Presumed optic neuritis of non-infectious origin in dogs treated with immunosuppressive medication: 28 dogs (2000-2015)

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Objective: To describe the clinical findings, magnetic resonance imaging features, management and outcome of canine cases with presumed optic neuritis of non-infectious origin that were presented to a UK referral centre from January 2000 to December 2015.

Materials and Methods: The clinical database was searched for optic neuritis. Dogs with acute-onset vision impairment, systemic immunosuppressive treatment and follow-up of ≥6 months were included. Information collected included: age; gender; breed; clinical signs and duration; physical, ophthalmic and neurological examination findings; concurrent systemic disease; and results of electroretinogram, magnetic resonance imaging, cerebrospinal fluid analysis, polymerase chain reaction and serology testing for *Toxoplasma gondii*, *Neospora caninum* and canine distemper virus, haematology and serum biochemistry profiles, abdominal ultrasound, thoracic radiography, treatment and outcome.

Results: Twenty-eight dogs were included, with a total of 48 affected optic nerves. Age at presentation ranged from 6 months to 10.5years. Fundoscopic evidence of optic nerve disease was present in 34 of 48 (71%) optic nerves. Magnetic resonance imaging revealed enlargement of 32 of 48 (67%) nerves and contrast enhancement of 28 of 48 (58%) nerves. Cerebrospinal fluid analysis performed in 25 of 28 (89%) dogs revealed pleocytosis (>5 nucleated cells/uL) in 11 of 25 (44%) and increased protein (>0.35g/L) in 11 of 25 (44%). Immunosuppressive prednisolone was administered to all dogs. Prednisolone was used alone in 9 of 28 (32%) dogs; the remaining 19 dogs received a combination of prednisolone with cytosine arabinoside, cyclosporine and/or azathioprine. Vision was recovered in 24 eyes (50%) of 18 affected dogs.

Clinical significance: A positive response to treatment was observed in 64% of dogs with presumptively diagnosed optic neuritis treated with immunosuppressive medication.

Key Words: Canine, optic neuritis, CN II, neuro-ophthalmology, optic nerve.

INTRODUCTION

The optic nerve (CN II) is formed by the axons of the retinal ganglion cells, whose soma are found in the innermost part of the retina (Glass & DeLahunta 2009). In dogs, the majority of the axons within CN II will cross at the level of the optic chiasm to synapse at the lateral geniculate nuclei or the pretectal nuclei (Glass & DeLahunta 2009). A complete lesion of CN II causes unilateral vision loss and an afferent deficit in the menace response, dazzle reflex and pupillary light reflex pathways (Glass & DeLahunta 2009).

Differential diagnoses for acute onset of blindness in dogs include sudden acquired retinal degeneration syndrome (SARDS) (Montgomery *et al*. 2008), retinal detachment, glaucoma (Grozdanic *et al*. 2007), retrobulbar disease (Mason *et al*. 2001), optic neuritis (ON) and tumours affecting the visual pathways (Davidson *et al*. 1991, Seruca *et al*. 2010). Less commonly, conditions such as cerebrovascular ischaemic infarction, head trauma (Gelatt 1974) and metabolic diseases, such as hypertensive or hepatic encephalopathy, hypoglycaemia or hypoxia (O'Neill *et al*. 2013, Lidbury *et al*. 2016), have been described as causes for acute blindness. For this reason, the use of MRI in conjunction with full physical, neurologic and ophthalmic examination, cerebrospinal fluid (CSF) analysis and serological testing are paramount to detection and characterisation of ON in dogs (Armour *et al*. 2011).

ON is commonly characterised by a sudden onset of blindness with a dilated pupil, secondary to inflammation of CN II (Bianca & Brooks 2013). Infectious diseases associated with ON in dogs include: viral (*e.g*. canine distemper virus (Richards *et al*. 2011), tick-borne encephalitis virus (Stadtbaumer *et al*. 2004), fungal (*e.g*. cryptococcosis (Jergens *et al*. 1986), blastomycosis (Treviño 1966), histoplasmosis (Gwin *et al*. 1980)) and bacterial infections (*e.g*. Ehrlichiosis (Leiva *et al*. 2005). Other causes of canine ON include traumatic, nutritional (*e.g*. Vitamin A deficiency (Fischer & Jones 1972)] and toxic [*e.g*. closantel intoxication (McEntee *et al*. 1995)) aetiologies. Furthermore, ON has also been reported in association with an extension of sterile inflammatory disease of the central nervous system (*e.g*. granulomatous meningoencephalitis [GME]) (O'Neill *et al*. 2005). In many dogs, this inflammatory process is deemed idiopathic and is presumed to be immune-mediated on the basis of clinical response to immunosuppressive treatment (Fischer & Jones 1972).

