamus to the eye (Figure 1) (Maggs, 2018). These consist of central, preganglionic and postganglionic neurons (Van Den Broek, 1987).

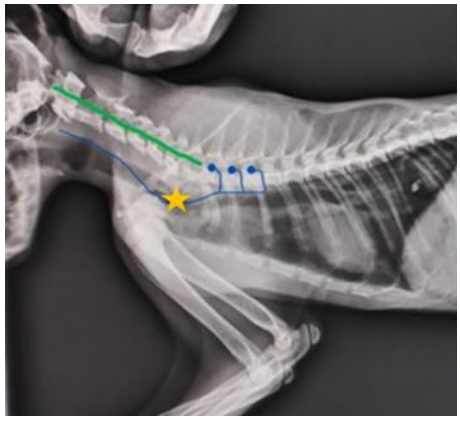

Figure 1: Green line: Central neurons (lateral tectotegmental spinal cord tract); blue line: preganglionic neurons; blue dots (left to right): T1, T2, T3; star symbol: middle cervical ganglion (original picture).

The central line includes certain parts of the spinal cord, starting from the forebrain (Viscasillas *et al.*, 2013). Efferent neurons originating from the hypothalamus pass through the brainstem and proceed from the tectum, the local area in the dorsal part of the midbrain, and the tegmentum, which forms its body (Mughal *et al.*, 2009). This line extends to the first three thoracic spinal cord segments (Viscasillas *et al.*, 2013). They synapse on the preganglionic cell bodies located in the lateral gray horns of the first three thoracic vertebrae (de Lahunta, 2020). From here, the nerves connected to the secondary neuron line leave the spinal cord line and pass to the thoracic sympathetic trunk. This line is called the preganglionic line (Viscasillas *et al.*, 2013). From here, it separates from the spinal cord segment via the ventral root (Figure 2). Immediately after separation, it follows a cranial path and proceeds to the thoracic sympathetic trunk through the ramus communicans and intervertebral foramen (Zwueste *et al.*, 2019). Here, preganglionic neurons passing through the cervicothoracic ganglion and then the cervical ganglion unite with the vagosympathetic trunk in the carotid sheath. Although they proceed adjacent to the vagus nerve, they do not unite and move away from each other after traveling a short distance (Figure 1) (Viscasillas *et al.*, 2013). Preganglionic nerves reaching the cranial cervical ganglion unite with the third nerve line called postganglionic. The nerves coming out of this ganglion form a plexus at the level of the internal carotid artery. This plexus is called carotid plexus. Nerves emerging from the carotid plexus divide into branches. While some of them pass through the tympanic bulla, some of them proceed along the medial side of the bulla without entering the calvarium. While the branching nerves innervate

the nasociliary nerve and from there the iris dilator muscle, some of them innervate the eyelids and the eye. However, unlike cats, sympathetic innervation of the third eyelid smooth muscles is not provided in dogs (Zwueste *et al.*, 2019).

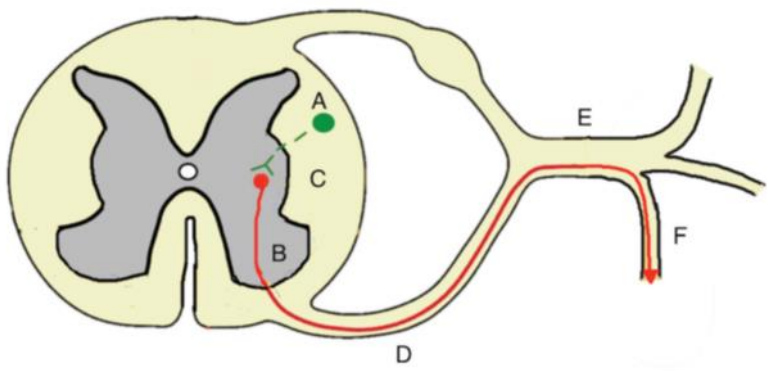

Figure 2: Cross-section of thoracic spinal cord segment. Central line (A). Will synapse onto preganglionic line (B) in intermediolateral horn of gray matter (C). Preganglionic nerve line exits via ventral nerve root (D), courses within spinal nerve (E), and then divides as ramus communicans (F) (Zwueste *et al.*, 2019).

