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Case Report
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Ischemic Optic Neuropathy in a Dog with Acute Bilateral Blindness and Primary Systemic Hypertension

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A 6-year-old neutered female Jack Russell terrier was investigated for sudden onset prechiasmatic bilateral blindness, left circling, reduced proprioception in the right pelvic limb and right facial allodynia. Electroretinography was normal. Magnetic resonance imaging (MRI) examination revealed that the right optic nerve and the optic chiasm were hyperintense on diffusion weighted imaging and hypointense on apparent diffusion coefficient map consistent with ischemic optic neuropathy. A concurrent lacunar infarct was detected in the left rostral colliculus. Primary systemic hypertension was diagnosed based on blood pressure measurement and no detectable abnormalities on hematology, comprehensive serum biochemistry, urinalysis including protein/creatinine and cortisol/creatinine ratios and thoracic/abdominal imaging. Prednisolone for 10 days and amlodipine long-term were administered. Vision was not recovered after 7 months. Repeat MRI supported the diagnosis of ischemic lesions and revealed a recent striatocapsular infarct. Ischemic optic neuropathy is a well-recognized cause of blindness in humans and should be included as a differential diagnosis for acute prechiasmatic blindness in dogs.

Key words: Infarct; Ophthalmic artery; Optic nerve; Optic neuritis.

Case Description

A 6-year-old neutered female Jack Russell terrier presented to the ophthalmology and neurology departments of the Animal Health Trust for investigation of sudden onset bilateral blindness 48 hours before referral. The dog was reported to be playing completely normally when she suddenly became at first unable to follow objects particularly coming from the right and then bilaterally blind within 24 hours. At presentation, no abnormalities were detected at general examination. Neurologic and ophthalmologic examination revealed obtunded mental status, compulsive circling to the left, decreased proprioception in the right pelvic limb, allodynia of the right side of the head and mydriasis, absent menace response, vision, dazzle, and pupillary light reflexes bilaterally. No abnormalities were detected at funduscopic examination. Neurologic localization was multifocal affecting retinae, optic chiasm or optic tracts bilaterally, and the left forebrain. Considering the acute and progressive nature of the clinical signs and the multifocal localization, an inflammatory/infectious disease was deemed the most likely differential diagnosis. Vascular accidents and middle fossa neoplasia extending to the optic chiasm were also considered. Hematology and serum biochemistry were unremarkable. Electroretinography revealed normal mixed rod/cone response bilaterally. High-field magnetic resonance imaging (MRI)[a] of the head revealed a focal, well-defined intra-axial lesion in the left rostral colliculus causing no mass effect. The lesion was hyperintense on T2-weighted and fluid-attenuated inversion recovery sequences and isointense in T1-weighted and gradient echo (GRE) sequences compared to normal gray matter. No contrast enhancement was evident.[b] The affected area was hyperintense on diffusion weighted imaging (DWI) and hypointense on the apparent diffusion coefficient (ADC) map, compatible with an ischemic infarct. Hyperintense signal on DWI and hypointense signal on the ADC map were also detected in the right optic nerve extending to the optic chiasm, compatible with ischemic optic neuropathy (ION) and chiasmal infarction (Fig 1). On transverse postcontrast 3D spoiled gradient echo (3D SPGR) sequences of the orbits, the right optic nerve appeared much more defined from the surrounding mildly enhancing retrobulbar tissues compared to the left optic nerve (Fig 2). No abnormalities were detected at cerebrospinal fluid analysis. Urine analysis, including protein to creatinine and cortisol to creatinine ratios, and serum thyroxine,

Abbreviation:

ADC	apparent diffusion coefficient
DWI	diffusion weighted imaging
GCA	giant cell arteritis
IOA	internal ophthalmic artery
ION	ischemic optic neuropathy
MRI	magnetic resonance imaging