The aims of this study were to describe the clinical findings, MRI features, management, outcome and long-term follow- up of canine cases presumptively diagnosed with idiopathic/ immune-mediated ON.

MATERIALS AND METHODS

Medical records of all dogs seen in a UK referral centre for evaluation of acute onset of vision impairment between January 2000 and December 2015 were reviewed. Inclusion criteria included all canine cases with presumptive diagnoses of ON that underwent complete physical examination, ophthalmic examination (performed by a veterinary ophthalmologist or veterinary ophthalmology resident), neurological examination (performed by a veterinary neurologist or veterinary neurology resident), full haematology and comprehensive serum biochemistry pro- files, serological titres or polymerase chain reaction testing [per- formed on blood or CSF] for infectious diseases (*Toxoplasma gondii*, *Neospora caninum*, Canine distemper virus); 1.5T MRI scanner (Signa Echospeed, General Electric, Milwaukee, WI) of the head; and a minimum of 6 months' follow-up (either at the referral centre or via telephone updates with the owner/ referring veterinary surgeon) during which there was no evidence of progression that would be incompatible with, or call into question, a diagnosis of a primary inflammatory condition. All MRI studies included fast spin echo T2-weighted sequences (repetition time [TR] 2200-5420ms; echo time [TE] 80.47– 89.22 ms; slice thickness 2–5 mm) and pre- and post-intravenous injection of contrast medium (gadolinium, Bayer's Gadovist® (*gadobutrol*)) transverse fast spin echo T1-weighted sequences (TR 260–760ms; TE 9.00–14.00ms; slice thickness 2–5mm). Further sequences were performed at the imager's discretion; however, all studies included sequences in transverse, dorsal and sagittal planes. MRI abnormalities were categorised as absent if no lesions were noticed, isolated ON (I-ON) if only the optic nerve or nerves showed signs consistent with inflammation and multi-focal if other areas of the brain exhibited signs consistent with inflammation. Cases were excluded if there was evidence of pathology involving the visual pathway(s) caudal to the optic chiasm or within the ocular visual axis that could explain the clinical signs, evidence of retinal/optic nerve head disease not compatible with ON, evidence of infectious or neoplastic disease, significant abnormalities on haematology and serum biochemistry profiles, abnormal electroretinography (ERG) or progression of neuro- logical disease despite appropriate immunosuppressive treatment (which could bring into question a presumptive diagnosis of an inflammatory aetiology). Cases considered stable on treatment (i.e. no

improvement but no progression) were not excluded, nor were cases that relapsed with tapering of therapy.

Patient information collected included: breed, gender and neuter status, age at diagnosis, clinical signs exhibited at and before presentation, duration of clinical signs, MRI findings, CSF analysis, treatment administered (medication(s) used, length of treatment, length of treatment at immunosuppressive doses), recovery of CN II function (recovery of menace response and pupillary light reflexes) and outcome. Follow-up was performed through a combination of clinical re-examination at the referral centre, evaluation of post-diagnosis clinical records and telephone conversations with the owner. For dogs in which the final clinical re-examination at the referral centre was within 6 months of diagnosis, subsequent clinical information was collected by telephone conversations with the owner and/or the referring veterinary surgeon. Visual function was assessed based on the presence or absence of the menace response and dazzle reflex with intact facial nerve function. A successful outcome was defined as recovery of visual function in one or both affected eyes and recovery of menace response and pupillary light reflexes (partial or complete)

RESULTS

A total of 28 dogs met the inclusion criteria. The individual breeds are shown in Table 1, and signalment is detailed in Table 2. The majority of dogs were of small breeds (<10 kg; 16/28, 57%), followed by large breeds (>25kg; 9/28, 32%) and medium breeds (10–25kg; 3/28, 11%). Of the 28 dogs, 7 (25%) were entire females, 8 (29%) neutered females, 4 (14%) entire males and 9 (32%) neutered males. The mean (median; range) age at presentation was 5.9 years (5.8 years; 0.6–10.5 years).

The most frequent clinical signs at the time of presentation were acute onset of visual impairment (27/28, 96%) and mydriatic pupils (12/28, 43%). Blepharospasm (1/28, 4%) and exophthalmos (1/28, 4%) were also reported. The menace response and dazzle reflex were absent in one eye in eight dogs (8/28, 29%) and both eyes in 20 cases (20/28, 71%), giving a total of 48 affected eyes.