Clinical Findings

Horner's Syndrome is a combination of many ipsilateral eye and side tissue symptoms that occur as a result of sympathetic innervation disorder of the eye and surrounding tissues (Jaggy A, 2010). These symptoms are hypersensitivity, anisocoria characterized by asymmetric pupil, miosis, ptosis, enophthalmos and third eyelid protrusion (Simpson *et al.*, 2013). The most common of these symptoms is considered miosis and is usually unilateral. While mydriasis is visible in dim light in a healthy eye, it is not seen in an eye with Horner's Syndrome. Thus, clinical diagnosis can be made (Van Den Broek, 1987).

The use of some pharmacological substances facilitates clinical diagnosis. Cocaine, in particular, has a very important place in clinical diagnosis because it inhibits the reuptake of norepinephrine. However, the fact that it is difficult to find and its use is limited increases the interest in other pharmacological substances (Mughal *et al.*, 2009).

1. Miosis and Anisocoria

The most common symptom in Horner's Syndrome is unilateral miosis, defined by reduced pupil size (Van Den Broek, 1987). This may occur as a result of a brachial plexus lesion (Crispin SM, 2005). In such a case, the absence of the ipsilateral cutaneous truncus reflex is also observed (Fitzmaurice, 2010). Additionally, miosis can also be seen alone (Freeman, 2020).

The innervation of the pupil is connected sympathetically to the iris dilator muscle and parasympathetically to the iris sphincter muscle through the innervation of the oculomotor nerve in the preganglionic nerve network (Freeman, 2020). The sympathetic innervation of the iris dilator muscle, which is a smooth muscle in the affected eye, is insufficient (Maggs, 2018). When sympathetic innervation is interrupted, if not damaged, only parasympathetic stimulation is provided. This causes the pupil size to become smaller (Freeman, 2020). As a result, the sizes of the two pupils

differ and an asymmetry occurs. This asymmetry is called anisocoria. In dim light, in unconscious animals or in times of fear, anisocoria becomes highly visible (Fitzmaurice, 2010).

Affected eyes should be examined in both dim light and bright conditions. In a bright environment, the pupil of the affected eye shrinks more than the healthy pupil; in a dim environment, the size of the healthy pupil enlarges more than the affected eye (de Lahunta, 2020).

2. Ptosis

Ptosis is the drooping of the upper eyelid as a result of the interruption of the sympathetic innervation to the eyelids in certain pathologies (Zwueste *et al.*, 2019). Upper eyelid stimulation is provided sympathetically by stimulating the levator palpabrae superioris and its extension, the Müller muscle (Jaggy A, 2010). Sometimes, in sympathetic denervations, the lower eyelid rises upwards and this is called reverse ptosis (Martin, 2007). In such a case, as the upper eyelid descends, the lower eyelid also rises, and as a result, the palpebral fissure narrows (Fitzmaurice, 2010). This may also cause eye discharge (Featherstone, 2011).

3. Enophthalmos

Interruption of the sympathetic innervation of the eye and surrounding tissues not only affects the upper and lower eyelids, but also causes the innervation of other sympathetic muscles to be interrupted. It is also possible that the retractorbulbi muscle, which is innervated by the abducens cranial nerve, which ensures the eye's outward posture, may be affected (de Lahunta, 2020). Interruption of sympathetic innervation disrupts the tone of the smooth muscles of the eye and causes the eyeball to shift slightly backward within its orbit. This is called enophthalmos (Van Den Broek, 1987).

Apart from the retractorbulbi muscle, ptosis and reverse ptosis are another condition that causes narrowing of the palpebral fissure and an increase in enophthalmos (Mughal *et al.*, 2009). However, in humans, affecting the retractorbulbi muscle only causes ptosis and the resulting narrowing of the palpebral fissure, resulting in an enophthalmia-like appearance (Kong, 2007; Zwueste *et al.*, 2019). On the other hand, it causes third eyelid prolapse in dogs (Zwueste *et al.*, 2019).

