Case Report

JVC Journal of Veterinary Clinics

pISSN 1598-298X • eISSN 2384-0749
J Vet Clin 2023;40:360-364
https://doi.org/10.17555/jvc.2023.40.5.360

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Ophthalmic Manifestations of Cavernous Sinus Syndrome in a Yorkshire Terrier Dog

Sehan Shin
Sol Kim
Seonmi Kang
Jihye Choi
Kangmoon Seo*

Department of Veterinary Clinical Sciences, College of Veterinary Medicine and Research Institute for Veterinary Science, Seoul National University, Seoul 08826, Korea

*Correspondence: kmseo@snu.ac.kr

ORCID
Sehan Shin:
https://orcid.org/0009-0000-1399-2860
Sol Kim:
https://orcid.org/0000-0003-2309-4620
Seonmi Kang:
https://orcid.org/0000-0001-8017-0891
Jihye Choi:
https://orcid.org/0000-0002-1258-7158
Kangmoon Seo:
https://orcid.org/0000-0001-6645-7116

Abstract A 7-year-old castrated male Yorkshire Terrier presented for a palpable mass of the right neck with ophthalmic signs of conjunctival hyperemia and anisocoria with fixed mydriatic pupil of the right eye. Clinical examination findings included the absence of direct and consensual pupillary light reflexes, external and internal ophthalmoplegia, and corneal hypoesthesia with incomplete blinking of the right eye. Magnetic resonance imaging and computed tomography revealed a mass extending from the right cavernous sinus to the orbital fissure with neighboring bone lysis. Cytological examination of fine-needle aspiration samples of the mass revealed a neuroendocrine tumor. The owner declined further diagnosis and did not wish to care for the dog receiving chemotherapy. This study describes the importance of investigating neuro-ophthalmic findings, which might provide clues for the localization of lesions, including tumors, to aid in diagnosis.

Key words Yorkshire Terrier, dog, cavernous sinus syndrome, ophthalmoplegia, mydriasis.

Received July 29, 2023 / Revised September 6, 2023 / Accepted September 25, 2023

Introduction

The cavernous sinus is a coupled venous sinus that stretches from the orbital fissure to the petro-occipital canal and is positioned bilaterally on the floor of the calvarium (2,5,9,10). The oculomotor (CN III), trochlear (CN IV), and abducens (CN VI) cranial nerves and the ophthalmic and maxillary branches of the trigeminal (CN V) cranial nerve pass through the cavernous sinus and extend into the orbital fissure (2,5,9,10). Cavernous sinus syndrome (CSS) is closely associated with cranial nerve impairment caused by neoplastic or inflammatory lesions around the cavernous sinus (5,9,10).

Clinical manifestations commonly observed in patients with CSS include external and internal ophthalmoparesis, ptosis and reduced sensation of cornea and periorbita. These signs occur because of impaired innervation of the extraocular muscles by CN III, IV, and VI, as well as disrupted pupillary constriction controlled by the parasympathetic efferent pathway of CN III. Ventrolateral strabismus can also present itself when external ophthalmoparesis develops as a consequence of CN III denervation (5,9,10). When CN VI is compromised, which controls the retractor bulbi muscle and the lateral rectus muscle, it leads to the occurrence of medial strabismus and the absence of bulbar retraction. Sensory abnormalities, including absent or diminished corneal sensation and hypoalgesia in the periorbital region, are frequently observed in patients with CSS. These deficits arise from denervation of the ophthalmic and maxillary branches of CN V (5,9,10). All aforementioned clinical signs are confirmed through ophthalmic examinations.

Many reports concerning cavernous sinus syndrome have been published in human medicine and veterinary medicine (1,3-6,9-11). The purpose of this case study is to describe the ophthalmic presentation and note the diagnosis of a cavernous sinus tumor in a dog with neuro-ophthalmologic deficits.

Case Report

A 7-year-old castrated male Yorkshire Terrier presented with conjunctival hyperemia and anisocoria with fixed mydriatic pupil in the right eye (Fig. 1A). The owner reported that conjunctival hyperemia and mydriasis in the right eye had first been noted one month earlier, and topical antibiotics and anti-inflammatory eye drops had been administered. Additionally, the dog had been diagnosed with right submandibular lymph node enlargement by a veterinarian one month prior.

