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CASE REPORT

Suspected bacterial ventriculitis in a nine-month-old Goldendoodle

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Bacterial ventriculitis is an uncommon, often fatal complication of intracranial bacterial infection. This case report describes a nine-month-old spayed female Goldendoodle that presented with a history of acute onset generalised seizures. The initial clinical examination, neurological examination and minimum database laboratory tests were unremarkable, and the dog was diagnosed with probable idiopathic epilepsy. Three weeks thereafter, the patient developed breakthrough clustering orofacial and generalised seizures. Magnetic resonance imaging (MRI) findings were consistent with bacterial ventriculitis. Broad-spectrum antibiotic and supportive therapy was initiated pending cerebrospinal fluid (CSF) analysis, serology and bacterial culture; however, the patient died eight hours after initiating treatment. To our knowledge, this is the first case report of suspected bacterial ventriculitis in a dog in South Africa and describes its atypical clinical presentation, progression and unique MRI findings.

Keywords: bacterial ventriculitis, seizures, idiopathic epilepsy, magnetic resonance imaging, dog

Introduction

Bacterial infection of the central nervous system (CNS) is rare in dogs. Only 7–13% of reported infectious and inflammatory CNS disease cases had a bacterial origin, with 4.3–6.8% having an intracranial location (Tipold 1995; Gonçalves et al. 2022). Intracranial bacterial infection may arise secondary to haematogenous spread, local extension from otitis media/interna, foreign body migration or traumatic/iatrogenic inoculation (Radaelli & Platt 2002). Commonly isolated bacteria include *Escherichia coli*, *Streptococcus*, *Staphylococcus* and *Klebsiella* (Rawson et al. 2023; Tipold 1995). Ventriculitis is an uncommon, poorly defined, often fatal, complication of intracranial infection (Agrawal et al. 2008). Literature describing ventriculitis in dogs is limited to case reports (Dennis et al. 2005; Harvey et al. 2021; Headley et al. 2017; Saito et al. 2002; Wu & Chang 2015). This report describes the presentation, clinical progression and magnetic resonance imaging (MRI) findings of a dog with suspected bacterial ventriculitis.

Patient presentation

A nine-month-old, 28.5 kg, spayed female Goldendoodle presented for the investigation of three acute onset generalised seizures in the preceding week with normal interictal behaviour. Phenobarbitone (2.7 mg/kg PO q12h, Sedabarb 30 mg, Ranbaxy Pharmaceuticals LTD) was initiated prior to initial presentation. There was no history of trauma or toxin exposure. Vaccinations, deworming and parasiticide therapy were current.

The physical and neurological examinations were unremarkable. Haematology, urinalysis and serum biochemistry (Table I) were unremarkable. Post-prandial bile acid concentration was mildly elevated (Table I), but too mild to support overt hepatic insufficiency, and therefore rendering hepatic encephalopathy

Table I: Complete blood count and serum biochemistry results

Complete blood count [a]				Serum biochemistry [b]			
Test	**Result**	**Units**	**Reference range**	**Test**	**Result**	**Unit**	**Reference range**
Red cell count	5.3	$x10^{12}$/L	5.5–8.5	**Glucose**	6.1	mmol/L	3.89–7.95
Haemoglobin	13.3	g/dL	12.0–18.0	**Total serum protein**	54	g/L	50–67
PCV	37.9	%	37.0–55.0	**Albumin**	30.1	g/L	25–35
MCV	72.1	fL	60.0–75.0	**Globulins**	23.9	g/L	25–35
MCHC	35.1	g/dL	33.7–39.1	**Alanine aminotransferase**	42	U/L	10–60
Reticulocyte count	38.4	$x10^9$/L	0–80.0	**Alkaline phosphatase**	136	U/L	0–200
White cell count	7.2	$x10^9$/L	6.0–15.0	**Urea**	6.7	mmol/L	3.6–8.9
Segmented neutrophils	3.9	$x10^9$/L	3.0–11.5	**Creatinine**	72	µmol/L	20–110
Band neutrophils	0.0	$x10^9$/L	0.0–0.3	**Phosphate**	2.1	mmol/L	0.5–2.6
Lymphocytes	2.68	$x10^9$/L	1.0–4.8	**Sodium**	146	mmol/L	135–155
Monocytes	0.51	$x10^9$/L	1.0–1.4	**Potassium**	4.8	mmol/L	3.8–5.8
Eosinophils	0.14	$x10^9$/L	0.1–1.2	**Chloride**	112	mmol/L	107–113
Basophils	0.0	$x10^9$/L	0–0.1	**Pre-prandial bile acids**	1	µmol/L	0–15
Platelet count	275	$x10^9$/L	200–500	**Post-prandial bile acids**	16	µmol/L	0–15

