Review Article Compte rendu

A review of Horner's syndrome in small animals

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Abstract — Horner's syndrome arises from dysfunction of the oculosympathetic pathway and is characterized by miosis, enophthalmos, protrusion of the third eyelid, and ptosis. It has been recognized in a wide variety of breeds and ages in small animal patients. The oculosympathetic pathway is a 3-neuron pathway. The central/first order neuron arises from the hypothalamus and extends down the spinal cord. The preganglionic/second order neuron arises from the first 3 thoracic spinal cord segments and travels through the thorax and cervical region until it synapses at the cranial cervical ganglion. The postganglionic/third order neuron travels from this ganglion to the orbit. Topical application of cocaine is the gold standard for differentiating Horner's syndrome from other causes of miosis. Topical 1% phenylephrine allows for identification of a post-ganglion Horner's syndrome. Numerous etiologies have been reported for Horner's syndrome, but idiopathic disease is most common. Ancillary diagnostics include otoscopic examination, thoracic radiographs, or advanced imaging. Treatment and prognosis are determined by the etiology.

Résumé — Examen du syndrome de Horner chez les petits animaux. Le syndrome de Horner provient d'une dysfonction de la voie oculo-sympathique et est caractérisée par la miose, l'enophtalmie, la protrusion de la troisième paupière et la ptose. Elle a été reconnue chez une grande variété de races et d'âges chez les patients petits animaux. La voie oculo-sympathique est une voie à trois neurones. Le neurone central/de premier ordre provient de l'hypothalamus et s'étend vers le bas sur la colonne vertébrale. Le neurone préganglionnaire/de deuxième ordre provient des trois premiers segments thoraciques de la colonne vertébrale et se déplace dans le thorax et la région cervicale jusqu'à la synapse au ganglion cervical crânien. Le neurone postganglionnaire/de troisième ordre se déplace de ce ganglion jusqu'à l'orbite. L'application topique de cocaïne est le test de référence pour la différenciation du syndrome de Horner des autres causes de miose. La phényléphrine topique 1 % permet l'identification d'un syndrome de Horner postganglionnaire. Plusieurs étiologies ont été signalées pour le syndrome de Horner, mais la maladie idiopathique est la plus commune. Les diagnostics auxiliaires incluent l'examen otoscopique, des radiographies thoraciques ou une imagerie avancée. Le traitement et le pronostic sont déterminés par l'étiologie.

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Introduction

Horner's syndrome is a phenomenon that arises from dysfunction of the oculosympathetic pathway and is characterized by the constellation of miosis, enophthalmos, protrusion of the third eyelid, and ptosis (Figure 1). It was described as early as 1727, when Francois Pourfour du Petit severed intercostal nerves in dogs and noted ipsilateral ocular effects (1). The classic combination of clinical signs was more fully described later, however, through the independent work of Claude Bernard and Johann Friedrick Horner (1,2).

Horner's syndrome is well-known in small animal medicine and has the potential to affect any breed of cat or dog, although there is a lack of consensus on the population most likely to be affected. One study failed to identify breed predispositions (3) while another suggested that golden retrievers, Labrador retrievers, collies, Shetland sheepdogs, weimaraners, and Doberman pinschers are over-represented (4). A disparate age range can also be found in the literature, with patients presenting anywhere from 5 wk to 17 y of age in dogs, and up to 14 y of age in cats (5,6). It is therefore important to be able to recognize the signs,

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Figure 1. Clinical manifestation of unilateral Horner's syndrome in the right eye of a cat. Note the miosis, enophthalmos, and prolapsed third eyelid. Ptosis was also present, but the eyelids are being retracted in the photo to emphasize the anisocoria.