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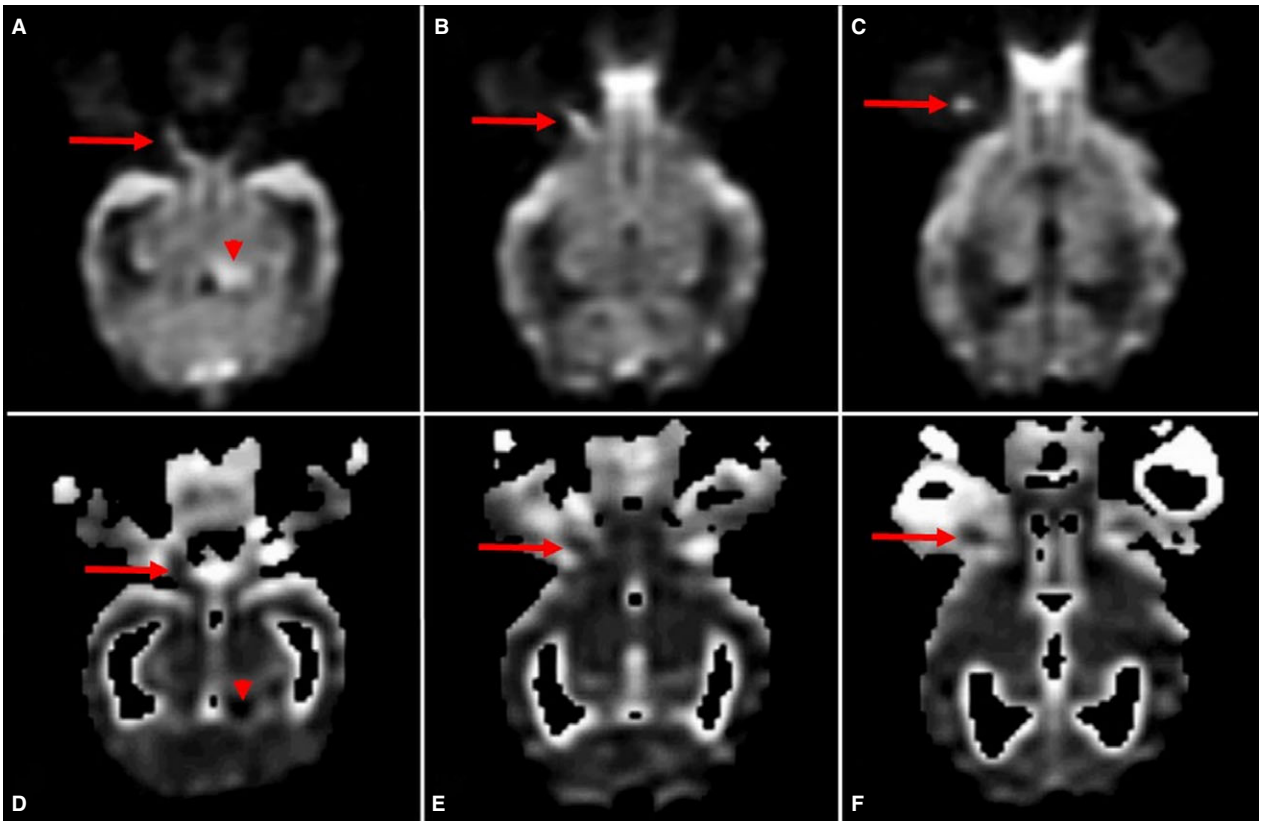

Fig 1. **A, B, C**: DWI of the brain. The arrows show the hyperintense signal of the right optic nerve from the chiasm (**A**) rostrally (**B**, **C**); the arrowheads indicate the mesencephalic infarct. **D, E, F**: ADC map of the brain at the same levels, showing the hypointense signal of the affected structures.