Fundoscopic examination revealed signs consistent with ON in 20 dogs (71%) affecting 34 eyes (71%). The most common signs were peripapillary retinal detachment, optic nerve head (ONH) inflammation (exudates, haemorrhages), ONH atrophy, hyperpigmentation of the non-tapetal fundus and white deposits on the non-tapetal fundus (Table 3). ERG was performed in 17 dogs and was bilaterally normal in all cases (Table 2).

Five dogs (5/28, 18%) presented other neurological signs apart from deficits within the visual pathway, with two of these dogs displaying two or more additional neurological signs. These neurological deficits included: proprioceptive deficits in one or more limbs (3/28, 11%), unilateral facial paresis (1/28, 4%), horizontal nystagmus (1/28, 4%), mild proprioceptive ataxia of all four limbs (1/28, 4%), decreased facial sensation on one side (1/28, 4%), hyperaesthesia on palpation over the cranium (1/28, 4%) and moderate pelvic limb ataxia secondary to previous peripheral vestibular disease (1/28, 4%). Four of this dogs displaying additional neurological signs presented with fundic lesions suggestive of ON.

MRI changes consistent with ON were seen in most dogs (26/28, 93%). Examples of the MRI findings are depicted in Fig 1. These included CN II enlargement (32/48 eyes, 67%), contrast enhancement of the CNII (28/48eyes, 58%), enlargement of the optic chiasm (10/28 dogs, 36%), changes suggestive of encephalitis/meningoencephalitis/meningoencephalomyelitis (5/28 dogs, 18%), contrast enhancement or thickening of the meninges (4/28 dogs, 14%), contrast enhancement or T2-weighted hyperintensity within non-nervous tissues adjacent to the CN II (6/48 eyes, 13%) and CN II atrophy (1/48 eyes, 2%). In three dogs (3/28, 11%), the CN II changes were the sole finding(s) on MRI. Most dogs (19/28, 68%) demonstrated two or more concurrent MRI abnormalities in addition to CN II changes, and seven (7/28, 25%) had only one concurrent MRI abnormality in addition to CN II changes.

Five dogs displaying bilateral signs of blindness showed MRI features suggestive of inflammation in only one CNII, while the contralateral CNII appeared normal on MRI. All five dogs presented fundic changes suggestive of ON, bilaterally in three and unilaterally in two cases. Among this group, ERG was performed and was normal in three dogs. In addition, a further two bilaterally blind dogs exhibited no MRI abnormalities in either CN II (Table 2). The presumptive diagnosis of ON in these two cases was based on the presence of fundic abnormalities (both cases) and the normality of the ERG result in one case (Table 2).

After MRI, CSF was collected from either the cerebellomedullary cistern or via lumbar puncture in 25 cases (25/28, 89%). For the remaining three cases, MRI findings were suggestive of increased intracranial pressure, and this procedure was deemed unsafe. CSF analysis was abnormal in most dogs (15/25, 60%; Table 2). Pleocytosis alone (>5 nucleated cells/uL) was present in four cases (4/15, 27%) and albuminocytological dissociation (protein >0.35g/L) in four dogs (4/15, 27%). A combination of pleocytosis and increased protein level was present in seven dogs (7/15, 47%). The pleocytosis was lymphocytic in four dogs (4/11, 36%), monocytic in four dogs (4/11, 36%), mixed mono- nuclear in three dogs (3/11, 27%) and neutrophilic in one dog (1/11, 9%).

Treatment

The treatment and follow-up information is detailed in Table 4. The treatment protocol varied among cases depending on clini- cian preference and experience, owner constraints (financial, ease of administration, availability of follow-up treatment), patient temperament and medical history; however, all dogs received immunosuppressive doses of prednisolone. Prednisolone was used alone in nine dogs (9/28, 32%), and the remaining dogs received a combination of prednisolone and cytosine arabino- side (7/28, 25%), cyclosporine (4/28, 14%), azathioprine (1/28, 4%), cytosine arabinoside and cyclosporine (3/28, 11%), cytosine arabinoside and azathioprine (2/28, 7%) or cyclosporine and azathioprine (2/28, 7%).

Outcome

The combinations of treatment and recovery of vision are summarised in Table 5. A total of 24 affected nerves (24/48, 50%) recovered function in 18 dogs (18/28, 64%). The median time for recovery of vision was 10.5 days (range 2–60 days) after starting immunosuppressive treatment.

The median duration of treatment was 365days (56– 2920 days) for the dogs that recovered vision and 180 days (21–1095 days) for those that did not. The median duration of treatment at immunosuppressive doses was 20 days (0–210 days) for dogs that recovered vision and 35days (7–1095days) for those that did not.