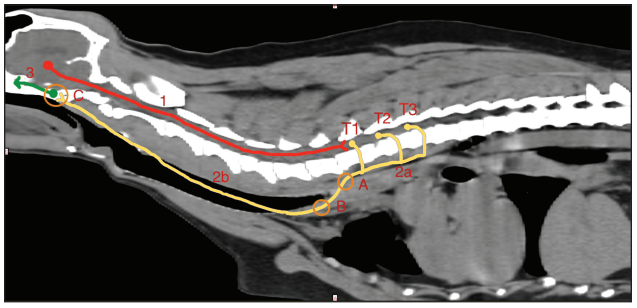

Figure 2. Schematic representation of the oculosympathetic pathway superimposed over a sagittal cervical and thoracic CT image. The central/first order neuron begins within the hypothalamus and travels through the lateral tectotegmental spinal tract (1). The preganglionic/second order neuron begins within the gray matter of the first 3 thoracic spinal cord segments (T1, T2, T3). Its axon continues through the ramus communicans and travels though the thorax within the sympathetic trunk (2a). It will pass through but not synapse within the cervicothoracic ganglion (A) and middle cervical ganglion (B). The sympathetic trunk fuses with the vagus nerve and travels through the cervical region as the vagosympathetic trunk (2b), ultimately synapsing in the cranial cervical ganglion (C). The post-ganglionic axon will then enter the calvarium and continue to the orbit.

understand the underlying neuroanatomy, possible differential diagnoses, available diagnostic tools, treatment options, and expected prognosis. It is on this basis that we provide this review.

Neuroanatomy

Sympathetic innervation to the eye is a 3-neuron pathway. The central or first order neuron begins within the hypothalamus and travels through the brainstem to the lateral tectotegmentospinal tract, which is located within the lateral funiculus of the spinal cord white matter (7–9). The synapse with the preganglionic, or second order, neuron occurs within the intermediolateral horn of the gray matter of the first 3 thoracic spinal cord segments (Figure 2).

The axon of the preganglionic neuron exits the spinal cord segment with the ventral nerve root and travels a brief distance within the spinal nerve before separating as the ramus communicans just as the spinal nerve divides into the dorsal and

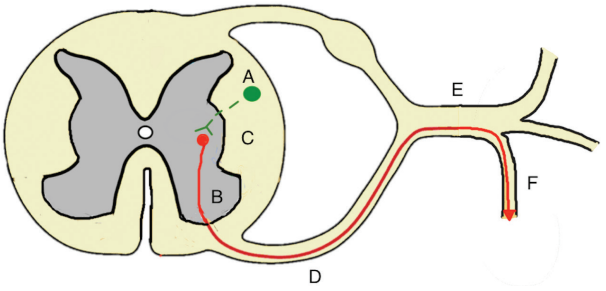

Figure 3. Cross section of the first 3 thoracic spinal cord segments. The central/first order axon travels from the brain through the spinal cord *via* the lateral tectotegmentospinal tract, located within the lateral funiculus of the white matter (A). It will synapse with the preganglionic/second order cell body (B) within the intermediolateral horn of the gray matter (C). The preganglionic axon exits the spinal cord *via* the ventral nerve root (D), travels a short distance within the spinal nerve (E) and then separates as the ramus communicans (F).

ventral branches (Figure 3), lateral to the intervertebral foramen (10,11). The ramus communicans joins the thoracic sympathetic trunk ventrolateral to the vertebral bodies and as the sympathetic pathway travels cranially through the mediastinum it passes through the cervicothoracic ganglion, which is near the surface of the cranial lung lobe, and the middle cervical ganglion (10,11). The nerve does not synapse as it passes through either of these ganglia (Figure 2). At the level of the thoracic inlet the sympathetic trunk fuses with the vagus nerve within a common epineurium (12). This is in contrast to humans, in which the cervical sympathetic trunk and the vagus nerve are adjacent but distinct entities (13). The vagosympathetic trunk courses through the cervical region to the head where the sympathetic trunk once again deviates from the vagus nerve and terminates in the cranial cervical ganglion (9). The cranial cervical ganglion is located ventromedial to the tympanic bulla, and this is where the preganglionic axon synapses with the postganglionic/third order neuron cell body (14). The active neurotransmitter at the ganglion is acetylcholine, which is released by the preganglionic telodendria and binds to nicotinic cholinergic receptors on the postganglionic cell body (11).

