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IMAGING DIAGNOSIS - UNILATERAL TRIGEMINAL NEURITIS MIMICKING PERIPHERAL NERVE SHEATH TUMOR IN A HORSE

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Abstract

A 16-year-old Warmblood gelding presented with a non-healing corneal ulcer and absent corneal sensation in the left eye. A lesion affecting the maxillary and ophthalmic branches of the left trigeminal nerve was suspected. Magnetic resonance (MR) imaging identified marked thickening of the ophthalmic and maxillary branches of the left trigeminal nerve. The nerve was iso- to hypointense on T1-weighted and T2-weighted images with heterogeneous enhancement. A peripheral nerve sheath tumor was suspected, however granulomatous neuritis was histopathologically confirmed. These inflammatory changes can result in severe nerve enlargement and should be considered with MR findings suggestive of peripheral nerve sheath tumor.
Signalment, History and Clinical Findings

A 16-year-old Warmblood gelding was presented with a two-week history of a non-healing corneal ulcer in the left eye. On presentation there was a mid depth stromal ulcer of the left eye with a 4-5 mm fringe of perilimbal vascularisation. The ocular defect covered 70% of the cornea with severe corneal edema precluding deeper ocular examination. A focal area of cellular infiltrate was present at 10 o’clock at the margin of the ulcer and also ventrally along the edge of the ulcer. There was minimal ocular discharge and the eye was open and comfortable. The right eye was normal to ocular examination. Touch testing of the left corneal surface revealed no corneal sensation. A neurological examination was requested.

Neurological examination revealed normal mental status, posture and gait. Postural reactions were normal in all four limbs. Cranial nerve examination revealed decreased sensation at the medial and lateral canthus of the left eye, the cornea of the left eye, over the maxilla on the left, and in the left nostril. Palpebral reflex was decreased in the left eye, but the menace response was present. Direct pupillary light reflex (PLR) could not be assessed in the left eye due to the severity of the corneal ulcer and edema; however, a normal consensual PLR was present on the right eye. The rest of the neurological examination was normal. Pre-referral haematology and serum biochemistry did not reveal any abnormalities.

Based on the history, ophthalmic and neurologic examination, a lesion affecting the maxillary and ophthalmic branches of the left trigeminal nerve (CN V) was suspected. The main differential diagnoses were neoplasia and inflammatory/infectious diseases. A MR
imaging study of the head was recommended in order to investigate the underlying cause.

A temporary tarsorrhaphy was placed in the left eye and the horse was started on topical ocular serum and chloramphenicol eye drops every 4 hours.

**Imaging, Diagnosis and Outcome**

Magnetic resonance imaging of the head was performed under general anesthesia using a 1.5-T superconducting magnet (GE Signa Echospeed System, General Electric Medical System, Milwaukee, WI). The horse was positioned in right lateral recumbency and images were obtained in three planes (dorsal, sagittal, and transverse). Sequences included T2-weighted (T2W) fast spin echo (FSE), T1-weighted (T1W) FSE before and after administration of intravenous contrast medium (20 ml, gadobenate dimeglumine, MultiHance®, Bracco Imaging SpA, Milan, Italy). 3D- Spoiled Gradient Echo (SPGR) pulse sequence was also acquired in transverse plane after contrast medium administration.

The MR images showed severe enlargement of the ophthalmic and maxillary branches of the left trigeminal nerve from the level of middle cranial fossa, extending rostrally through the orbital fissure and round foramen respectively, measuring about 2 cm in diameter compared to 0.4 cm on the right side. The left infraorbital nerve was markedly thickened along the length of the infraorbital canal. The trigeminal nerve enlargement was visible on all sequences, however the T1W images acquired in transverse and sagittal planes showed better definition of the lesion. The left orbital fissure, round foramen, and infraorbital canal were enlarged by the markedly thickened left trigeminal nerve. The bony margin of these structures surrounding the emerging left trigeminal nerve was thinned, presumably secondary to pressure atrophy. The nerve was iso- to hypointense to grey matter on T1W,
T2W FSE, and 3D-SPGR and exhibited heterogeneous, mainly peripheral enhancement on T1W sequence after contrast administration (Fig. 1). The imaging findings were consistent with an extensive, diffuse left trigeminal neuropathy. The main differential diagnosis was a peripheral nerve sheath tumor. Cerebrospinal fluid was collected from the cerebellomedullary cistern and the analysis (nucleated cell count, total protein, and cytology) was within normal limits.

Ultrasonographic examination (Philips HDI 5000, Bothell, USA) of the infraorbital nerve at its exit from the infraorbital canal was performed using a 8.5 MHz microconvex array transducer and 12 MHz linear array transducer in order to obtain a fine needle aspirate or tru-cut biopsy; however, the nerve did not appear abnormal at this level precluding non-invasive sampling.

The ulcer initially improved with evidence of healing and epithelialisation but then rapidly progressed to a large descematocoele requiring either surgical repair or enucleation. Given the poor prognosis the owner declined any further treatment and elected to have the horse euthanized. Post mortem examination confirmed gross enlargement of the left orbital fissure, round foramen, and infraorbital canal in addition to the ophthalmic and maxillary branches of left CN V (Fig. 2). Histopathology revealed that the trigeminal nerve was markedly expanded by a densely cellular population of fibroblasts arranged in parallel bundles depositing moderate amounts of fibrillar eosinophilic matrix. Admixed were large numbers of infiltrating macrophages, lymphocytes, plasma cells, neutrophils, multinucleated giant cells and eosinophils. Inflammatory cells are focused upon nerve
fascicles, with rupture of the perineurium and extension of inflammatory cells into the interfascicular interstitium (Fig. 3). There was marked myelin degeneration with associated axonal swelling (spheroids). The left infraorbital nerve at its exit from the infraorbital canal, which was accessible to ultrasound examination, appeared mildly enlarged. Histopathology at the same level revealed an extensive expansion of the fibrous connective tissue surrounding the nerve fascicles, with small aggregates of lymphocytes. All these findings were consistent with a severe granulomatous neuritis affecting the ophthalmic and maxillary branches of the left trigeminal nerve.