Dogs that recovered vision exhibited clinical signs for a median duration of 4.5days (1–60 days) before referral, whereas clinical signs were present for a median duration of 7 days (3–35 days) in dogs that did not recover vision. The duration of clinical signs noted by the owner before referral exceeded 1 week for 2 of the 19 dogs (11%) that recovered vision and 3 of 9 dogs (33%) that did not recover vision. Recovery of vision was more prevalent in neutered dogs (94% recovered vision) than entire dogs (27% recovered vision).

Five dogs (5/28, 18%) relapsed after tapering the dose of immunosuppressive drugs. However, four of these dogs (4/5, 80%) again recovered vision after a return to immunosuppressive doses of medication.

DISCUSSION

This study presents the retrospective evaluation of a series of canine cases diagnosed with presumptive idiopathic ON. Idiopathic ON is considered an ocular form of GME. CN II involvement in GME can occur as part of the disseminated or focal forms or as an entity of its own (O'Neill *et al*. 2005). Affected dogs may initially present solely with ophthalmologic

signs but subsequently develop other neurological signs associated with disseminated central nervous system lesions (O'Neill *et al*. 2005). In dogs, ON is often deemed idiopathic and presumed to be immune-mediated (Fischer & Jones 1972), while in humans, ON is most commonly considered to be idiopathic and may occur alone or in association with other disease pro- cesses such as demyelinating lesions (multiple sclerosis being the most common cause), autoimmune disorders and infectious and inflammatory conditions (Hoorbakht & Bagherkashi 2012).

In the cases presented in this study, the presumptive diagnosis of ON was made based on complete physical, neurological and ophthalmic examinations; blood tests; ERG (in the absence of fundic lesions); and MRI and CSF findings consistent with previous reports (Davidson *et al*. 2002, O'Neill *et al*. 2005). In this study, the response to immunosuppressive treatment and exclusion of other possible causes of ON, with consistent MRI findings (enlargement and enhancement of the CN II) and an elevation of CSF nucleated cell count, might indicate the presence of an immune-mediated component. Progression of clinical signs despite treatment with immunosuppressive agents can indicate an underlying infectious or neoplastic disorder. Given the difficulty of obtaining an ante-mortem definitive diagnosis, although it introduced a degree of bias in our population through exclusion of dogs whose signs progressed, only patients with static or improving signs while receiving appropriate immunosuppressive treatment were included in the present study to minimise the risk of misdiagnosis.

Based on the fundoscopic findings, canine ON can be classified as intra-bulbar ON (where fundic abnormalities are present) and retrobulbar ON (where fundic abnormalities are absent) (Fischer & Jones 1972). In the present study, most cases presented with fundic lesions such as peripapillary haemorrhage, retinal detachment, ONH inflammation, ONH atrophy and hyperpigmentation of the non-tapetal fundus. Similar findings were found in another study, where ONH swelling and elevation were described in all dogs (n = 50) diagnosed with ON (Davidson *et al*. 2002). In another retrospective study (n = 96), fundoscopic findings included ONH elevation (n = 96), peripapillary retinal oedema or separation (n = 37), retinal haemorrhage or dilation of retinal vasculature (n = 23) and multiple inflammatory foci in the peripapillary region (n = 13) (Smith *et al*. 2017). In contrast to human medicine, in which retrobulbar ON represents two-thirds of human ON cases (Hoorbakht & Bagherkashi 2012), retrobulbar ON has been described in only four dogs (Smith *et al*. 2017). In the eight cases in the present study with normal ocular fundoscopic examination, the presumed diagnosis of retrobulbar neuritis was made through the presence of MRI abnormalities such as CN II

enlargement, enlargement of the optic chiasm or contrast enhancement of the ON and normal ERG.

In the present study, slightly more males than females were affected, and it seemed that recovery of vision was more likely in neutered than entire dogs. The mean age of dogs with ON in the present study (5.9years) is similar to the mean age of 6.34years reported in a previous study (Davidson *et al*. 2002). The present study showed that more than half of affected dogs were of small breeds, with the most commonly affected breeds being the Lhasa Apso and West Highland white terrier. This is similar to reported GME cases, in which middle-aged small-breed dogs are commonly affected (O'Neill *et al*. 2005). In contrast, large-breed dogs were most commonly affected by ON in another study (Smith *et al*. 2017). Therefore, further studies are necessary to determine whether a breed predisposition exists.