Unfortunately, the exact pathway of the postganglionic neuron is not as well-defined as the more proximal portions. Once the axons exit the cranial cervical ganglion, they form a plexus around the internal carotid artery (11). Some of the fibers pass through the tympanic bulla on the ventral surface of the petrosal portion of the temporal bone while others run medial to the bulla before entering the calvarium (9,10). Postganglionic fibers may also continue with the internal carotid artery and enter the calvarium *via* the tympanooccipital fissure and carotid canal (9,15). Once within the calvarium, the postganglionic fibers course ventral to the trigeminal ganglion and exit with the ophthalmic branch of the trigeminal nerve through the orbital fissure (Figure 4), entering the orbit (9,10,15,16). The fibers become the nasociliary nerve and then ultimately the long ciliary nerve, which supplies the iris dilator muscle and blood vessels of the uveal tract (10). Fibers also supply the smooth muscles of the periorbita and the eyelids. The term orbitalis

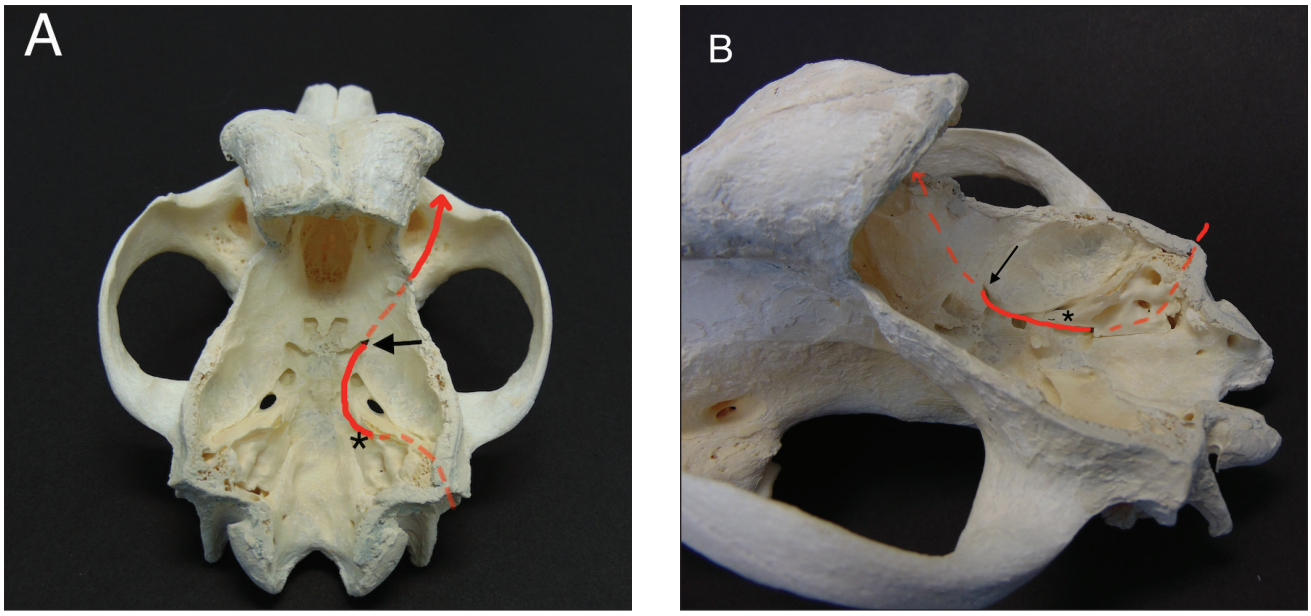

Figure 4. One proposed pathway of the third order/post-ganglionic neuron, shown travelling through the calvarium from a dorsal (A) and oblique (B) perspective. After passing through the tympanic bulla, the nerve enters the calvarium and travels ventral to the trigeminal nerve within the trigeminal canal (asterisk). It exits the calvarium *via* the orbital fissure (arrow) and enters the orbit

muscle *(musculus orbitalis)* has been inconsistently applied to this group of muscles, sometimes referring to the periorbital muscles alone and sometimes also including the muscles of the dorsal, ventral, and third eyelids (17). Cats have sympathetic innervation of the smooth muscles within the third eyelid, a feature that is absent in dogs (17). A portion of postganglionic fibers is designated to travel from the cranial cervical ganglion with the external carotid artery and supply arteries of the face and ears, as well as sweat glands (10). Norepinephrine is the primary neurotransmitter acting at the synapses between the postganglionic telodendria and the effector organs, binding to α-adrenergic receptors (11).