[a] Sysmex XT 2000i, Sysmex
[b] Indiko Clinical Chemistry Analyzer, Thermo Fisher Scientific

unlikely as the cause of the seizures. Phenobarbitone concentration was within therapeutic range. The patient was moderately hypertensive (systolic pressure 174 mm Hg) which was likely situational given the scarcity of idiopathic hypertension and the low likelihood of secondary hypertension given the patient signalment and unremarkable clinical examination, urinalysis, haematology and serum biochemistry. The patient was diagnosed with probable idiopathic epilepsy based on previously defined criteria (De Risio et al. 2015).

Management and outcome

Phenobarbitone treatment was continued. Levetiracetam (20 mg/kg PO q8h until seizure-free for 24 hours, Keppra 100 mg/ml, GlaxoSmithKline South Africa LTD) pulse therapy was added pending phenobarbitone concentration testing. Midazolam (0.2 mg/kg IN, Dormicum 15 mg/3 ml, Roche) was dispensed for emergency application during seizures. Follow-up blood pressure measurement was recommended for two weeks later. MRI of the head and CSF analysis was advised should the patient suffer status epilepticus, cluster seizures or develop interictal neurological abnormalities.

Three weeks hereafter, the patient presented to an emergency service due to clustering orofacial and recurrent generalised seizures. Seizure activity persisted despite an increase in phenobarbitone dosage (3.8 mg/kg PO q12h total dose). Potassium bromide (600 mg/kg PO administered over five days; thereafter continuing with 30 mg/kg PO q24h; Potassium bromide 300 mg/ml, Kyron Prescriptions LTD) was initiated as a third anti-epileptic drug (AED). Progressive sedation was noted from day three of bromide therapy and the patient became stuporous from day six of bromide therapy, one day prior to re-admission. No further seizures were noted.

Upon re-admission, follow-up blood pressure measurement was unremarkable (systolic pressure 120 mm Hg). Follow-up neurological examination showed the patient to be recumbent and stuporous with bilateral pelvic limb hyperreflexia and normal thoracic limb spinal reflexes. Neurolocalisation was consistent with a forebrain lesion and, given the patient's signalment and rapid progression of clinical signs, an infectious cause was prioritised.

The dog was premedicated with butorphanol (0.2 mg/kg IV, Dolorex 10 mg/ml, MSD Animal Health) and diazepam (0.2 mg/kg IV, Valium 10 mg/2 ml, Pharmaco Distribution LTD), induced with propofol (1 mg/kg IV per bolus, Propoven 1%, Fresenius Kabi, South Africa) to effect and placed in dorsal recumbency for MRI of the head using a 1.5 Tesla scanner (Optima™ MR450w, GE Medical Systems). The study consisted of T2-weighted images in the sagittal and transverse planes, T2* images in the transverse plane, pre- and post-contrast T1-weighted SPGR images in the transverse plane with reconstructions in the dorsal and sagittal planes, a FLAIR sequence in the dorsal plane, and dorsal plane DWI and ADC maps. Post-contrast imaging was performed immediately after injection (0.2 mmol/kg of 0.5 mmol/ml gadopentetate dimeglumine, Magnevist, Bayer LTD). All images were obtained at 3 mm slice thickness, except the SPGR images which were at 1.2 mm. There was severe ring-like ependymal