At first presentation, a complete ophthalmic examination was performed. Tear production values (Schirmer Tear Test-1 [STT-1]; Merck Animal Health, Madison, NJ, USA) were 9 mm/min in the right eye and 10 mm/min in the left, and the intraocular pressures (Tonovet; iCare, Helsinki, Finland) measured 15 mmHg in the right eye and 16 mmHg in the left. The menace response and dazzle reflexes were positive in both eyes. The absence of right direct/consensual pupillary light reflex (PLR), right oculocephalic reflex was noted. A cotton swab was utilized to induce the corneal reflex, strategically placed within the patient's visual blind spot to prevent the patient from perceiving it as a potential threat and subsequently triggering a menace response. Right corneal reflex displayed a slight impairment, but there was a clear observation of globe retraction. Incomplete blinking was also observed; however, the palpebral reflex was normal. Slit-lamp biomicroscopic examination (SL-D7; Topcon, Tokyo, Japan) revealed corneal degeneration and conjunctival hyperemia of the right eye. Fluorescein staining (Flu-Glo; Akorn Pharmaceuticals, Decatur, IL, USA) revealed absence of corneal ulcer in both eyes. Indirect ophthalmoscopy (Vantage Indirect ophthalmoscope; Keeler, Windsor, UK), which was performed to evaluate the posterior segment, showed no remarkable findings. The patient's medical history and neurological examination indicated the absence of systemic neurological symptoms.

Since an ocular manifestation due to an intracranial problem was suspected on neurologic examination, computed tomography (CT) was performed. The transverse view of the head CT images showed that a mass of soft-tissue density was located in the right cavernous sinus region. Bone lysis of the basilar part of the right occipital bone, right tympanic bulla, and right stylohyoid bone was noted, suggesting the possibility of invasion of the surrounding tissues (Fig. 2A). Invasions of the right common carotid artery and internal jugular vein were also observed (Fig. 2B). Moreover, one pulmonary nodule in the right cranial lobe and mild enlargement of the cranial mediastinal lymph node, tracheobronchial lymph node, sternal lymph

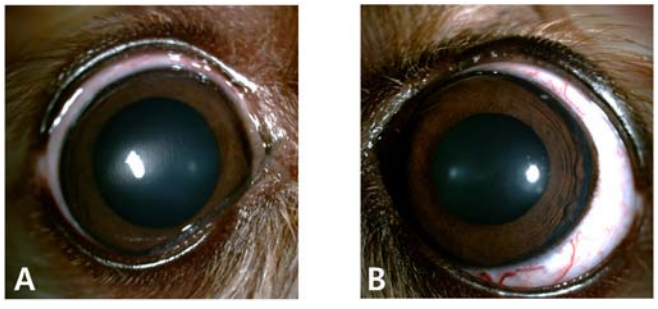

Fig. 1. Clinical photographs of both eyes in the patient. (A) The right eye. Fixed mydriatic condition is clearly evident. (B) The left eye.

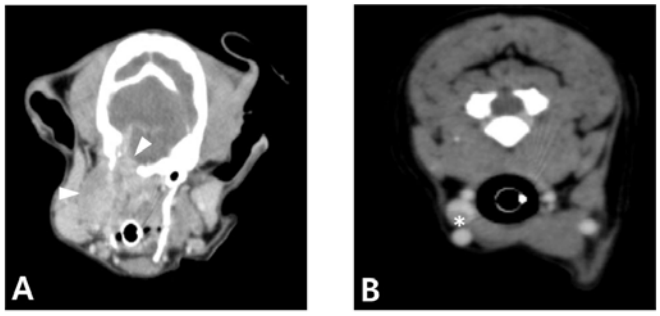

Fig. 2. Contrast-enhanced, transverse computed tomographic (CT) images of the cranium at the level of the cavernous sinus area. (A) The arrowhead shows marked soft-tissue density and bone lysis around the cavernous sinus. (B) The asterisk notes the invasion of the cavernous sinus mass to the right jugular vein.