Clinical signs

Horner's syndrome is classified based upon the level of dysfunction within the oculosympathetic pathway — central, preganglionic, or postganglionic — but the signs will be the same regardless of a lesion's location in small animals. It should be noted that with a central lesion it is very unlikely that Horner's syndrome will be the only observed clinical sign. Other expected neurological deficits with a brainstem or spinal cord lesion include altered mentation, paresis, postural reaction deficits, or dysfunction of other cranial nerves. Ataxia may also be observed with a central lesion. The character of the ataxia is most likely to be proprioceptive. This is due to concurrent involvement of the general proprioceptive pathways as they traverse through the spinal cord and brainstem, some of which travel within the lateral funiculus and are close to the tectotegmentospinal tract (9). If the underlying pathology is extensive enough, involvement of the central vestibular system may occur, and a more vestibular ataxia may be noted (9).

Miosis

Miosis of the affected eye is the most commonly identified component of Horner's syndrome and develops secondary to loss of innervation of the iris dilator muscle (10). The iris sphincter muscle, which is innervated by the parasympathetic component of cranial nerve III, is then allowed to act unopposed and leads to pupillary constriction (18). The iris dilator muscle also has a unique feature in that it has dual innervation by both the sympathetic and parasympathetic systems (17). The sympathetic component is what allows the iris dilator muscles to contract and the pupil to dilate. The parasympathetic innervation conversely prevents contraction of this muscle. When the sympathetic pathway is compromised, the inhibitory effect of the parasympathetic innervation further prevents pupil dilation and exacerbates the miosis. (17). Anisocoria will develop with unilateral lesions and is most pronounced under scotopic conditions as the affected eye cannot dilate to the same degree as the normal eye (16). The properly functioning iris sphincter muscle, however, still allows the affected eye to fully constrict under photopic conditions. Indeed, the anisocoria may actually be difficult to appreciate in a brightly lit room. Pupillary light reflexes and vision will remain intact in the affected eye (18).

Ptosis

Ptosis, or drooping of the upper eyelid, leads to a narrowed palpebral fissure in the affected eye (14). The dogma is that ptosis develops because of loss of sympathetic tone in the thin muscles of the eyelids (occasionally referred to as Müller's muscle) (1,2). There are some that argue, however, that this muscle is of minor importance in veterinary species and that the ptosis is secondary to enophthalmos (3,10).

Table 1. Summary of pharmacological diagnosis and localization of Horner's syndrome.

Drug	Mechanism of action	Use	Effect
Cocaine (5% or 10%)	Prevents norepinephrine reuptake	Confirm Horner's syndrome	Dilates Horner's pupil No effect on normal pupil
Apraclonidine (0.5% or 1%)	Weak α-1 adrenergic agonist	Confirm Horner's syndrome	Dilates Horner's pupil (not validated in veterinary patients)
Phenylephrine (0.1% or 1%)	Direct sympathomimetic	Localize Horner's syndrome	Dilates with postganglionic lesion < 20 min No effect on preganglionic, central lesions or normal eye
Hydroxyamphetamine (1%)	Indirect sympathomimetic	Localize Horner's syndrome	Dilates with preganglionic or central lesion, normal eye < 45 min No effect on postganglionic lesion

Enophthalmos

The circular periorbital smooth muscles help maintain the globe in an anterior position within the orbit (9,17). When these muscles relax due to a loss of sympathetic input, the retractor bulbi muscles are without antagonism and they actively retract the globe into the orbit, producing enophthalmos (10,14,18). The absence of the retractor bulbi muscle in humans results in ptosis only (19).

Third eyelid protrusion

Although the degree to which the third eyelid protrudes is variable between cases, it is the second most commonly reported clinical sign (3). The protrusion is passive in dogs and secondary to the enophthalmos (14). In cats there is an additional active component due to the presence of sympathetically mediated smooth muscle within the third eyelid. With a Horner's lesion, the muscle can no longer maintain the eyelid in a retracted position (16,17).