The increasing use and availability of MRI in veterinary medicine has provided better contrast resolution for the visualisation of the orbit and CN II (Dennis 2000). Hence, MRI is the method of choice to evaluate the cranial nerves in companion animals with cranial neuropathies (Parry & Volk 2011). In this study, MRI allowed excellent depiction of the anatomy of CN II due to its excellent soft-tissue contrast and better delineation of the entire visual pathway (Seruca *et al*. 2010). However, no abnormalities were seen on MRI in two bilaterally blind dogs. In the first case, CSF analysis was within normal limits, and the second exhibited slight albuminocytologic dissociation (0.36 g/L). In both these cases, the diagnosis was made based on abnormalities evident on ophthalmic examination and, in one case, a normal ERG result. There are only three recent studies published in veterinary literature regarding ON in which both MRI and CSF were performed. The first (Seruca *et al*. 2010) included two cases of ON in association with meningoencephalitis. One dog in that study exhibited T1- and T2-weighted images and short time inversion recovery hyperintensity and contrast enhancement of both CN II, with lymphocytic pleocytosis of the CSF (Seruca *et al*. 2010). However, results of MRI and CSF were unremarkable in the second dog (Seruca *et al*. 2010). The second study reported that only 2 of 13 dogs demonstrated pathologic CSF alterations (Armour *et al*. 2011). The third study included 96 dogs grouped into I-ON, multifocal meningoencephalitis of unknown origin (MUE), microbial infection, neoplasia, orbital inflammation and suspected ivermectin toxicosis (Smith *et al*. 2017). Forty-two cases were diagnosis with I-ON, with these subdivided into 17 confirmed and 25 unconfirmed cases. A total of 35 cases were confirmed with MUE. CSF was significantly higher in dogs with MUE compared with I-ON (Smith *et al*. 2017). In the current study, CSF analysis was abnormal in 60% dogs. The CN II are brain tracts rather than nerves per se and, as such, are

sur- rounded by the subarachnoid space that contains CSF (Bianca & Brooks 2013). Therefore, ON alone may cause some CSF abnormalities. In human medicine, Sanberg & Bynke (1973) reported pleocytosis in 60% and increased total protein concentrations in 24% of CSF samples from 25 patients with I-ON.

The correlation between different treatment protocols and recovery of vision or the likelihood of relapse of clinical signs was not analysed as case numbers within each group were low. Large prospective studies with standardised treatment protocols are necessary to evaluate these. Potentially worthy of future investigation may be evaluation of the response to azathioprine. In our study, this was the only medication with which all treated dogs (4/4) recovered vision in at least one eye [compared with 7/12 (58%) dogs treated with a protocol including cytosine arabino- side, 4/8 (50%) dogs treated with a protocol including cyclosporine and 18/28 (64%) dogs treated with prednisolone alone or in combination with at least one other immunosuppressive agent]. However, in addition to the very small number of cases who received azathioprine, it must also be noted that three of these dogs also received a third immunosuppressive agent. Larger case numbers with standardised treatment protocols would be necessary to comment further on the efficacy of azathioprine compared with other immunosuppressive agents.

The median duration of clinical signs before referral was shorter in dogs that recovered vision compared with those that did not. This may suggest that prompt diagnosis and treatment could be important in obtaining a successful outcome; however, further studies with greater case numbers would again be necessary to investigate this further.

Prognosis has generally been considered guarded for recovery of vision in dogs with ON. In previous studies, 30–33% of dogs diagnosed with ON recovered partial or complete vision after starting therapy (Davidson *et al*. 2002, Smith *et al*. 2017). In contrast, our results showed a partial or complete recovery of vision in response to treatment in 64% of dogs.

The cases included in our study were presumptively diagnosed with ON. Histopathological confirmation is required for definitive diagnosis of ON, with reported features including marked loss of ganglion cells and mild to moderate astrogliosis within the CN II fibre and ganglion cell layers in the retina (Maehara *et al*. 2009). However, as obtaining a definitive diagnosis may require sampling of the affected CN II, the nature of diagnosis alone would prevent evaluation of the response to treatment. The retrospective nature of the study meant that exclusion of all other potential aetiologies (such as fungal infection, tick-borne encephalitis or ehrlichiosis) was not possible, although as these diseases are of low prevalence in the UK, they were considered very unlikely.

There are many limitations to this study, the majority because it is a retrospective analysis of a presumptively diagnosed condition and the low number of included cases. Another limitation is the lack of ERG in 11 cases – however, of the 10 dogs for which no recovery of vision was reported, 7 were reported to have normal ERG. Therefore, although the potential for concurrent SARDS cannot be excluded in the remaining three dogs that did not recover vision, it could be ruled out as a contributing factor in 70% of non-responders. Despite these limitations, the results obtained potentially indicate a better response to treatment than has been previously reported – a prospective multi-centre study would assist in confirming this finding.

