Clinical signs, imaging findings and outcome in twelve cats with internal ophthalmoparesis/ophthalmoplegia

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Abstract:

OBJECTIVE

To retrospectively evaluate the clinical signs, imaging findings and outcome of feline internal ophthalmoparesis/ophthalmoplegia.

PROCEDURE

Medical records were reviewed from 2008 to 2015. Inclusion criteria included cats that presented with internal ophthalmoparesis/ophthalmoplegia, underwent diagnostic imaging, and had follow-up information available.

RESULTS

Twelve cases of feline internal ophthalmoparesis/ophthalmoplegia were identified. Nine cats were unilaterally affected, and three cats were bilaterally affected. Affected cats had a median age of 10.54 years (range 5.75 to 13.17), and both sexes of varying breeds were affected (9 males; 3 females). Clinical signs including abnormal mental status (n = 9; 75%) and additional neurologic abnormalities (n =10; 83%) were observed. Magnetic resonance imaging and/or computed tomography (MRI/CT) of the head were performed in ten cats, revealing a mass lesion in all cases with varying locations. Multicentric lymphoma was diagnosed in two cats via abdominal ultrasound and cytology. All twelve cats were euthanized due to deterioration of clinical signs and/or quality of life concerns. Median time from diagnosis to euthanasia was 3.5 days (range 0 to 80 days).

CONCLUSIONS

Feline internal ophthalmoparesis/ophthalmoplegia rarely presents as the sole clinical sign in a referral hospital. Advanced imaging (MRI/CT) may be necessary to reach a definitive

diagnosis in these cases. However, abdominal ultrasound would be advocated in cats with systemic clinical signs as a less expensive and less invasive diagnostic test to further investigate the possible etiology of internal ophthalmoparesis/ophthalmoplegia prior to advanced imaging. Feline cases with internal ophthalmoparesis/ophthalmoplegia associated with other intracranial signs and/or systemic clinical signs have a poor prognosis.

Keywords: Imaging, feline, internal ophthalmoplegia, oculomotor, neuro-ophthalmology, parasympathetic.

Abbreviations:

CN – cranial nerve

CSF – cerebrospinal fluid

CT – computed tomography

MRI – magnetic resonance imaging

OD – oculus dexter (right eye)

OS – oculus sinister (left eye)

OU – oculus uterque (both eyes)

PLR – pupillary light reflex

VOR – vestibulo-ocular reflex

Introduction

Internal ophthalmoparesis/ophthalmoplegia is characterized by decreased (ophthalmoparesis) or absent (ophthalmoplegia) motor function of the iris sphincter and ciliary body muscle. This is due to loss of parasympathetic innervation from the oculomotor nerve [cranial nerve (CN) III], observed clinically as areflexive mydriasis.[1]

Documented cases of feline and canine internal ophthalmoparesis/ophthalmoplegia are limited in the veterinary literature. Most of the literature in dogs and cats with internal ophthalmoparesis/ophthalmoplegia are case reports with middle cranial fossa syndrome (also known as cavernous sinus syndrome).[2-11] Middle cranial fossa syndrome is a clinical disorder characterized by ipsilateral internal ophthalmoparesis/ophthalmoplegia, paresis or plegia of the extra-ocular muscles (also known as external ophthalmoparesis/ophthalmoplegia) and decreased to absent facial and corneal sensation.[12,13] These clinical signs are due to a dysfunction of several cranial nerves that course at the level of the middle cranial fossa.[12,13] These cranial nerves include: CN III (motor and parasympathetic component), CN IV (trochlear nerve), CN VI (abducens nerve), the ophthalmic branch of the CN V (trigeminal nerve), and postganglionic sympathetic nerve fibers. The maxillary branch of the CN V, which passes through the round foramen, can also be affected. This is usually due to an intracranial mass or retro-bulbar mass invading the orbital fissure or the middle cranial fossa. Case reports in dogs have included: chondrosarcoma, lymphoma, meningioma, primitive neuroectodermal tumors, metastatic invasion of thyroid carcinomas, neuroendocrine carcinoma and an aneurysm as the underlying cause.[2-7] Reports in cats have included: osteochondroma, lymphoma, squamous cell carcinoma, chondrosarcoma, trauma, orbital abscessation and infectious diseases (feline infectious peritonitis/Cryptococcus) as the underlying cause.[7-11]