4. Third Eyelid Protrusion

It is a condition in which the third eyelid protrudes slightly and covers the front of the eye, resulting from sympathetic denervation of the smooth muscles (Fitzmaurice, 2010). Unlike humans, this condition, which is seen only in animals, can develop secondary to enophthalmia (Crispin SM, 2005).

In a healthy eye, as a result of the contraction of the retractorbulbi and rectus muscles, the third eyelid passively protrudes outwards and closes the eye. In Horner's Syndrome, when the eyeball returns to the orbit due to enophthalmos, the eyelid also protrudes (de Lahunta, 2020).

Diagnosis

To diagnose Horner's Syndrome, it is necessary to first detect the clinical symptoms and determine the location of the sympathetic innervation interruption. Once the location of the lesion in the 3rd order neuron pathway is determined, the ethiology can be found. Although it is suggested

that the syndrome may be due to pre- and post-ganglionic innervation interruption, it is also thought that it may occur as a result of demyelination, trauma or vascular problems (Freeman, 2020).

The presence of lesions, infectious diseases, tumoral structures, trauma, and even diseases that may cause innervation interruption, such as otitis media, also play a role in the ethiology of Horner's Syndrome (Zwueste *et al.*, 2019).

Differantial Diagnosis

Since Horner's syndrome has similar clinical findings to many ophthalmological diseases, a differential diagnosis list should be created by taking into account other diseases in the same localization. The clinical findings of Horner's syndrome can be confused with eye diseases such as uveitis and ulcerative keratitis, which veterinarians frequently encounter in the clinic, but other findings may not be accompanied in these diseases (Zwueste *et al.*, 2019). While miosis can occur unilaterally in cases such as corneal ulceration and keratitis, bilateral miosis can also be observed in hepatic encephalopathy (Van Den Broek, 1987).

Redness occurs in the conjunctiva as a result of third eyelid protrusion. This condition can be confused with diseases such as uveitis or glaucoma (Williams, 2002). If it is bilateral, it should be differentiated from dehydration and tetanus (Van Den Broek, 1987). Red eye is distinguished from keratoconjunctivitis sicca using the "Shirmer Tear" test, and keratitis is distinguished using the "Fluorescein" test (Stades, 2007).

Localization and Ethiology

For localization, the central, pre- and postganglionic sympathetic nervous system to the eye must be taken into account (Van Den Broek, 1987). In dogs, especially Golden Retrievers, lesion localization is much more important but also difficult, as it is generally idiopathic (Maggs, 2018).

The central nerve line is the sympathetic pathway extending from the hypothalamus, which includes the cervical segments of the hypothalamus, brainstem and spinal cord, to the T1, T2 and T3 segments of the spinal cord (Van Den Broek, 1987). Any interruption in the sympathetic nerve network passing through here may result from trauma, infection, focal myelopathy, spinal fracture or luxation, embolism and intervertebral disc disease of the spinal cord (Freeman, 2020; Maggs, 2018). Lesions on the first 5 cervical vertebrae can cause upper motor neuron symptoms as well as miosis, ptosis, enophthalmos, and third eyelid luxation. While white matter lesions occurring between the cervical sixth and eighth lesions or lesions occurring in the gray matter of the medulla spinalis between the first three thoracic vertebrae cause almost all symptoms of Horner's Syndrome, they can also cause serious symptoms such as tetraparesis (de Lahunta, 2020). Neuropathies that also affect the nucleus of the trigeminal cranial nerve in the pons cause Horner's Syndrome (Mayhew 2002). In addition, infections and polyradiculoganglioneuritis may also affect the trigeminal cranial nerve and cause the disease (Panciera *et al.*, 2002).

In lesions affecting the hypothalamus, not only Horner syndrome occurs, but also the body's homeostasis is disrupted and non-neurological symptoms such as polydipsia/polyuria are also observed. Additionally, lesions in the brainstem or the first cervical segment of the spinal cord cause upper motor neuron symptoms (Van Den Broek, 1987).