This retrospective study provides valuable information for veterinarians regarding the clinical findings, MRI features, management and outcome of canine cases with presumed ON of non-infectious origin. The term idiopathic immune-mediated ON is used for cases of ON in which no aetiologic diagnosis is found and that respond to immunosuppressive therapy. Although clinical signs and ocular abnormalities may be helpful in reaching a presumptive diagnosis of ON, this study emphasises the relevance of performing an MRI to identify retrobulbar involvement and rule out structural lesions (such as tumours) in situations where surgical biopsy is not possible. A positive response to treatment was observed in 64% of dogs with presumptively diagnosed ON treated with immunosuppressive medication; however, further comparative studies are required to demonstrate the safety and effectiveness of this intervention.

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Conflict of interest

None of the authors have a financial or personal relationship with other people or organisations that could inappropriately bias the content of the paper.

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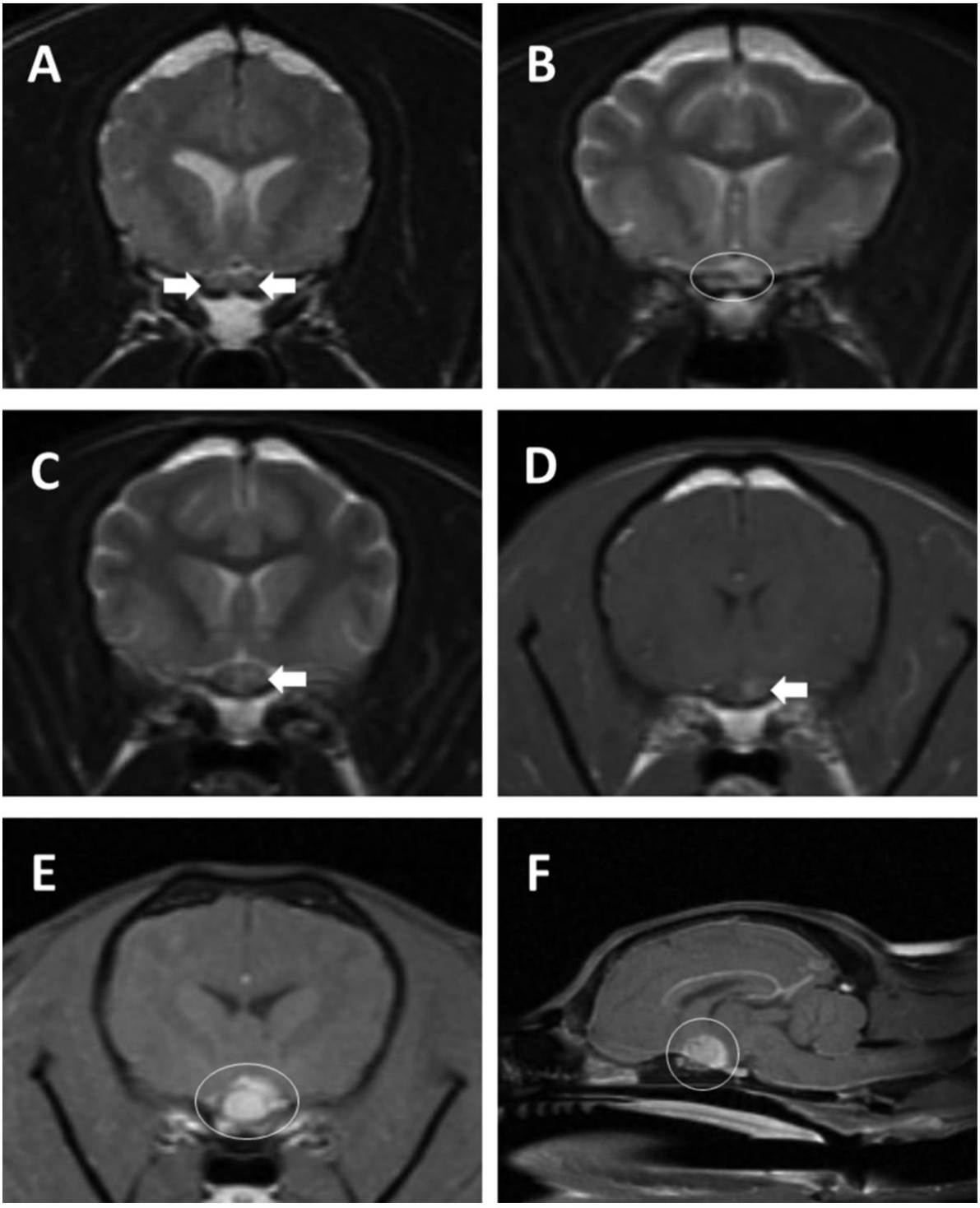