Lesions affecting the CN III alone and causing internal ophthalmoparesis/ophthalmoplegia as the sole clinical signs are more rarely reported. Dysautonomia and pharmacological blockage with mydriatic agents, such as atropine, in both dogs and cats, has to be considered.[14-17] In dogs, it has been reported in the literature secondary to intracranial meningiomas, intracranial suprasellar germ cell tumors, toxic contact (e.g. to Datura stramonium) or as an idiopathic cause.[18-25] Feline reports in the literature are confined to metastasis of a renal cell carcinoma, thiamine deficiency, viruses (e.g. feline leukemia virus) and as an idiopathic cause, all of which should be considered in our feline patients.[26-29]

Internal ophthalmoparesis/ophthalmoplegia is more commonly reported in the human literature. It has been reported secondary to a diabetic neuropathy, autoimmune disease, ophthalmoplegic migraine, trauma, cavernous sinus thrombosis, and compressive lesions such as intracranial aneurysms and space occupying lesions.[30–38]

The aims of this study were to describe the clinical features, imaging findings, and outcome of feline cases presented with internal ophthalmoparesis/ophthalmoplegia.

Materials and methods

Medical records from the Royal Veterinary College, Queen Mother Hospital were reviewed from 2008 to 2015. Inclusion criteria were as follows: (1) cats that presented with internal ophthalmoparesis/ophthalmoplegia; (2) had complete medical records (including ophthalmic and neurologic examinations performed by a board certified ophthalmologist and neurologist, respectively); (3) underwent diagnostic imaging; and (4) had follow-up information available.

Ophthalmic examination must have included: a neuro-ophthalmic examination (menace response, palpebral reflex, corneal reflex, dazzle reflex, pupillary light reflex (PLR) direct and consensual), Schirmer tear testing, examination of facial symmetry, a complete slit-lamp

examination, indirect funduscopy and rebound tonometry. Neurologic examinations must have included: assessment of mental status, gait, posture, cranial nerves, postural reactions, spinal reflexes and areas of possible hyperesthesia. The criteria for the clinical diagnosis of internal ophthalmoparesis were a mydriatic eye with a decrease in the direct PLR, a decreased consensual PLR (from the contra-lateral eye to the affected side), and intact vision. Internal ophthalmoplegia was considered when the direct and consensual PLR were absent in a mydriatic eye, but the vision was intact. Vision was assessed primarily by the menace response. However, in some cats, other means of testing, including a cotton ball test and navigation around the room, were used if the menace response was decreased to absent. Iris atrophy, iris hypoplasia, glaucoma, posterior synechia, and other causes of iris muscular dysfunction had to be ruled out for the case to be included. Data retrieved from the medical records included: signalment, history, physical, ophthalmic and neurologic examinations at presentation, imaging findings, ancillary diagnostic tests, cerebrospinal fluid analysis when available, treatment and outcome/follow-up. Post-mortem findings were recorded if available.

Magnetic resonance imaging and CT findings were reviewed independently by a board certified neurologist (EB) and a board certified radiologist (RL). The images were described for each case. Ultrasound and radiographic findings were also reviewed when available (RL).

Short-term outcome was defined as survival or non-survival 48 hours after diagnosis. The long-term outcome was assessed, when available, at 1, 2 and 3 months after diagnosis. Follow-up information was obtained by telephone consultation with the owner and/or the referring veterinarian and combined with information from the medical records, including any gross pathology and histopathology reports.

Results

Internal ophthalmoparesis/ophthalmoplegia was identified in twelve cats. The cats had a mean age of 10.33 years, and a median age of 10.54 years (range 5.75 to 13.17). Breeds affected were eight Domestic Short-hair cats and one of each of the following: Domestic Long-hair, Tonkinese, British Short-haired, and Burmese cat. Nine cats were male (neutered n = 9; 75%) and three cats were female (spayed n = 2; 17%, or intact n = 1; 8%).