Many cranial nerves are affected in diabetic people. As a result, diseases such as facial paralysis and optic neuritis develop, which causes Horner's Syndrome. Diabetic neuropathy has also

been reported in dogs and may lead to ocular sympathetic dysfunction and Horner's Syndrome (Miller *et al.*, 2018). However, although unilateral Horner's Syndrome has been reported in diabetic dogs, bilateral occurrence is very rare, even in naturally occurring diseases (Holland, 2007). Apart from these, diseases that can be seen together with Horner's Syndrome include pachymeningitis, vestibular disease, otitis media and interna (de Lahunta, 2020; Fitzmaurice, 2010).

The preganglionic pathway extends from the first 3 thoracic vertebrae to the cranial cervical ganglion, and the origin of the sympathetic innervation interruption here may be idiopathic or may result from traumatic, neoplastic, infectious or brachial plexus block (Van Den Broek, 1987). The presence of a lesion in the preganglionic sympathetic pathway can be confirmed by pharmacological tests, radiography, computed tomography (CT) and Magnetic Resonance Imaging (MRI) (Zwueste *et al.*, 2019). The most common causes of preganglionic sympathetic innervation interruption include trauma, surgical complications and spinal neoplasias (Melián *et al.*, 1996). Interruptions occurring here may affect the motor neuron system and cause motor dysfunctions in the front and hind legs. Additionally, a lesion in the ventral roots can cause paralysis with damage to the brachial plexus. Respiratory disorders may occur as a result of a lesion in the chest (Van Den Broek, 1987).

The cause of sympathetic innervation interruption in the postganglionic pathway can be seen as a result of the presence of a lesion or a post-operative complication (Freeman, 2020). Horner Syndrome due to thyroid carcinoma has also been reported in dogs (Melián *et al.*, 1996). While a lesion in the middle ear may cause vestibular symptoms (head shaking, loss of balance), a lesion in the retrobulbar tract may cause damage to the 2nd, 3rd, 4th and 6th cranial nerves (Van Den Broek, 1987). To detect the presence of the lesion, palpation, ear and orbit CT and MRI evaluation can be performed (Zwueste *et al.*, 2019). It is also known that otitis media affects the sympathetic nerve network. Otitis media may cause Horner's syndrome in dogs and may also affect trigeminal and facial sympathetic innervation (Gotthelf, 2004). Dogs are less prone to Horner syndrome of otitis media/interna origin than cats due to their bulla structure, but imaging of the tympanic bulla is performed for localization (Kennis, 2013).

Pharmacological Lesion Localization

Pharmacological tests are widely used test models for lesion localization (Zwueste *et al.*, 2019). In human medicine, it has been reported that cocaine applications are especially successful in distinguishing patients with Horner's Syndrome from people with similar symptoms but different diseases (Kardon *et al.*, 1990).

When the sympathetic innervation of the eye is interrupted (in cases such as Horner's Syndrome), the affected eye narrows more than the unaffected eye, resulting in anisocoria (Freeman, 2020). Norepinephrine is a neurotransmitter that binds to α-adrenergic receptors (Zwueste *et al.*, 2019). As a result of innervation interruptions in the sympathetic pathway, norepinephrine release decreases (Lee, 2019). The most commonly used agent among pharmacological substances is cocaine, which is a norepinephrine reuptake inhibitor secreted from the ends of nerve cells and is used in 5-10% solution (Zwueste *et al.*, 2019). Norepinephrine accumulates in receptors. The healthy pupil dilates, but the affected pupil does not respond to norepinephrine and does not dilate because it is denervated. Even in 1932, the use of cocaine in Horner's Syndrome was mentioned (Thompson *et al.*, 1971). Although cocaine is very effective in finding lesion localization in patients with Horner's Syndrome, its use is also difficult (Kanagalingam *et al.*, 2015). Because its acquisition and

storage are subject to strict controls (Zwueste *et al.*, 2019). The use of apraclonidine has been recommended for this purpose (Bremner, 2019).