Vascular effects

A loss of sympathetic input can lead to ipsilateral peripheral vasodilation, although this is an uncommonly reported manifestation in small animals (16). The vasodilation may manifest as a warm pinna or hyperemia of the nasal planum and/or conjunctiva (14,20). There is 1 report of a seal point Siamese cat with loss of pigment from the mask on the side of its face (20). The discoloration was attributed to a local increase in temperature and reduced temperature-dependent melanocyte activity following vasodilation (14,20).

Partial Horner's

An incomplete or partial Horner's syndrome is well-described in humans and is characterized by ophthalmic signs (miosis and ptosis) without facial anhidrosis; one of the cardinal signs amongst human patients (19,21). These cases are seen with postganglionic lesions and are often associated with internal carotid artery dissection, due to the close association of sympathetic fibers with the internal carotid adventitia (21). Reference is made to a partial Horner's in dogs with brachial plexus lesions in which only a miosis is seen, but a suitable anatomical explanation has not been provided (16). Miosis is also associated with acute forebrain and midbrain disease, although it is unknown if this is due to loss of sympathetic function (a partial Horner's) or due to loss of upper motor neuron inhibition of the oculomotor nerve (9).

Differential diagnoses

Neuro-ophthalmology is a uniquely challenging arena, perhaps related to the complexity of the anatomy and the diversity of diagnostic tests and etiologies. Although seemingly simple, the first task a clinician faces with anisocoria is determining which pupil is abnormal. This involves the recording and comparison of pupil size in both photopic and scotopic conditions. Generally, the non-mobile pupil is the abnormal one and with unilateral Horner's syndrome the anisocoria is less obvious in photopic conditions and worsens substantially in scotopic conditions, related to a lack of dilation in the latter by the affected pupil. It is an important distinction to make as the differentials for mydriasis are quite different from those for miosis. For example, iris atrophy, glaucoma, Adie's syndrome, and cavernous sinus syndrome may be important considerations for a mydriatic pupil and would require a different complement of ancillary diagnostics (22).

Once the miotic pupil is determined to be the abnormal one, the important differential diagnoses for Horner's syndrome include undetected unilateral or bilateral uveitis, endophthalmitis, panophthalmitis, and focal ulcerative keratitis. These conditions can be excluded by a thorough ophthalmologic examination. Based on our experience, mild uveitis as a primary condition, or one that develops secondary to focal ulcerative keratitis, is overlooked most frequently by veterinarians. Like Horner's syndrome, it may be bilateral or unilateral, and typically is very mild in cases of either a primary uveitis or a uveitis that develops secondary to a focal subclinical corneal ulcer and is usually accompanied by conjunctival and episcleral hyperemia. Conjunctival hyperemia is generally not present in Horner's syndrome in domestic animals. The intraocular pressures are usually reduced with uveitis and the pupils usually dilate fully when topical parasympatholytics are applied to subtle cases of uveitis, while in cases of Horner's syndrome pupils will only dilate by a very small amount. These are important but subtle ophthalmologic findings that reward the thorough clinician. Additional findings include mild aqueous flare, synechiae, uveal follicles, granulomas or tumors, and corneal scars, vascularization and edema, which are all important signs of uveitis and keratitis, respectively. For those clinicians who have dilated the pupil with a topical parasympatholytic agent it is important to recognize that the miotic pupil with Horner's syndrome will only dilate by a millimeter or so (pupillary escape) as the residual parasympathetic tone is released in the affected globe.

Table 2. Etiologies for Horner's syndrome.