The results of the physical, ophthalmologic and neurologic examinations are summarized in Table 1. Unilateral internal ophthalmoparesis (right eye only (OD) n = 1; 0.08%) (Fig. 1) or ophthalmoplegia {(total n = 8; 67%), OD = 4; 33%, left eye (OS) = 4; 33%} was present in nine cats (75%). One cat (case 4), presented with unilateral internal ophthalmoparesis (OD), however, this progressed to bilateral internal ophthalmoplegia 14 days following initial presentation. Bilateral internal ophthalmoparesis was present in one cat (case 10) at presentation. Case 11 had internal ophthalmoparesis OD and internal ophthalmoplegia OS.

The neurologic examination at presentation revealed: obtunded mental status (n = 9; 75%), abnormal behavior (circling n = 3, 25%; pacing n = 1, 8%; compulsive behavior n = 1, 8%), proprioceptive ataxia in all four limbs (n = 3; 25%), ambulatory tetraparesis (n = 1; 8%), postural reactions deficits (n = 4; 33%), and seizures (n = 2; 17%). In addition, the neuro-ophthalmic examination included deficits in CN III (motor component), IV, V (ophthalmic and maxillary branch), VI and VII ipsilateral to the mydriasis. Clinical signs of these deficits included: an absent or decreased palpebral reflex (n = 5; 42%), absent or decreased menace response with normal vision (n = 3; 25%), absent/decreased corneal reflex (n = 3; 25%), a decreased (n = 1; 8%) or absent (n = 3; 25%) vestibulo-ocular reflex (VOR) (unilateral n = 3; 25%, or bilateral n = 1; 8%); and decreased facial sensation (areas innervated by the ophthalmic and maxillary branches n = 1; 8%).

149 Abnormal imaging findings are summarized in Table 2: MRI only (n = 4; 34%), MRI and
150 ultrasound (n = 3; 25%), CT only (n = 1; 8%), CT and ultrasound (n = 1; 8%), CT and MRI
151 (n = 1; 8%), ultrasound only (n = 2; 17%). In addition, thoracic radiographs were performed
152 in cases 2, 4, and 6. Magnetic resonance imaging (Fig.2) or CT scans (Fig.3) of the head were
153 performed in most cats (n = 10; 84%). This revealed a mass lesion in all cases in varying
154 locations: middle cranial fossa (n = 7; 58%); extra-axially between the midbrain and pons (n
155 = 1; 8%); retro-bulbar space (n = 1; 8%); and intra-nasally, extending to the orbital fissure (n
156 = 1; 8%). The two cats with abdominal ultrasound only, had intestinal thickening, mass-like
157 lesions or abnormal kidneys that were diagnosed by fine needle aspirates and cytology as
158 large cell lymphoma. Their neurologic signs were suspected to be due to multi-centric
159 lymphoma and further investigations, including MRI, were offered but declined by the
160 owners due to quality of life concerns, and they requested for euthanasia of both cats.

161 Cerebrospinal fluid (CSF) analysis was only performed in one case (Case 4). CSF analysis
162 from the cerebellomedullary cistern showed atypical large mononuclear cells (76%) small
163 mononuclear cells (21%), non-degenerate neutrophils (1%), occasional activated
164 macrophages (2%) and a protein concentration of 0.06g/l. This case was diagnosed with
165 multi-centric lymphoma following fine needle aspiration and cytology of a colonic lesion.

166 Follow-up information is summarized in Table 2. All twelve cats were euthanized due to
167 clinical deterioration or concerns of quality of life. There was a short-term outcome (48 hours
168 after diagnosis) of 50% survival and 50% non-survival. All cases with an initial short-term
169 survival outcome were euthanized within 3 months of diagnosis. The median time between
170 presentation and euthanasia was 3.5 days (range 0 to 80 days). Two cats had post-mortem
171 examinations performed (Cases 7 and 10). Case 7 was diagnosed with a round cell neoplasm
172 consistent with lymphoma observed in the hypothalamic area (middle cranial fossa), optic
173 chiasm, local meninges and stomach. This case had MRI and CT of the head performed with

lesions noted on the left side of the middle cranial fossa, however no abdominal imaging had been performed. Case 10 was diagnosed with a macroadenoma of the pituitary gland; the lesion location was consistent with the ante-mortem CT findings.