Apraclonidine acts as an α-2 adrenergic agonist in the central nervous system. It is generally used in the treatment of increased intraocular pressure in humans (Morales, 2000). It inhibits the release of noradrenaline by activating α-2 receptors. As a result, a narrowing of the pupil occurs. However, denervation in Horner's Syndrome causes upregulation of α-1 receptors, thus dilating the pupil (Bremner, 2019). In this way, when dropped into the healthy and affected eyes, it corrects anisocoria within 30-45 minutes with the application of 0.5% to 1% apraclonidine (Zwueste *et al.*, 2019).

Alternatively, topical phenylephrine can be used. Phenylephrine is an α-adrenergic agonist that can be administered in solutions up to 10%. While it can be used in dogs, it is not effective in cats (Martin, 2019). 1% phenylephrine solution dilates the pupil during postganglionic interruptions. On the other hand, while a very small amount of expansion is observed in preganglionic denervations, no expansion is observed in central denervations (Syam *et al.*, 2004). The duration of action is less than 20 minutes, and less than 8 minutes in 10% solutions. In cases lasting more than 20 minutes but less than 45 minutes, denervation can be thought to be in the preganglionic nerve line (Freeman, 2020).

The use of 1% hydroxyamphetamine is also a widely used pharmacological agent for localization because it is a sympathomimetic substance and stimulates the release of norepinephrine from postganglionic neurons (Zwueste *et al.*, 2019). In the use of hydroxyamphetamine, the pupil does not dilate because norepinephrine production will not occur or will be incomplete in the eye with postganglionic lesion (Mughal *et al.*, 2009). However, expansion is observed within 45 minutes in healthy eyes and eyes with central or preganglionic lesions (Zwueste *et al.*, 2019).

Prognosis and Treatment

Treatment depends on the underlying disease and its prognosis. These processes may be inflammatory, neoplastic or neuronal (Esson, 2015). However, it may not require treatment as it usually heals spontaneously and does not cause a systemic disease (Viscasillas *et al.*, 2013). This is particularly due to the commonly idiopathic course of the disease. Most symptoms do not reduce the patient's quality of life and disappear after a while (Zwueste *et al.*, 2019). However, in a study published in 2008 (Cho *et al.*, 2008), it was reported that acupuncture treatment was applied to a dog with idiopathic Horner's syndrome, and the clinical symptoms improved from the second day of treatment, and it was suggested that acupuncture was an effective treatment method for Horner's Syndrome.

For treatment, accurate localization and detection of the underlying disease is required. While regression and recovery can be expected in Horner's syndrome with correct treatment, recovery is not possible in the presence of neoplasia (Van Den Broek, 1987). In Horner's syndrome caused by infection, it is possible to improve Horner's syndrome by treating the underlying disease. In some cases, systemic anti-inflammatory drugs can be used for treatment (Esson, 2015). Imaging techniques such as CT, MRI, neurological examinations and pharmacological tests are needed to find the cause (Zwueste *et al.*, 2019).

Conclusion

Horner's syndrome is a syndrome characterized by miosis, ptosis, enophthalmos and protrusion of the third eyelid. Various etiologies, such as lesions and inflammations, cause disruption of sympathetic innervation and create the syndrome. But it usually has an idiopathic course. Lesions are localized as central, preganglionic and postganglionic neuron pathways. Interruption of sympathetic innervation can not only cause Horner's syndrome, but also cause diseases in many eyes and adjacent tissues. Prognosis and treatment depend on the underlying ethiology. For this reason, neurological examination and radiological imaging techniques can be used to determine the localization of the lesion causing Horner's syndrome, as well as pharmacological tests. Depending on the underlying ethiology or symptomatic treatment, the symptoms of Horner's Syndrome may disappear after a while. However, this situation may vary depending on the underlying disease or lesion. Failure to use correct diagnosis and diagnostic methods in the presence of a lesion may cause the disease to have more extensive consequences. For this reason, more consistent diagnosis and lesion localization are critical for the prognosis of the disease.