Location	Etiology	Number of animals	Reference
Postganglionic	Neoplasia		
	Neuroblastoma	1	31
	Carotid body paraganglioma	3	32
	Idiopathic	11	28
	Iatrogenic		
	Post-operative TECA-LBO	11	7
	Infectious		
	Otitis media/interna	22	28,33
Preganglionic	Idiopathic	112	28,33–35
	Iatrogenic		
	Brachial plexus block	1	8
	Epidural ropivacaine	1	36
	Vagus nerve stimulator placement	1	13
	Thoracic surgery	3	37,8
	Traumatic		
	During birth	1	5
	Brachial plexus avulsions	30	3,39
	Neoplastic		
	Mediastinal lymphoma	1	40
	PNST of vagus nerve	1	12
	Infection		
	Tick paralysis — *Ixodes holocyclus*	2	41
Central	Traumatic		
	Air pellet — spinal cord	1	42
	Infectious		
	Neospora	1	43
	Other		
	Fibrocartilagenous embolism — cervical	1	10
Unspecified	Diabetic polyneuropathy	1	44

TECA-LBO — total ear canal ablation and lateral bulla osteotomy; PNST — peripheral nerve sheath tumor.

Diagnostic testing

The gold standard test for Horner's syndrome in all animals is the topical application of 1 drop of a 5% or 10% solution of cocaine (23). Cocaine prevents the reuptake of norepinephrine by the presynaptic membrane of the postganglionic neuron, leading to pupillary dilation (24). A lesion affecting any part of the oculosympathetic pathway will prevent the normal release of norepinephrine, which means that even in the face of cocaine there is insufficient accumulation of norepinephrine within the synapse to affect pupil size. In bilateral Horner's cases neither pupil will dilate substantially with topical cocaine and unilateral cases will manifest with worsening anisocoria as the affected pupil will dilate minimally and the unaffected pupil will completely dilate (25). Cocaine testing in humans will confirm the diagnosis of Horner's when the anisocoria exceeds 0.8 mm (24,25). Although cocaine testing is diagnostic it unfortunately does not localize the sympathetic pathway lesion. It is often not completed by veterinary ophthalmologists as the product is a strictly controlled substance and the ophthalmic solution must be compounded. Additionally, it requires a separate visit without parasympatholytic ocular application to be diagnostic. Many ophthalmologists simply use the minimal dilation of the miotic pupil to parasympatholytics and the complete ophthalmologic examination to rule out subtle uveitis and keratitis.

Apraclonidine has been used with increasing frequency in human medicine due to the challenges of working with cocaine. It has a weak α-1 adrenergic effect and when applied topically a normal pupil will be minimally affected while a Horner's syndrome pupil will dilate (26,27). This dilatory effect is seen with both pre- and postganglionic lesions (27); the respective reduction or complete absence of norepinephrine release induces upregulation of α receptors on the postsynaptic membrane of the iris dilator muscle (26,27). The up-regulation could be the result of an increased number of α receptors, reduced degradation or reduced absorption of catecholamines within the synapse, a phenomenon known as denervation hypersensitivity (16,28). The purpose of this response is to maximize the opportunity for activation of the effector organ in the face of insufficient neurotransmitter. The overall effect of 0.5% to 1% apraclonidine is a lessening of the anisocoria within 30 to 45 min (24–27). While used to treat glaucoma, apraclonidine has not been validated for diagnosing Horner's syndrome in veterinary patients and may induce mydriasis in a normal eye (29).

Pharmacological localization of Horner's lesions

Considerable confusion exists amongst veterinary clinicians and in the veterinary literature regarding the techniques for localization of Horner's syndrome. Given the diversity of systemic and local periocular conditions that can induce Horner's syndrome we stress the importance of a complete approach to localization that is usually completed in 2 or 3 visits depending on the availability of cocaine for initial confirmation of the diagnosis. We have provided a guide for pharmacologic localization in Table 1.

Third order Horner's syndrome that is unilateral is by far the most common presentation and localization of such a lesion is best accomplished by the application of a dilute direct sympathomimetic (phenylephrine) (28). A drop of 1% phenylephrine will create pupillary dilation and resolve enophthalmos, third eyelid protrusion, and ptosis in under 20 min, while it will not dilate the normal canine, feline, or equine pupil or a first or second order Horner's pupil (28,30). This is due to the denervation hypersensitivity following absence of endogenous norepinephrine in the affected eye. It is important to use such a dilute solution to ensure that only a hypersensitive pupil will respond, as even a normal pupil may dilate at higher concentrations (3,10,28). While 1% is most commonly reported in the veterinary literature, the authors have also had success using a 0.1% solution of phenylephrine. It is imperative that the phenylephrine be applied bilaterally and simultaneously; in unilateral cases the normal eye will not respond within the 20 min, acting as a control to confirm the hypersensitivity of the affected eye. When the Horner's syndrome is bilateral, both eyes will still respond and the resolution of signs is still expected within 20 min.