Discussion

We describe clinical signs, imaging findings and outcome in twelve cats with internal ophthalmoparesis/ophthalmoplegia. Despite several reports of middle cranial fossa syndrome in cats,[7-11] this is the first case series specifically looking at the presentation of internal ophthalmoplegia/ophthalmoparesis in cats.

Understanding of the neuroanatomical pathway of CN III is important prior to interpreting its dysfunction. Cranial nerve III is divided into motor fibers and parasympathetic fibers. The motor fibers innervate the ipsilateral extra-ocular muscles (dorsal rectus, medial rectus, ventral rectus, and ventral oblique) and the ipsilateral levator palpebrae superioris muscle. The parasympathetic fibers innervate the iris sphincter and ciliary body muscles. The PLR allows evaluation of the parasympathetic fibers of CN III. Following stimulation of the retina by a light stimulus, impulses travel via the optic nerve (CN II) to the optic chiasm, where the majority of the fibers (around 65% in the cat) cross over and continue as part of the contralateral optic tract. Some optic tract fibers bypass the lateral geniculate nucleus and course caudally to synapse in the pretectal nucleus (located in the rostral midbrain). The majority of the fibers of the pretectal nucleus (around 65%), cross over to the contralateral side, through the caudal commissure, and reach the parasympathetic nucleus of CN III (known in human neuro-anatomy as the Edinger–Westphal nucleus). The remaining fibers from the pretectal nucleus (around 35%) reach the ipsilateral parasympathetic nucleus of CN III.[1,13] Both the motor and the parasympathetic fibers emerge together in the lateral aspect of the interpeduncular fossa, on the medial side of the crus cerebri, and course rostrally in the

middle cranial fossa lateral to the pituitary gland, adjacent to but not in the cavernous sinus, where they meet the trochlear nerve (CN IV), abducens nerve (CN VI) and two branches of the trigeminal nerve (CN V) (ophthalmic and maxillary nerves).[1,13] All these nerves (except the maxillary branch) exit the cranial cavity through the orbital fissure. The maxillary branch of CN V exits through the round foramen. The motor fibers of CN III then abruptly branch to innervate the extraocular muscles. Located at the point of branching is the ciliary ganglion. In this ganglion, the preganglionic parasympathetic fibers synapse onto the postganglionic parasympathetic fibers. These postganglionic fibers, then known as the short ciliary nerves, pass along the surface of the optic nerve to the eyeball to innervate the smooth muscle of the ciliary muscle and the sphincter of the pupil causing pupillary constriction (Fig.4).[1,13] Provocative pharmacological testing of mydriasis can be performed by using 0.1% pilocarpine solution to assess the parasympathetic innervation of the oculomotor nerve to that eye.[39] However, the results of such tests can be unreliable.[40] Pharmacological testing was not performed in any of the cases of this study.

Obtunded mental status was seen in nine of the twelve cats at presentation (75%). This is likely due to the intracranial masses causing compression of the forebrain/brainstem. The menace response was absent or decreased in three cats, however, they had intact vision; the menace response deficits were considered likely to be due to their obtunded mental status.

The majority of our cases (n = 8) had internal ophthalmoparesis/ophthalmoplegia without external ophthalmoparesis/plegia. Five of these eight cats (cases 1, 8, 9, 10 and 12) were diagnosed with a middle cranial fossa mass. This could be explained by the fact that the preganglionic parasympathetic fibers are more superficial, medial and smaller in diameter than the motor fibers of CN III and therefore more at risk of being compressed by a lesion arising from the middle cranial fossa and causing mass effect.[1,41,42] Two of these 8 cases (cases 4 and 5) did not have advanced imaging of the head and the remaining case (case 6)

was diagnosed with a retrobulbar mass. In case 6, we could hypothesize that the mass affected mainly the postganglionic parasympathetic fibers after they branched away from the motor fibers. However, a post-mortem examination was not obtained in this case.