References

1. Abbas, A., Manjila, S., Singh, M., Belle, V., Chandar, K., & Miller, J. P. (2015). *Johann Friedrich Horner and the Repeated Discovery of Oculosympathoparesis: Whose Syndrome Is It?.* Neurosurgery, 77(3), 486–491. https://doi.org/10.1227/NEU.0000000000000832.
2. Boydel P. (2000). *Idiopathic horner syndrome in the golden retriever.* Journal of neuro–ophthalmology: the official journal of the North American Neuro–Ophthalmology Society, 20(4): 288–290.
3. Boydell P. (1995*). Idiopathic Horner 's syndrome in the golden retriever.* Journal of Small Animal Practice, 36: 382–384. https://doi.org/10.1111/j.1748–5827.1995.tb02958.x.
4. Bremner F. (2019). *Apraclonidine Is Better Than Cocaine for Detection of Horner Syndrome*. Front Neurol. Jan 31: 10:55. https://doi.org/10.3389/fneur.2019.00055.
5. Cho SJ, Kim O. (2008). *Acupuncture treatment for idiopathic Horner's syndrome in a dog*. J Vet Sci, 9(1): 117–9. https://doi.org/10.4142/jvs.2008.9.1.117.
6. Crispin SM. (2005). *Notes on Veterinary Ophtalmology*. Blackwell Publishing, Oxford, 77.
7. de Lahunta, Glass E, Kent M. (2020). *De Lahunta's veterinary neuroanatomy and clinical neurology*. Saunders Company, Philadelphia, fifth edition, 208, 219, 272, 355–362.
8. Esson DW. (2015). Clinical atlas of canine and feline ophthalmic disease. Wiley Blackwell, Ames, IA, 310.
9. Featherstone H, Holt E. (2011). *Small animal ophthalmology : what's your diagnosis?.* Wiley–Blackwell, Chichester, 183.
10. Fitzmaurice S. (2010). *Small animal neurology*. Elsevier Saunders, Edinburgh, first edition, 117–133.
11. Freeman PM, Ives E. (2020). A practical approach to neurology for the small animal practitioner, Rapid reference series. John Wiley and Sons, Hoboken, 75, 197, 202–207.
12. Gotthelf LN. (2004). *Diagnosis and treatment of otitis media in dogs and cats*. The Veterinary clinics of North America. Small animal practice, 34(2): 469–487. https://doi.org/10.1016/j.cvsm.2003.10.007.
13. Gould D, McLellan GJ. (2014). *BSAVA Manual of Canine and Feline Ophthalmology*. British Small Animal Veterinary Association, Gloucester, third edition, 205.

14. Holland CT. (2007). *Bilateral Horner's syndrome in a dog with diabetes mellitus.* The Veterinary record, 160(19): 662–664. https://doi.org/10.1136/vr.160.19.662.

15. Jaggy A. 2010. Small Animal Neurology. Schlütersche, Hannover, first edition, 421.

16. Kanagalingam S, Miller NR. (2015). *Horner syndrome: clinical perspectives*. Eye and brain, 7: 35–46. https://doi.org/10.2147/EB.S63633.

17. Kardon RH, Denison CE, Brown CK, Thompson HS. (1990). *Critical evaluation of the cocaine test in the diagnosis of Horner's syndrome.* Archives of ophthalmology Chicago, Ill. : 1960, 108(3): 384–387. https://doi.org/10.1001/archopht.1990.01070050082036.

18. Kennis RA. (2013). *Feline otitis: diagnosis and treatment*. The Veterinary clinics of North America. Small animal practice, 43(1): 51–56. https://doi.org/10.1016/j.cvsm.2012.09.009.

19. Kong YX, Wright G, Pesudovs K, O'Day J, Wainer Z, Weisinger HS. (2007). *Horner syndrome.* Clinical & experimental optometry, 90(5): 336–344. https://doi.org/10.1111/j.1444–0938.2007.00177.x.

20. Lee AG, Sinclair AJ, Sadaka A, Berry S, Mollan SP. (2019). *Neuro–Ophthalmology: Global Trends in diagnosis, treatment and management.* Springer, Cham, first edition, 122.

21. Maggs DJ, Miller PE, Ofri R. (2018). *Slatter's fundamentals of veterinary ophthalmology*. Elsevier, St. Louis, sixth edition, 408.