Firgure 1. All images are at the level of the optic chiasm. (A) Transverse T2-weighted image depicting bilaterally enlarged optic nerves (arrows), loss of differentiation between the white and grey matter and flattening of the sulci. (B) Transverse T2-weighted image demonstrating asymmetry between the right and left optic nerves at the level of the optic chiasm (circled). (C) Transverse T2-weighted image depicting hyperintensity diffusely affecting the left optic

nerve and extending to the chiasm. (D) Transverse post-contrast T1-weighted image of the dog depicted in (C), revealing multi-focal areas of contrast enhancement in the left optic nerve at the level of the optic chiasm. (E and F) Transverse (E) and midline sagittal (F) post-contrast T1-weighted images depicting severe enlargement of the optic chiasm with uniform contrast enhancement (circled)

Table 1. Breed distribution.

	Breed	Number dogs (%)
Small breed <10kg	Lhasa Apso	4 (14%)
	West Highland White Terrier	4 (14%)
	Cavalier King Charles Spaniel	2 (7%)
	Jack Russell Terrier	2 (7%)
	Small size crossbreed	2 (7%)
	Shih Tzu	1 (3%)
	Bichon Frisé	1 (3%)
Medium breed 10-25 kg	French Bulldog	2 (7%)
	Springer Spaniel	1 (3%)
Large breed >25kg	Golden Retriever	3 (10%)
	Labrador Retriever	1 (3%)
	Airedale Terrier	1 (3%)
	Boxer	1 (3%)
	Chow Chow	1 (3%)
	Greyhound	1 (3%)
	German Shepherd	1 (3%)

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Table 2. Signalment, clinical findings, ERG, CSF and MRI results (*n* = 28).

Case	Signalment (size age sex)	Duration of clinical signs prior to referral (days)	Lack of menace response and dazzle reflex	ERG result	CSF nucleated cell count (cells μl)	CSF total protein (g/l)	MRI (unifocal or multifocal)
1	SB 4y FN	2	Bilateral	NP	0	0.17	Multifocal
2	SB 6y FN	Unknown	Bilateral	Positive	NP	NP	Multifocal
3	SB 8y MN	14	Bilateral	Positive	4	0.29	Multifocal
4	SB 3y 7m FN	7	Bilateral	NP	44	0.47	Multifocal
5	SB 3y FE	11	Bilateral	Positive	NP	NP	Multifocal
6	SB 6y 5m MN	3	Bilateral	NP	34	0.34	Unifocal
7	SB 6y FE	3	Bilateral	NP	32	0.76	Multifocal
8	SB 10y 1m ME	1	Bilateral	Positive	2	0.24	Unifocal
9	SB 5y 6m MN	5	Bilateral	Positive	10	0.41	Multifocal
10	SB 4y 6m MN	3	Bilateral	NP	53	0	Multifocal
11	MB 5y 4m FE	2	Bilateral	Positive	NP	NP	Multifocal
12	MB 7y 6m FN	3	Bilateral	NP	1	0.23	Multifocal
13	MB 2y 7m ME	3	Bilateral	NP	NP	NP	Unifocal
14	LB 1y 6m MN	1	Bilateral	Positive	3	0.28	Absent

15	LB 3y 2m FN	7	Bilateral	NP	5	0.36	Absent
16	LB 7y MN	7	Bilateral	Positive	0	0.21	Unifocal
17	LB 4y ME	4	Bilateral	Positive	3	0.27	Multifocal
18	LB 6m ME	5	Bilateral	NP	49	0.95	Unifocal
19	LB 10y FN	7	Bilateral	Positive	3	0.93	Multifocal
20	LB 8y 9m ME	14	Bilateral	Positive	3	0.64	Multifocal
21	SB 4y 6m FE	35	Left	Positive	1	0.15	Unifocal
22	SB 8y 9m ME	7	Left	NP	14	0.37	Multifocal
23	SB 4y FN	1	Left	Positive	760	1.65	Multifocal
24	SB 3y 6m MN	6	Left	Positive	23	0.23	Unifocal
25	LB 10y 5m FN	7	Left	Positive	0	0.18	Multifocal
26	SB 8y 8m MN	4	Right	NP	377	0.61	Multifocal
27	LB 9y 5m FN	60	Right	Positive	5	0.44	Multifocal
28	SB 7y ME	4	Right	Positive	11	0.26	Multifocal

SB Small breed, *MB* Medium breed, *LB* Large breed, *FE* Female entire, *FN* Female neutered, *ME* Male entire, *MN* Male neutered, *y* Year old, *NP* Electroretinography not performed, *Absent* no signs of inflammation within the optic nerves or central nervous system, *I-ON* isolated optic neuritis; only optic nerve(s) displayed MRI changes consistent with inflammation, *Multi-focal* MRI changes consistent with inflammation were not confined to the optic nerve(s), affecting other parts of the central nervous system and/or adjacent soft tissue structures

Table 3. Most common abnormalities identified on fundoscopic examination.