In cats, clinical signs of external ophthalmoparesis/ophthalmoplegia include ptosis, ventrolateral strabismus and a decreased (paresis) or absent (plegia) VOR.[13] In this case series, panopthalmoparesis/ophthalmoplegia (internal and external ophthalmoparesis/ophthalmoplegia) was only seen in the form of an ipsilateral decreased or absent VOR (n=4); ptosis or static ventrolateral strabismus were never observed. The VOR evaluates CN VIII (sensory component to the reflex) and III, IV, and VI (motor component).[39] The VOR is induced by movement of the head from side to side in a horizontal plane which elicits an involuntary rhythmic eye movement. This reflex can be decreased to absent due sensory component dysfunction (CN VIII), motor component dysfunction (CN III, CN IV, CN VI) or myopathy of the extraocular muscles.13 None of the cats presented with vestibular dysfunction, therefore a dysfunction of the sensory component of this reflex was not considered the cause of the decreased/absent VOR. All four of these cats (cases 2, 3, 7, 11) were diagnosed by MRI/CT with a mass lesion in the middle cranial fossa. The nerves involved in the motor component of the VOR (CN III, IV, VI) pass through the middle cranial fossa where they exit the skull through the orbital fissure.[13] This anatomical relationship can explain why panophthalmoparesis/ophthalmoplegia was seen in these cats.

Lymphoma is the second most common intracranial neoplasm after meningioma in cats.[43-45] It can be associated with feline leukemia virus.[28] Lymphoma should be included as one of the major differential diagnoses in cats presented with internal ophthalmoplegia.[43-45] Systemic clinical signs were seen in ten of the twelve cases in this study. Cases 4 and 5 had an abdominal ultrasound prior to MRI/CT due to the presence of inappetance, weight loss, and diarrhea (case 4). In both of these cases, due to lesions found on abdominal ultrasound,

lymphoma was diagnosed by fine needle aspiration and cytology. Due to these findings, advanced imaging was declined by the owners. This is similar to the findings of Inumura *et al.,* who suspected CN III failure due to metastasis of a renal carcinoma. A third case, case 7, was diagnosed with intracranial and gastric lymphoma on post-mortem examination. In hindsight, an abdominal ultrasound with cytology could have possibly provided a pre-mortem diagnosis of lymphoma. As demonstrated by these cases, in cats with concurrent systemic signs abdominal ultrasound should be considered prior to any advanced imaging to better understand the clinical signs, and potentially reach a diagnosis.

Inherent limitations of retrospective studies impacted these results. A final post-mortem examination was only performed in two cases, thus limiting any definitive comments about the nature of our findings. The medical records were at times incomplete, although follow-up information and outcome was obtained for all cases. Another limitation of this study was the small number of cases and a referral only population. It is possible that cases presenting in general practice with feline internal ophthalmoparesis/ophthalmoplegia alone, in an otherwise healthy cat, are often not referred, and so our population is biased towards more critically unwell animals with a worse prognosis. Future prospective studies documenting larger populations of cats with internal ophthalmoparesis/ophthalmoplegia, in both a referral and first opinion setting, would be beneficial to understand the true clinical outcome of cats with internal ophthalmoparesis/ophthalmoplegia.

Conclusion

Feline internal ophthalmoparesis/ophthalmoplegia often presents with other clinical signs in a referral hospital population. A thorough history, physical examination, and neurologic and ophthalmic examinations are essential for clinical reasoning and to effectively select the most indicated diagnostic tests. Cats with intracranial lesions can present with

panophthalmoparesis/ophthalmoplegia or internal ophthalmoparesis/ophthalmoplegia as the sole clinical sign. Advanced imaging may be necessary to reach a definitive diagnosis, but abdominal ultrasound can be helpful in some cases with systemic disease. Cats with systemic and neurologic deficits related to internal ophthalmoparesis/ophthalmoplegia have a guarded prognosis due to the high prevalence of neoplasia in this population.