Discussion

The etiology of the progressive granulomatous inflammation of the left trigeminal nerve in this case remains undetermined. Granulomatous inflammation affecting the cranial nerves has been associated with polyneuritis equi (PNE); however, clinical experience has suggested that horses with PNE presenting primarily with cranial nerve deficits eventually also show cauda equina deficits. Moreover, the most common clinical signs reported when the cranial nerves are involved include atrophy of the muscles of mastication, dysphagia, head tilt, facial nerve paresis and head shaking. In the present case, the neurological examination did not reveal involvement of any other cranial nerve or any signs of cauda equina dysfunction (poor tail tone, faecal and urinary incontinence, pelvic limb weakness or pelvic limb muscle atrophy) at the time of presentation. However, a subclinical PNE affecting this area could not be ruled out because the cauda equina was not assessed on post-mortem examination. The underlying cause of PNE remains unknown, but an
underlying immune-mediated process has been suggested.\textsuperscript{5,7} Corticosteroids and azathioprine have been proposed as potential treatments to slow progression of the disease.\textsuperscript{4}

The MR imaging features of peripheral nerve sheath tumor (PNST) affecting the cranial nerves have not been described in horses. There is a case report of lingual PNST in a horse, where MR imaging revealed a large, round, well defined and encapsulated mass with mixed signal intensity on T2W and T1W images.\textsuperscript{8} Some consistent, although nonspecific, MR imaging features of PNST in dogs include diffuse thickening of the nerve that is typically iso to hyperintense on T2W FSE sequences and iso-to hypointense on T1W FSE sequences to normal muscle with heterogeneous contrast enhancement.\textsuperscript{9,10} Similar findings in our case, together with the chronicity of the changes and degree of enlargement, suggested an ante-mortem diagnosis of PNST; however, histopathology confirmed a severe granulomatous neuritis.

There is a report of a trigeminal nerve sarcoid granuloma mimicking a trigeminal PNST in a person.\textsuperscript{11} This case had a similar expansile mass of the trigeminal nerve and was thought to be a PNST; however, histopathology confirmed a sarcoid granuloma. Equine sarcoïds are attributed to non-productive infection with bovine papillomavirus.\textsuperscript{12,13} Histopathology typically reveals fibroblast proliferation with spindle cells often arranged in bundles, oval nuclei and small nucleoli. Peripheral nerve sheath tumor can histologically be difficult to distinguish from sarcoïds. Differentiation can be made with immunohistochemistry staining for S-100 protein.\textsuperscript{14} However, histopathology in the present case was not consistent with sarcoid granuloma.
The MR imaging findings in this horse confirmed the clinical diagnosis of trigeminal neuropathy and led clinicians to consider the possibility of further investigating the area of the affected nerve to reach a final diagnosis. On ultrasonographic examination the infraorbital nerve appeared normal at its exit from the infraorbital canal. Given the normal appearance of the nerve, fine needle aspiration was not attempted. Nevertheless, post-mortem examination of the nerve at this level revealed some abnormalities and fine needle aspiration or a surgical biopsy could have provided more diagnostic information than anticipated.

In conclusion, granulomatous neuritis should be considered as a differential diagnosis in horses with MR imaging findings suggestive of a trigeminal nerve sheath tumor. These inflammatory changes can result in severe enlargement of the nerve mimicking a nerve sheath tumor. Therefore, a surgical biopsy may be indicated to further characterize these lesions in order to plan the best treatment approach.


Figure captions

Figure 1  
(A) Transverse T1-weighted (T1W) image at the level of the orbital fissure. (B) Transverse T1W image after contrast administration at the same level of Fig 1A. (C) Dorsal T1W image after contrast administration (TR=520ms, TE=15.5ms, slice thickness 5mm). There is enlargement of the ophthalmic and maxillary branches of the left trigeminal nerve from the level of middle cranial fossa, through the orbital fissure and round foramen respectively. The infraorbital branch of the maxillary branch of the trigeminal nerve is markedly enlarged along the length of the infraorbital canal (arrow) (C). The nerve was iso- to hypointense to grey matter on T1W (A) with heterogeneous, mainly peripheral enhancement on T1W sequence (B) after contrast administration. There was bony remodelling and secondary enlargement of the left orbital fissure (arrow) (A,B).
Figure 2  View of the inner cranial vault after removal of the brain. Gross enlargement of left orbital fissure and round foramen is visible (arrow). The ophthalmic and maxillary branches of left trigeminal nerve (black asterisk) are enlarged compared to the right trigeminal nerve (white asterisk).
Histopathology from a section of the left trigeminal nerve from the affected horse (original magnification x 40 (A) and x 200 (B)). Haematoxylin and eosin showed revealed that the trigeminal nerve was markedly expanded by a densely cellular population of fibroblasts arranged in parallel bundles depositing moderate amounts of fibrillar eosinophilic matrix. Admixed were large numbers of infiltrating macrophages, lymphocytes, plasma cells, neutrophils, multinucleated giant cells and eosinophils. Proliferation of fibroblasts, and associated deposition of collagen, has resulted in marked thickening of the perineurium. A densely cellular infiltrate is observed, extending into the nerve fascicles through the endoneurium. This infiltrate is composed of lymphocytes, plasma cells, macrophages, multinucleated giant cells, and small numbers of eosinophils. Leukocytic infiltration is associated here with neuronal destruction.