When the Horner's syndrome has been present for longer than 3 wk and a pupil fails to respond to 1% phenylephrine, one assumes a first or second order lesion. Bilateral application of 1 drop of 10% phenylephrine is pursued and again the response is timed. Both the normal and affected pupil should dilate within 20 to 40 min.

As discussed, dilation of the pupil is noticed sooner and with a lower concentration of phenylephrine with a postganglionic lesion. A possible explanation for this is that when the postganglionic neuron is affected there is a complete depletion of norepinephrine within the synapse, leading to maximum sensitivity of the post-synaptic membrane to exogenous adrenergics (28). When the lesion is preganglionic, however, small quantities of norepinephrine continue to be released by the still-functional postganglionic neuron. While a degree of denervation hypersensitivity is still present it is not as complete and thus the response to topical adrenergics is not as pronounced (28).

It is very important that the clinician be cognizant of the time required for denervation hypersensitivity to develop when using phenylephrine to localize a Horner's syndrome. If testing is conducted before onset of the hypersensitivity, a case could be falsely localized as preganglionic. Unfortunately, there is variability in the literature regarding the time of onset of denervation hypersensitivity, with ranges as wide as 2 to 10 d and 2 to 3 wk being reported (6,18). Many of the sources cited are also review articles. The authors of this review paper use 2 to 3 wk to help reduce the likelihood of a false negative result. The same concerns exist for the use of apraclonidine, although this has not been referenced in veterinary medicine. Another marked area of ambiguity in the literature is why apraclonidine induces pupillary dilation with either second or third order lesions, while dilute phenylephrine only acts with third order lesions, even though both pharmacological agents rely on denervation hypersensitivity.

Hydroxyamphetamine (1%) is an alternative method of distinguishing a third order from a first and second order lesion. As an indirect sympathomimetic it will stimulate the release of norepinephrine from the intact postganglionic nerve terminal, thus leading to pupil dilation in normal eyes and those affected by a first or second order lesion (18). The dilation should be noted within 45 min. An affected postganglionic neuron (a third order lesion), however, has a reduced or absent supply of norepinephrine and the pupil will not dilate (10). Concerns have been raised, however, regarding increased rates of false negative or false positive results when compared to dilute phenylephrine (16).

There has yet to be developed a pharmacological method for differentiating a first and second order Horner's syndrome (24). As a reminder, the development of a first order lesion in the absence of other thalamic, brainstem or myelopathic deficits is very unlikely (16).

Etiologies of Horner's syndrome

Once a diagnosis of Horner's syndrome has been made and the lesion localized to a postganglionic, preganglionic, or central location, the underlying etiology must be considered. Case reports have documented an astonishing array of possibilities, including those that are idiopathic, iatrogenic, neoplastic, traumatic, and infectious in nature. A summary of described etiologies is provided in Table 2.

Idiopathic Horner's syndrome

Idiopathic Horner's syndrome merits specific discussion as it represents approximately half of the presentations amongst dogs (14). Although any breed can be affected, golden retrievers are predisposed with an incidence of 2.6% compared with other breeds at 0.03% (33,34). Collies may also be at increased risk (35). A mean age of 5 to 8 y is commonly reported in the literature, although animals between the ages of 4 and 13 y have been affected (3,33,34). Of Horner's syndrome cases documented in cats, approximately 40% are idiopathic (3). Clinical signs are acute in onset, can be unilateral or bilateral, and can be due to both pre- and post-ganglionic lesions (16). As the name suggests, an underlying cause has not been identified and a diagnosis of idiopathic Horner's syndrome can only be made after excluding all other possible causes. It is not unreasonable, however, to make a presumptive diagnosis in a patient with an acute onset of signs, an unremarkable physical examination and the absence of other neurological deficits (16).