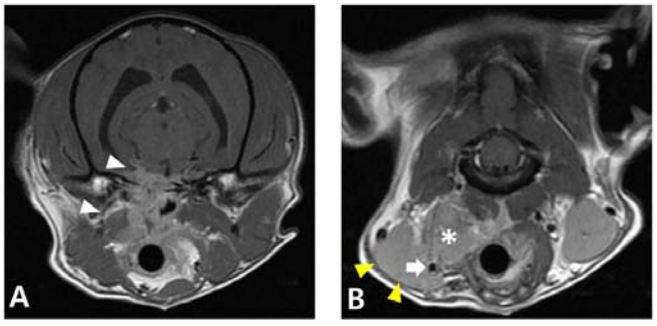

Fig. 3. (A) T1-weighted magnetic resonance imaging reveals mass ranging from right ventral petrosal sinus and tympanic bulla to multiple muscles including digastric muscle, pterygoid muscle, cleidocephalic muscle, and sternocephalic muscle (arrowheads). (B) The mass included the right external carotid (arrow) artery. Right internal artery was obscured by the mass. Dislocation of the mandibular gland (yellow arrowheads) by mass (asterisk) was also noted.

node, and right hepatic lymph node were also confirmed in the transverse view of the CT scan, indicating pulmonary and lymph node metastases might be suspected.

Magnetic resonance imaging (MRI) was performed to rule out other retrobulbar diseases. MRI of the skull revealed a mass with T1 hyperintensity, T2 isohypointensity, and T1-contrast enhancement located in the right cavernous sinus and the ventral part of the right midbrain (Fig. 3A). The mass extended from the right ventral petrosal sinus and tympanic bulla to multiple muscles, including the digastric, pterygoid, cleidocephalic, and sternocephalic muscles. The right common, external, and internal carotid arteries were also included (Fig. 3B). Similarly, meningeal enhancement was observed peripherally around the mass.

Samples for cytological examination were collected from the cranial and caudal parts of the palpable mass of the right neck using fine-needle aspiration (FNA). Cytological analysis of the

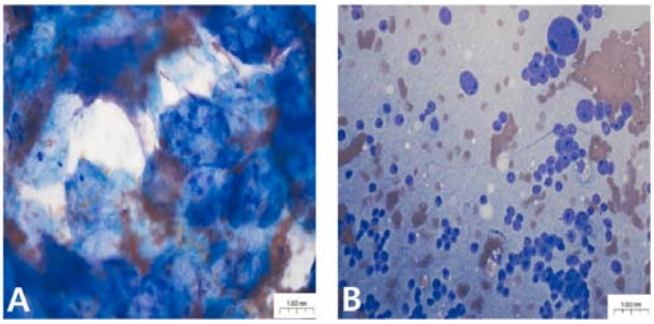

Fig. 4. The cytologic appearance of a fine-needle aspirate (FNA) from the palpable mass of the right neck. (A) The cranial part of the mass. It showed round to oval cells with low to moderate cellularity. Irregularly shaped vacuoles were also detected in the cytoplasm. Salivary gland hyperplasia was suspected. (B) The caudal part of the mass. Round cells showed a moderately increased nucleus/cytoplasm ratio. Several prominent nucleoli with moderately increased anisokaryosis were noted. Neuroendocrine tumor was suspected.

cranial part revealed round-to-oval cells with low-to-moderate cellularity. Irregularly shaped vacuoles are observed in the cytoplasm. No nucleoli or mitotic figure were observed (Fig. 4A). Cytological analysis of the caudal region revealed round cells with naked nuclei and moderate cellularity. The round cells showed a moderately increased nucleus/cytoplasm ratio. Several prominent nucleoli with moderately increased anisokaryosis were observed (Fig. 4B). Mitotic figures were also observed. The FNA sample was suspected to be a neuroendocrine tumor. An explorative orbitotomy to collect biopsy samples from the mass was dismissed by the owner.

Discussion

This study describes the clinical features of a cavernous sinus syndrome in a Yorkshire Terrier. A mass in the right cavernous sinus affected the cranial nerves within the cavernous sinus. As a result, mydriasis, decreased corneal sensation, incomplete blinking, and paralysis of the extraocular muscles occur. Therefore, these conditions were considered to have led to keratoconjunctivitis, corneal degeneration, and conjunctival hyperemia in the right eye.