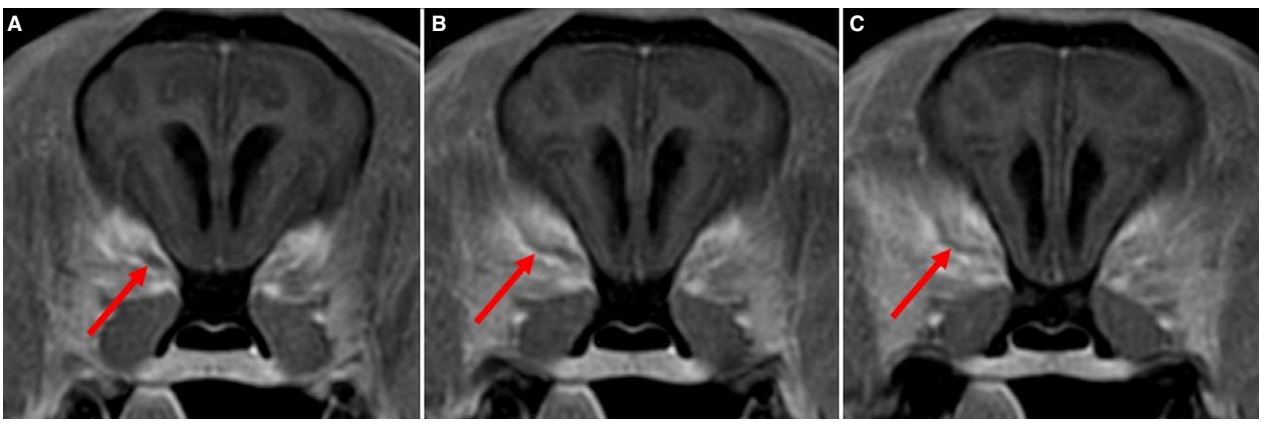

Fig 2. Transverse postcontrast 3D SPGR fat suppressed images of the brain at the level of the orbits from caudal (**A**) to rostral (**B, C**) showing the hypointense right optic nerve (arrows).

free thyroxine, and thyroid-stimulating hormone were within normal limits. Thoracic and abdominal radiography and abdominal ultrasound did not reveal any abnormality. Serology for *Toxoplasma gondii* and *Neospora caninum* was negative. As an underlying vasculitis causing the multiple ischemic infarcts could not be excluded, the dog was administered prednisolone[c] (1 mg/kg q12h per os). In the first 24 hours of hospitalization, serial oscillometric blood pressure measurements revealed an average of 183/79 (mean 110) mmHg. Amlodipine[d] (0.12 mg/kg q12h per os) was administered and continued long-term. After detection of primary systemic hypertension as the most likely underlying cause of the multiple ischemic infarcts, prednisolone dosage was tapered and stopped over 10 days. All neurologic deficits resolved within 2 days, with the exception of pupil size, pupillary light reflexes, and vision which were not recovered after 6 weeks. At that stage, blood pressure measurements returned to normal limits. A repeat MRI was initially declined by the

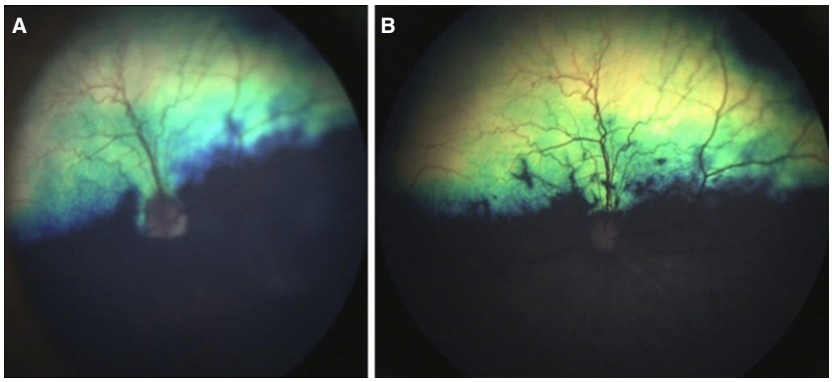

Fig 3. **A**: Funduscopy of the right eye at initial examination revealing no abnormalities. **B**: Funduscopy of the right eye at 7 months showing optic nerve head atrophy, attenuated retinal vessels, moderate diffuse tapetal hyper-reflectivity, and multifocal to mildly diffuse nontapetal hypopigmented lesions.

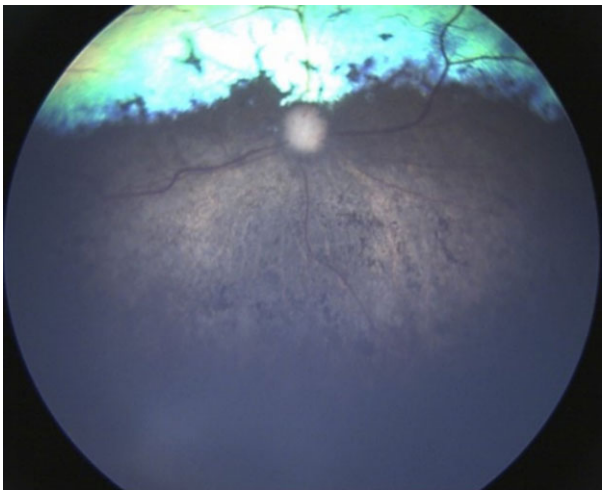

Fig 4. Funduscopy of the right eye at 7 months. Detail of the multifocal to mildly diffuse nontapetal hypopigmented lesions.