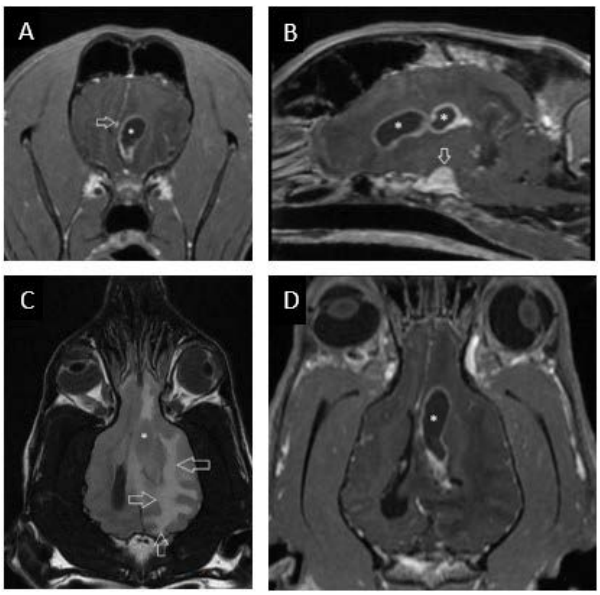

Figure 1: A. Transverse, B. Left parasagittal, C. Dorsal FLAIR, Dorsal SPGR post-contrast images of the brain. The asterisks indicate the left ventricular lumen, with peripheral contrast uptake of the ependymal layer [A, B and D]. The lack of suppression can be visualised on the FLAIR image [C]. The arrow [A] indicates the midline shift of the falx cerebri due to mass effect, the meningeal contrast uptake within the left cavernous sinus [B] and the severe perilesional FLAIR hyperintensity [C] consistent with white matter oedema.

contrast enhancement of the left ventricle, which contained non-enhancing T2-weighted hyperintense, T1 weighted hypointense but hyperintense to normal CSF, FLAIR non-suppressing material indicative of cellular or proteinaceous content. Some of the material in the middle of the ventricle was more rounded and T2W hypointense and T1W isointense, but non-enhancing. The rostral horn of the left ventricle was rounded, dilated and extended in a rostral direction, creating obvious ventricular asymmetry. This region was focally hyperintense on DWI and hypointense on the ADC map, consistent with restricted diffusion. There was asymmetrical plaque-like meningeal contrast uptake of the left cavernous sinus. A few small T1W, T2W and T2* weighted hypointense non-enhancing regions, were present within the cavernous sinus, most likely representing haemoglobin degradation products. There was severe white matter FLAIR hyperintensity surrounding the left lateral ventricle, affecting the entire left cerebral hemispheral corona radiata, consistent with perilesional oedema and resulting in severe mass effect, including compression and distortion of the left thalamus, mild subfalcine and infratentorial herniation, and marked midline shift to the right. There was mild segmental but extensive meningeal contrast uptake, affecting both lepto- and pachymeninges. The extracranial structures such as the caudal nasal passages, nasopharynx/nasopharyngeal meatus, orbits and ears were normal, without close proximity to the above pathology.

These findings indicated severe unilateral (left lateral) ventriculitis and meningitis, especially of the left cavernous sinus, and severe perilesional oedema resulting in marked mass effect. The most likely differential diagnosis for the lesion was infectious but with an origin not demonstrated (no otogenic spread, no cranial defect, no nasal spread/cribriform penetration noted). Non-

Table II: Cerebrospinal fluid analysis

Test	Result	Unit	Comments
Total protein [a]	2.72	g/L	
Total nucleated cell count [b]	2128	cells/µL	77% non-degenerate neutrophils 10% small mononuclear cells 13% large mononuclear cells
Bacterial culture			
Aerobic [c]	No growth		
Anaerobic [d]	No growth		
Serology [e]			
Canine distemper virus	Weak positive		IgG IFA (1:10 single screening dilution)
Toxoplasma gondii	Negative		IgG IFA (1:10 single screening dilution)
Neospora caninum	Negative		IgG IFA (1:10 single screening dilution)
Ehrlichia canis	Negative		IgG IFA