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393

Figure 1: 6.75 year-old, male neutered, Domestic Short-hair cat (case 1) with anisocoria due to internal ophthalmoplegia of the right eye.

Figure 2: MRI of the brain from a 6.75 year-old, male neutered, Domestic Short-hair cat with right-sided internal ophthalmoplegia (case 1) (A and D: mid-Sagittal plane; B, C, E and F: transverse plane at the level of the pituitary fossa plane). There is a large clearly marginated, bi-lobed mass in the middle cranial fossa (predominantly on the right). The mass is hyperintense, with areas of hypointensity compared to the normal grey matter on T2W FSE (A, B) and on FLAIR (C) images. The mass is hypointense to the normal grey matter on T1W (E) and demonstrates strong contrast enhancement on T1W (D, F).

Figure 3: Pre-contrast CT images of the brain from a 10 year-old, male neutered, Domestic Short Haired cat, with bilateral internal ophthalmoplegia with a rounded hyperattenuating large pituitary mass extending bilaterally and dorsally. Medium-frequency reconstruction images are presented in a brain window (WL 50, WW 100) A: Transverse plane at the level of the pituitary fossa, B: sagittal plane reconstruction, C: dorsal plane reconstruction at the level of the middle cranial fossa.

Figure 4: Neuroanatomic pathway of the pupillary light reflex. (A) Dorsal and (B) lateral views. Retina (1), optic nerve (2), optic canal (3), optic chiasm (4), optic tract (5), pretectal nucleus (6), parasympathetic component of the oculomotor nucleus (Edinger Westphal nucleus) (7), oculomotor nerve (8), orbital fissure (9), ciliary ganglion (10), and short ciliary nerve (11).

Table 1. Signalment and clinical signs in twelve cats with internal ophthalmoplegia/ophthalmoparesis. The affected CN is annotated in brackets.

Case	Signalment Breed Age (y) Sex	Duration mydriasis (d)	Side of mydriasis	Parasympathetic component CN III	Motor component CN III	Other ophthalmic signs	Other neurological signs	Systemic signs
1	DSH 6.75 MN	7	OD	Plegia	NA	None	Obtunded Pacing Seizures	Dehydration
2	Burm. 9.41 FE	5	OS	Plegia	Plegia	None	OS: absent palpebral reflex (CN V), absent corneal reflex (CN V, VI)	Inappetence Pyrexia
3	DSH 13.17 FN	21	OS	Plegia	Plegia	OS: diffuse corneal opacity OU: aqueous flare, uveitis and iridal haemorrhages	↓ L facial sensation (V) OS: absent palpebral reflex (CN V), absent corneal reflex (CN V)	Chronic hepatic lipidosis Pancreatitis Enteropathy Constipation
4	DSH 11.08 MN	3	OD	Paresis	NA	None	None	Weight loss Inappetence Diarrhoea Heart murmur
4* 14d after		17	OU	Plegia	NA	OD: corneal ulcer OS: focal white iridal mass	Obtunded OU: absent menace OD: absent palpebral reflex (V)	As before
5	DSH 13.00 MN	2	OD	Plegia	NA	None	Obtunded ↓ L sided postural reaction deficits	Pyrexia Inappetence Weight loss

Case	Signalment Breed Age (y) Sex	Duration mydruasis (d)	Side of mydriasis	Parasympathetic component CN III	Motor component CN III	Other ophthalmic signs	Other neurological signs	Systemic signs
6	BSH 12.25 MN	10	OS	Plegia	NA	OS: exophthalmus	Obtunded	Pancreatitis Coughing Weight loss L temporal m swelling Submand lymphadenopathy L nasal discharge
7	Tonk. 5.75 MN	2	OS	Plegia	Plegia	OU: 3rd eyelid protrusion	Obtunded	Hypothermia Inappetence Heart murmur
8	DSH 11.34 MN	30	OD	Plegia	NA	OU: scleral vessel congestion, edematous optic discs with areas of retinal detachment	Obtunded Seizures Proprioceptive ataxia Ambulatory tetraparesis Positional vertical nystagmus OD: ↓ menace response, absent palpebral reflex (CN V), ↓ corneal reflex (V)	Anorexia
9	DSH 15.00 FN	3	OD	Plegia	NA	None	Obtunded Circling to the R L PL and TL postural reaction deficits	Inappetence