Finding	Number affected dogs (%) (*n* = 28 dogs)	Number bilaterally affected dogs (%) (*n* = 28 dogs)	Number unilaterally affected dogs (%) (*n* = 28 dogs)	Total number affected eyes (%) (*n* = 48 eyes)
ONH swelling	17 (61)	12 (43)	5 (18)	29 (60)
Peri-ONH retinal detachment	4 (14)	2 (7)	2 (7)	6 (12)
ONH atrophy	3 (11)	1 (4)	2 (7)	4 (8)
White deposits non-tapetal fundus	2 (7)	2 (7)	0	2 (4)
ONH haemorrhage	2 (7)	0	2 (7)	2 (4)

ONH optic nerve head

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Table 4. Treatment, progression and follow-up for dogs with suspected optic neuritis (*n* = 28).

Case	Immunosuppressive drugs used	Length of treatment (days) at immunosuppressive doses	Total length of treatment (days) *	Relapse during tapering of drug(s) dose	Recovery optic nerve function
1	Prednisolone, azathioprine	14	120	No	Right eye only
2	Prednisolone, cytosine arabinoside, cyclosporine	150	460	No	Right eye only
3	Prednisolone, cytosine arabinoside, azathioprine	14	1095	No	Left eye only
4	Prednisolone, cyclosporine	210	719	Yes	Complete (bilateral)

5	Prednisolone, cyclosporine	81	180	Yes	No
6	Prednisolone, cytosine arabinoside	74	2005	No	Left eye only
7	Prednisolone, cytosine arabinoside	1095	1095	No	No
8	Prednisolone, cytosine arabinoside	150	365	No	Right eye only
9	Prednisolone, cytosine arabinoside	90	90	No	Right eye only
10	Prednisolone	3	210	Yes	Complete (bilateral)
11	Prednisolone, cyclosporine, azathioprine	7	1550	No	Left eye only
12	Prednisolone, cytosine arabinoside, azathioprine	21	561	No	Complete (bilateral)
13	Prednisolone, cytarabine arabinoside, cyclosporine	60	60	No	No
14	Prednisolone	7	425	No	Left eye only
15	Prednisolone	0	70	No	Complete (bilateral)
16	Prednisolone	14	365	No	Complete (bilateral)
17	Prednisolone	7	51	No	No
18	Prednisolone	14	56	No	Complete (bilateral)
19	Prednisolone, cytosine arabinoside	20	180	Yes	Left eye only
20	Prednisolone	14	21	No	No
21	Prednisolone, cytosine arabinoside	54	210	No	No
22	Prednisolone, cytosine arabinoside, cyclosporine	35	300	No	No
23	Prednisolone, cytosine arabinoside	53	180	Yes	No

24	Prednisolone	0	2920	No	Complete (unilateral)
25	prednisolone	14	90	No	No
26	Prednisolone, cyclosporine	30	150	No	Complete (unilateral)
27	Prednisolone	44	545	No	Complete (unilateral)
28	Prednisolone, cyclosporine	21	810	No	No
*_Length of treatment_ is determined from the start of immunosuppressive treatment to the termination of treatment due to veterinarian advice, the end of the study period or the point at which the dog is lost follow-up					

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Table 5. Drug combination and recovery of vision in at least one affected eye (n = 28 dogs).

Treatment	Number dogs treated (%)	Recovery vision (%)
PRED (%) only	9/28 (32)	6/9 (67)
PRED + CYT (%)	7/28 (25)	5/7 (71) P = 1
PRED + CYCL (%)	4/28 (14)	2/4 (50) P = 0.371
PRED + AZA (%)	1/28 (4)	1/1 (100) P = 0.273
PRED + CYT + CYCL (%)	3/28 (11)	1/3 (33)
PRED + CYT + AZA (%)	2/28 (7)	2/2 (100)
PRED + CYCL + AZA (%)	2/28 (7)	1/2 (50)
PRED prednisolone, CYT Cytosine arabinoside, CYCL Cyclosporine, AZA Azathioprine		

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