[a] Pyrogallol red method, Indiko Clinical Chemistry Analyzer, Thermo Fisher Scientific.
[b] Modified Fuchs-Rosenthal counting chamber.
[c] Cultured aerobically on sheep blood tryptose agar, MacConkey agar without crystal violet and nutrient broth for 7 days.
[d] Cultured anaerobically on blood tryptose agar prepared with sheep blood for 7 days.
[e] Immunofluorescence antibody test.

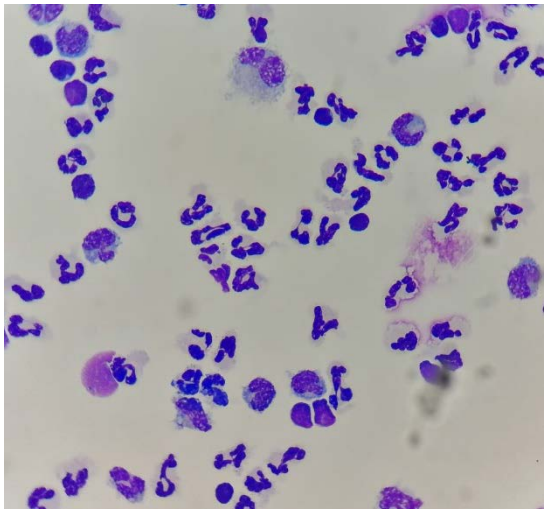

Figure 2: Light microscopy of the CSF. There is a severe neutrophilic pleocytosis.

infectious inflammatory disease, vascular disease, congenital causes, or neoplasia were considered inconsistent with the MRI changes.

A cerebellomedullary cistern cerebrospinal fluid (CSF) collection was performed the following day for cytology, serology and bacterial culture. Cytology indicated a severe neutrophilic pleocytosis (Table II) with no microorganisms seen. Given the MRI and preliminary CSF findings, a bacterial cause was considered most likely, and the patient was diagnosed with presumptive bacterial ventriculitis.

AED therapy was continued. Empirical broad-spectrum antibiotic therapy was initiated as amoxicillin-clavulanic acid (20 mg/kg IV q12h, Sandoz Co-amoxyclav 1.2 g, Sandoz SA LTD). Prednisolone (0.5 mg/kg IV q24h, Prednisolone 1%, V-Tech LTD) was administered to reduce secondary inflammation and oedema. The patient deteriorated to a comatose state. This was suspected to be due to increased intracranial pressure and mannitol (0.5 g/kg IV, Sabax Osmitrol 20% in Viaflex, Adcock Ingram Critical Care LTD) was administered over 20 minutes. Further appropriate nursing care was provided. The patient died 36 hours after admission.

CSF serology and culture results (Table II) were received post-mortem. The patient tested weakly positive for canine distemper virus (CDV) IgG. A necropsy was performed by the primary author 12 hours after death and samples submitted to a reference laboratory for histopathology and microbiological testing. Gross pathology revealed a moderate haemopurulent pleural effusion likely secondary to post-mortem autolysis. The visceral organs displayed varying degrees of post-mortem autolytic changes with no primary infectious focus evident on histopathology. The meningeal blood vessels appeared tortuous and congested. Transverse sectioning of the brain at the midpoint revealed a large, focally extensive area of periventricular tissue, which appeared dull grey in colour and sunken, surrounding the left lateral ventricle. This lesion resulted in marked midline shift to the right. Aerobic bacterial culture of the pleural effusion yielded a mixed growth of *Pseudomonas* spp., *Enterobacter* spp. and *Enterococcus* spp. Aerobic culture of brain parenchyma isolated *Neisseria animaloris*. Fungal and anaerobic bacterial culture yielded no growth. Histopathology of the brain revealed significant lesions were mostly confined to the periventricular tissues. There was also mild neuropil and meningeal capillary congestion. During processing of brain samples for histopathology, much of the macroscopic lesions were friable and disintegrated resulting in large cavitary lesions in the periventricular tissues, which made the ventricles appear abnormally large and distended. Representative sections could not be evaluated from these areas. The evaluated section of periventricular tissue indicated lymphoplasmacytic vascular wall infiltration and perivascular accumulation. Mild fibrin exudation was evident in few blood vessels lumens. In the surrounding neuropil, there were small focal areas of malacia and the areas of neuropil showed less intense staining with rarefaction. Small numbers of macrophages were seen in these affected tissues. Pathogens could not be demonstrated in Gram- or periodic acid-Schiff-stained sections of the tissues. Immunohistochemistry of the brain was negative for CDV.