Ancillary diagnostics

Further diagnostics are often warranted to investigate the etiology of Horner's syndrome, and they are dependent on the location of the lesion as determined by the previously described pharmacological testing. In cases of post-ganglionic lesions, a thorough otoscopic examination should be done to evaluate for any evidence of otitis (45). A complete blood (cell) count and serum biochemistry are advisable, particularly since metabolic disorders such as diabetes mellitus have been associated with Horner's syndrome in a dog (44). Cervical and thoracic radiographs are indicated in cases of preganglionic lesions. Magnetic resonance imaging (MRI) is warranted in all cases of central lesions, but advanced imaging [computed tomography (CT) or

MRI] should also be considered when preliminary diagnostics fail to identify a cause in pre- and post-ganglionic cases as this will allow for complete evaluation of the oculosympathetic pathway as it traverses through the brain, spinal cord, mediastinum, neck, middle ear, and orbit. If a structural lesion can be identified, more invasive diagnostics such as myringotomy/bulla osteotomy with cerebrospinal fluid analysis or biopsy of masses may be required to determine the definitive etiological agent.

Treatment and prognosis

The treatment and prognosis of Horner's syndrome are obviously dependent upon the underlying etiology. It is possible that the degree of third eyelid protrusion will be enough to obscure patient vision, in which case symptomatic treatment with topical 1% or 10% phenylephrine can be used for short-term improvement of signs (16,33,34). Some animals will only show partial resolution of the signs, such as the ptosis and enophthalmos, but will have persistent miosis (6). When permanent deficits occur, they are largely considered to be cosmetic with minimal to no impact on the patient's quality of life (16).

Given that there is no specific etiology for idiopathic Horner's syndrome, there is no specific treatment. There is 1 report of using acupuncture to treat a dog with presumptive idiopathic disease (46). Two points were used without electrical stimulation and the needles were retained for 20 min. The signs had improved the day following treatment and the signs resolved within 3 d (46). It is important to remember that most cases of idiopathic Horner's syndrome will show spontaneous improvement in as little as 4 wk, although some dogs may not improve until 15 wk after onset (28,35). It is also unusual for dogs to have repeat episodes (28).

There is marked variability in the literature regarding the prognosis when Horner's syndrome is the result of iatrogenic and spontaneous injury. In 2 cases in which the inciting cause was application of local anesthetics (brachial plexus block, epidural), the signs completely resolved within several hours (8,36). Cats are at increased risk for developing Horner's syndrome following bulla osteotomies compared to dogs, with incidence rates of 58.3% and 3.3%, respectively (7). Post-operative signs tend to last 2 wk in dogs, while up to 25% of cats will have a permanent Horner's syndrome. Horner's syndrome secondary to thoracic surgery is likely to improve (37,38). Signs of Horner's syndrome can resolve following a brachial plexus injury, although resolution of the Horner's syndrome itself is not associated with return of function in the affected limb (39).

In cases of infectious disease, resolution of the Horner's syndrome is possible if the underlying cause is appropriately addressed (43,44). Permanent signs are, not surprisingly, associated with neoplasia of the oculosympathetic pathway (21).

In conclusion, Horner's syndrome manifests with consistent clinical signs that include ptosis, enophthalmos, miosis, and third eyelid prolapse. The lesions that induce Horner's syndrome are diverse and include inflammatory lesions, neoplasms, and trauma; these may all cause central, preganglionic or postganglionic lesions. Topical ophthalmic cocaine is the gold standard diagnostic test to confirm the presence of Horner's syndrome, although it is seldom used even in veterinary referral practice.

Localization of the lesion to the specific location within the oculosympathetic pathway involves bilateral topical application of initially dilute followed by more concentrated topical direct adrenergics with timed responses to the resolution of the signs. Indirect sympathomimetics may provide further support of lesion localization. While idiopathic disease is the most common cause of Horner's syndrome, many other etiologies exist and necessitate additional diagnostics such as radiographs, CT, or MRI. These steps will accurately identify the lesion location and may allow the clinician to confirm the etiology of the oculosympathetic lesion. CVJ

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