owner. At monthly telephone follow-ups, the owner reported the dog had a good quality of life despite no obvious signs of vision recovery. Monthly blood pressure measurements remained within normal limits. The dog was presented again for a repeat clinical examination after 7 months. Neurologic examination still revealed bilateral blindness, mydriasis, absent menace responses, and pupillary light reflexes. At that stage, funduscopy revealed moderate optic nerve head atrophy, attenuation of retinal vessels, subtle tapetal hyper-reflectivity, and multifocal to mildly diffuse hypopigmented lesions in the nontapetal fundus in both eyes (Figs 3 and 4). Bilateral vitreal degeneration was also detected. The electroretinogram was unchanged. A repeat MRI was performed revealing no evidence of a progressive lesion affecting the optic nerves. On DWI, the right optic nerve and the area of the previously detected mesencephalic infarct appeared hypointense, compatible with MRI signal evolution of ischemic infarcts. A new lesion compatible with a recent striatocapsular infarct was detected in the right internal capsule. Considering the presence of a further cerebral infarct, C-reactive protein was tested as an inflammatory serum marker for possible vasculitis and was within normal limits. Retrospectively, the owner reported an episode of sudden disorientation 1 week before presentation when the dog was very stressed by loud fireworks. No changes in the clinical signs or blood pressure abnormalities were detected over 5 months after the second MRI.

Herein, we reported a case of ION associated with primary systemic hypertension and concurrent cerebral infarcts in a dog with acute bilateral blindness. In this case, DWI and ADC map MRI sequences were essential to reach the diagnosis.

Ischemic optic neuropathy is a well-recognized differential diagnosis for acute blindness in humans.[1,2] Two forms are described, namely anterior and posterior ION according to the affected part of the optic nerve, with the former being the most common.[1–3] Anterior ION is characterized by ischemia of the optic nerve head which is almost entirely supplied by the caudal ciliary artery circulation.[4] At funduscopy, edema of the optic disk and frequently also peripapillary hemorrhages are detected.[1,2] Posterior ION instead is caused by occlusion of pial branches of the ophthalmic artery,[1] which is equivalent to the internal ophthalmic artery (IOA) in dogs.[5] In posterior ION, no changes are normally detected at funduscopy at presentation.[6] The IOA in dogs is a small (<0.5 mm diameter) paired artery arising from the rostral cerebral arteries and running on the dorsal aspect of the optic nerve, where it anastomoses with the external ophthalmic artery coming from the maxillary artery.[5] The blood supply to the optic chiasm in dogs is provided by small arteries arising from the rostral intercarotid artery.[5] The limit between the territories supplied by the IOA and the chiasmatic branches of the rostral intercarotid artery is unclear. In this dog, the entire caudal part of the right optic nerve and the right side of the optic chiasm appeared affected on DWI sequences and ADC map, compatible with an ischemic infarct of the territory supplied by the right IOA and possibly also of the chiasmatic branches of the rostral intercarotid artery. Considering the MRI findings and the negative funduscopy, a diagnosis of

posterior (caudal) ION was provided. The detected concurrent infarct in the left rostral colliculus supported the presence of an underlying disease as the cause of multifocal vascular accidents. In dogs with cerebral ischemic infarcts, an underlying disease has been reported to be recognized in 55% of cases.[7] In these dogs, systemic hypertension was commonly detected although always secondary to an underlying cause such as chronic kidney disease and hyperadrenocorticism.[7]