22. Martin CL, Pickett JP, Spiess BM. (2019). *Ophthalmic disease in veterinary medicine*. CRC Press/Taylor & Francis Group, Boca Raton, second edition, 53.

23. Martin TJ. (2007). *Horner's syndrome, Pseudo–Horner's syndrome, and simple anisocoria.* Current neurology and neuroscience reports, 7(5): 397–406. https://doi.org/10.1007/s11910–007–0062–y.

24. Mayhew PD, Bush WW, Glass EN. (2002). *Trigeminal neuropathy in dogs: a retrospective study of 29 cases (1991–2000)*. Journal of the American Animal Hospital Association, 38(3): 262–270. https://doi.org/10.5326/0380262.

25. Melián C, Morales M, Espinosa de los Monteros A, Peterson ME. (1996). *Horner's syndrome associated with a functional thyroid carcinoma in a dog*. The Journal of small animal practice, 37(12): 591–593. https://doi.org/10.1111/j.1748–5827.1996.tb02336.x.

26. Miller EJ, Brines CM. (2018). *Canine Diabetes Mellitus Associated Ocular Disease*. Topics in companion animal medicine, 33(1): 29–34. https://doi.org/10.1053/j.tcam.2018.03.001.

27. Morales J, Brown SM, Abdul–Rahim AS, Crosson CE. (2000). *Ocular effects of apraclonidine in Horner syndrome*. Archives of ophthalmology Chicago, Ill. : 1960, 118(7): 951–954.

28. Mughal M, Longmuir R. (2009). *Current pharmacologic testing for Horner syndrome*. Current neurology and neuroscience reports, 9(5): 384–389. https://doi.org/10.1007/s11910–009–0056–z.

29. Panciera RJ, Ritchey JW, Baker JE, DiGregorio M. (2002). *Trigeminal and polyradiculoneuritis in a dog presenting with masticatory muscle atrophy and Horner's syndrome.* Veterinary pathology, 39(1): 146–149. https://doi.org/10.1354/vp.39–1–146.

30. Pearche JMS. (2020). *Pourfour du Petit (1664–1741).* Revue Neurologique, 177(1–2): 7–10. https://doi.org/10.1016/j.neurol.2020.04.023.

31. Simpson KM, Williams DL, Cherubini GB. (2013). *Neuropharmacological lesion localization in idiopathic Horner's syndrome in golden retrievers and dogs of other breeds*. Veterinary Ophthalmology, 18(1): 1–5. https://doi.org/10.1111/vop.12096.

32. Stades FC. (2007). *Ophthalmology for the veterinary practitioner*. Schlütersche, Hannover, second edition, 16.

33. Syam P, Hussain B, Hutchinson C. (2004). Mixed infection (Pseudomonas and coagulase negative

staphylococci) microbial keratitis associated with extended wear silicone hydrogel contact lens. British journal of ophthalmology, 88(4): 579. https://doi.org/10.1136/bjo.2002.015776.

34. Thompson HS, Mensher JH. (1971). *Adrenergic mydriasis in Horner's syndrome*. Hydroxyamphetamine test for diagnosis of postganglionic defects. American journal of ophthalmology, 72(2): 472–480. https://doi.org/10.1016/0002–9394(71)91323–7.
35. Van Den Broek AHM. (1987). *Horner's syndrome in cats and dogs: a review.* Journal of Small Animal Practice, 28: 929–940. https://doi.org/10.1111/j.1748–5827.1987.tb01317.x.
36. Viscasillas J, Sanchis–Mora S, Hoy C, Alibhai H. (2013). *Transient Horner's syndrome after paravertebral brachial plexus blockade in a dog*. Veterinary anaesthesia and analgesia, 40(1): 104–106. https://doi.org/10.1111/j.1467–2995.2012.00770.x
37. Williams DL, Barrie K, Evans TF. (2002). *Veterinary ocular emergencies*. Butterworth–Heinemann, Oxford, first edition, 14.
38. Zwueste DM, Grahn BH. (2019). *A review of Horner's syndrome in small animals*. Can Vet J, 60: 81–88.