Case	Signalment Breed Age (y) Sex	Duration mydriasis (d)	Side of mydriasis	Parasympathetic component CN III	Motor component CN III	Other ophthalmic signs	Other neurological signs	Systemic signs
10	DSH 10.00 MN	21	OU	Plegia	NA	OS: enophthalmus	Obtunded Proprioceptive ataxia Compulsive behaviour	Diabetes mellitus Acromegaly
11	DLH 8.75 MN	30	OU	OS: plegia OD: paresis	Paresis	None	Obtunded Circling to the R ↓ L PL and TL postural reaction deficits Cervical hyperaesthesia	None
12	DSH 7.50 MN	Unknown	OD	Paresis	NA	None	Obtunded Circling to the R Proprioceptive ataxia ↓ R sided postural reaction deficits OD: ↓ menace response, ↓ palpebral reflex (VII)	None

Table 2: Abnormal imaging findings, pathology results and outcome in twelve cats with internal ophthalmoplegia/paresis

Abbreviations: AD, after diagnosis; abdo u/s, abdominal ultrasound; CN, cranial nerve; d, days; dx, diagnosis; euth, euthanized; FNA, fine needle aspirate; n/a, not applicable; L, left; LN, lymph nodes; MCF, middle cranial fossa; PM, post-mortem; R, right; submand, submandibular

Case	MRI/CT findings	Other imaging findings	Pathology findings	Outcome
1	MRI: Extra-axial intracranial mass in the MCF through the orbital fissure bilaterally, perilesional oedema and raised intracranial pressure	Abdo u/s: diffuse hepatopathy	n/a	Euth 5d AD
2	MRI: Focal extra-axial mass extending from the ventral part of the pons to MCF L>R, with extension into the left retrobulbar tissues.	n/a	n/a	Euth 8d AD
3	MRI: Extra-axial mass lesion in the L MCF with enlargement of the three branches of CN V	n/a	n/a	Euth 0d AD
4	n/a	Abdo u/s: Intramural colonic mass, intra –abdominal lymphadenopathy, hypoechoic and thickened pancreas Thoracic radiographs: mild cardiomegaly	FNA colonic mass dx large cell lymphoma	Euth 14d AD
5	n/a	Abdo u/s: Bilateral nephropathy, mesenteric lymphadenopathy and focal intestinal thickening	FNA kidney dx large cell lymphoma	Euth 1d AD
6	CT: ST thickening within L temporalis musculature extending into the retrobulbar space and in the L tympanic bulla. Fluid filling of the frontal sinuses and thickening of the lining of the L frontal sinus.	Abdo u/s: Polycystic hepathopathy, mesenteric lymphadenopathy, mild pancreatic disease	FNA subamnd LN dx lymphoma	Euth 70d AD

Case	MRI/CT findings	Other imaging findings	Pathology findings	Outcome
7	CT: ST attenuating material in R tympanic bulla Mild amount of ST attenuating material in the nasal cavity. Lung consolidation MRI: Large extra-axial mass in MCF (R>L)	n/a	PM: lymphoma	Euth 0d AD
8	MRI: Intranasal mass extending to the olfactory bulb, the MCF and orbital fissure	n/a	n/a	Euth 0d AD
9	MRI: Large pituitary mass extending bilaterally (R>L)	n/a	n/a	Euth 0d AD
10	CT: Large pituitary mass extending bilaterally. Thickened pancreas	n/a	PM: macroadenoma	Euth 20d AD
11	MRI: Large extra-axial mass in MCF (R>L)	n/a	n/a	Euth 80d AD
12	MRI: Large extra-axial mass in MCF	n/a	n/a	Euth 0d AD