In humans, both anterior and posterior ION are divided into arteritic and nonarteritic forms, depending on whether the cause is a primary vascular disease (mainly giant cell arteritis—GCA) or not.[1,2] Nonarteritic forms are reported to be the most frequent,[1,2,6] and hypertension is one of the most commonly associated underlying diseases.[3,8–10] As GCA is considered an ophthalmologic emergency in humans, ruling out this disease is mandatory in the diagnostic approach to these patients.[2,11] A final diagnosis of GCA in humans can be obtained with a biopsy of the temporal artery which was not performed in our case. Erythrocyte sedimentation rate and C-reactive protein can be used to support a diagnosis of GCA in humans, with a specificity of 97% when combined together.[12] C-reactive protein is more sensitive than erythrocyte sedimentation rate in diagnosing GCA, with a sensitivity of 86.7 and 100% in 2 different studies.[12,13] Contrast-enhanced MRI of the superficial cranial arteries can also be used to support a diagnosis of GCA in humans, with sensitivity and specificity of 88.7 and 75%, respectively.[14,15] In the dog described in this report, C-reactive protein was within normal limits, which could suggest that an underlying arteritis compatible with GCA would be less likely. Also, although occult forms (ie, without systemic signs) are reported in 21.2% of cases in humans, systemic signs are frequently described in GCA, which were not recognized in this dog.[16,17] Furthermore, the absence of progression/relapse of the clinical signs without treatment over 1-year follow-up in this case would not be typical of a vasculitis. In a study on primary and secondary vasculitis in dogs, all the 6 dogs with the central nervous system affected died or were euthanized while hospitalized due to poor response to treatment.[18]

Compared to the general population, people with hypertension and nonarteritic ION are more likely to develop cerebrovascular accidents.[8] In this dog, the presence of a concurrent mesencephalic infarct has helped guiding us toward the correct diagnosis, as in its absence, it is likely that DWI and ADC map sequences would have not been performed, and optic neuritis would have been suspected. Indeed, a normal appearance of the optic nerves is reported in dogs with optic neuritis[19] and ION had never been previously described in dogs. Serial blood pressure measurements are also not part of a standard diagnostic protocol in dogs with optic neuritis, and in the absence of the mesencephalic ischemic infarct, systemic hypertension could have been missed in this case. Differentiating between ION and optic neuritis is occasionally challenging also in human medicine, where signalment, history, clinical signs, specific visual field deficits, and funduscopic and MRI findings can help in differentiating between these conditions.[1,20,21] In a retrospective study, which included 366 patients with vision loss, 223 patients were diagnosed with optic neuritis and 143 with ION, supporting the high prevalence of this disease.[21] Initial funduscopic examination in our case did not reveal significant findings, which is compatible with what is reported in human posterior ION. Indeed, in human posterior ION no funduscopic changes are seen until 6–8 weeks after the injury when the optic nerve head may appear paler as a consequence of descending optic nerve atrophy.[6] At the 7 month follow-up, optic nerve head atrophy was detected also in our case, together with signs of mild retinal atrophy and vitreal degeneration. In our opinion, these further signs could have also been secondary to ION; however, even if considered less likely, other causes could not be fully excluded. In 64 humans with ION or optic neuritis, the MRI signal of the affected optic nerves has been reported to be abnormal in 5/32 and 31/32 cases, respectively.[20] However, the MRI studies did not include DWI or ADC map sequences. The use of DWI and ADC sequences is reported in humans with ION and can be extremely helpful in reaching the diagnosis.[22–25] As other lesions (eg, lymphoma) can also appear hyperintense on DWI, and considering the lack of recovery of vision in our patient, a neoplastic process affecting the optic nerves was not excluded until the recheck MRI was performed.[26] However, in the second MRI, the signal intensity of the affected areas had changed to hypointense in DWI and iso-hyperintense in ADC sequences, as typically described with ischemic infarcts.[27]

Prognosis for vision improvement in humans with nonarteritic ION is guarded although some spontaneous improvement has been reported.[3,6] Aggressive systemic corticosteroids treatment in nonarteritic ION was found to increase the chances of vision improvement in treated compared to untreated patients;[6,9] however, only one of these patients was clearly described to have vision loss with no light perception and that patient did not improve on corticosteroids treatment.[6] On the other hand, in arteritic ION the rapid use of systemic corticosteroids is strictly mandatory to prevent complete vision loss in patients that are still partially visual at presentation, but improvement of visual acuity remains rare (4%).[28] Although a longer and more aggressive course of corticosteroids could have been attempted in our patient, considering the bilateral blindness at presentation, the likelihood of vision recovery was deemed very low.

Footnotes

[a] Signa EchoSpeed 1.5T MRI, GE Healthcare, Milwaukee, WI
[b] Gadovist–gadobutrol, Bayer Pharma AG, Berlin, Germany
[c] Prednicare, Animalcare Ltd, York, UK
[d] Amodip, Ceva Animal Health Ltd, Amersham, UK

Acknowledgment

Conflict of Interest Declaration: Authors declare no conflict of interest.

Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

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