In humans, three disorders are associated with the orbital apex region: CSS, orbital apex syndrome, superior orbital fissure syndrome (1,4,11). Because these disorders affect CN III-VI and have comparable etiologies and diagnostic criteria, it is essential to conduct a differential diagnosis. Compared to CSS, orbital apex syndrome is distinguished by the presence of visual impairment, which results from impairment of CN II (1,4,8,11). Superior orbital fissure syndrome, which is characterized by lesions situated anterior to the orbital apex,

shares similar clinical presentations with CSS, including ophthalmoplegia, mydriasis, and corneal hypoesthesia (1,4,7,11). However, it is associated with CN III and IV, the ophthalmic branches of V and VI, whereas CSS is related to CN III and IV, the ophthalmic branch of V, the maxillary branches of V and VI, and the sensory plexus of the ophthalmic artery (1,4,7,11). Thus, superior orbital fissure syndrome does not manifest as symptoms of Horner's syndrome or paralysis of the cutaneous sensation in the lateral canthus. Given the close proximity of their occurrence, it is common for these two disorders to exhibit progression, in which one condition transitions into another, displaying an interrelated pattern (6).

Neoplasia is the most prevalent underlying cause of CSS, with lymphoma, thyroid adenocarcinoma, and neuroendocrine carcinoma being frequently observed (5,9,10). Infection is the next leading cause, with documented problems including feline infectious peritonitis, cryptococcosis, and toxoplasmosis (5,9,10). Inflammatory, vascular, and infrequent traumatic factors may also contribute (5,9,10).

MRI is a valuable tool for the early detection and diagnosis of CSS, providing the advantage of distinguishing it from other retrobulbar diseases that occur in the orbital apex region (3,5). However, it is difficult to differentiate between conditions present in the orbital apex using MRI alone due to the absence of certain clinical symptoms, convergence of multiple cranial nerves within the same anatomical space, and the possibility of one condition manifesting as another (12). CT assists in the diagnosis of CSS, especially when there is suspicion of tumor invasion into the surrounding bone tissue and osteolysis (3). Cerebrospinal fluid puncture can be used to exclude an infectious etiology, and has been particularly useful in cats (10). The usefulness of blood tests including complete blood count and serum chemistry are subject to debate. While one study reported their utility in differentiating between inflammatory and neoplastic causes (10), other studies have found non-specific associations between test results and disease (9). In this study, imaging data demonstrated bone lysis in multiple adjacent bones near the right cavernous sinus region, invasion of the right carotid vessels, and the presence of a mass extending from the right cavernous sinus region to the cervical muscles through the midbrain. These findings strongly indicate the presence of a neoplasm, which was likely responsible for the observed clinical manifestations. Cytological examination was additionally conducted at two locations on the prominent palpable mass of the right neck to distinguish neoplastic lesions. The presence of round cells with naked nuclei, significant anisokaryosis, and mitotic figures led to the suspicion of a neuroendocrine tumor.

Several veterinary studies have reported the treatment and prognosis of CSS. Management of CSS typically involves radiation therapy, chemotherapy, and medical intervention (5,9,10). In a previous retrospective study investigating bilateral CSS in dogs, four patients were followed up after receiving chemotherapeutic treatment. The median survival time (MST) for these patients was 199 days (9). In another retrospective study involving four dogs and eight cats, follow-up data were available for two dogs and one cat. The longest survival time recorded was 540 days in a dog that received cisplatin and etoposide (10). In another retrospective study investigating 11 dogs and two cats, the MST for anti-inflammatory steroid therapy was 360 days, whereas radiation therapy demonstrated 1,035 days (5). In this study, the owner refused further treatment and the patient's condition deteriorated rapidly, leading to the decision to euthanize the individual 60 days after diagnosis.

There are several limitations in the present study. Firstly, pharmacological testing by administering 0.1% pilocarpine was omitted, a procedure that assists in discerning lesions of the lower motor neuron of CN III through the rapid constriction of the pupil (10). Secondly, the forced duction test, which offers insights into mechanical restrictions of the eye, was not conducted.

Conclusions

The present report implies that CSS can be diagnosed by ophthalmic examination in dogs with neuro-ophthalmologic deficits. Additionally, MRI and CT can assist in the diagnosis and localization of tumors.

Conflicts of Interest

The authors have no conflicting interests.

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