Discussion

This case describes an unusual presentation of suspected intracranial bacterial infection in a dog. Previous reports of ventricle-associated bacterial infections in dogs were associated with *Actinomyces* spp. pyogranulomatous meningoencephalitis (Couto et al. 2000), *Enterococcus* spp. meningoencephalitis (Harvey et al. 2021), otogenic meningoencephalitis (Wu & Chang 2015), migrating foreign bodies (Dennis et al. 2005) and traumatic inoculation (Headley et al. 2017). In this patient, previously reported causes were excluded given patient history, MRI findings of the head and necropsy findings, and the origin of the infection remains unknown.

Generalised seizures were an uncommon presenting complaint in previous case reports of bacterial ventriculitis (Dennis et al. 2005; Harvey et al. 2021; Headley et al. 2017; Wu & Chang 2015). Seizures in this patient likely developed secondary to neuronal damage inflicted by bacterial toxins and the local inflammatory response in addition to increased intracranial pressure due to cerebral vasogenic oedema.

Literature describing MRI findings of bacterial ventriculitis in dogs is sparse. Characteristic findings in humans include ventricular debris, ependymal contrast enhancement, periventricular signal abnormalities and signs of meningitis (Fukui et al. 2001). In this dog, the most prominent findings were ependymal contrast enhancement, ventricular debris and periventricular signal abnormalities, which is similar to MRI findings in a dog diagnosed with cerebral ventriculitis associated with otogenic meningoencephalitis (Wu & Chang 2015). These characteristic MRI findings may prove useful in making a provisional diagnosis of ventriculitis, allowing earlier initiating of treatment pending CSF analysis.

Differential diagnoses for a severe neutrophilic pleocytosis include bacterial or fungal infection and steroid-responsive meningitis-arteritis (SRMA) (Chrisman 1992). Although not a common cause of seizures, there is a single case report of cerebral extension of SRMA in an intact male boxer with resultant seizures (Wrzosek et al. 2009); however, the histopathology was not consistent with SRMA in this patient.

Cytology and culture of the CSF fluid analysis in the case described here was unrewarding, as is often the case (Radaelli & Platt 2002; Rawson et al. 2023; Wu & Chang 2015). This may be due to low bacterial concentration; isolation of bacteria to the lesion and not in the CSF (Radaelli & Platt 2002) or antibiotic administration prior to sampling inhibiting bacterial isolation. The bacteria identified on post-mortem culture are common opportunistic bacteria and most likely represented post-mortem invaders.

Histopathology of the brain lesion was not characteristic for an intracranial bacterial infection in this patient. However, large portions of the macroscopic lesion were too friable for further processing, and it is therefore possible that lesions more characteristic of the underlying aetiology may have been missed due to the poor processing ability of these necrotic tissues.

Although the patient tested weak positive for CDV IgG on CSF evaluation, it is an unlikely cause of morbidity in this patient due to a complete vaccination history, lack of additional clinical signs associated with CDV infection, neutrophilic instead of mononuclear pleocytosis and negative immunohistochemistry. The presence of CDV antibodies was most likely due to contamination secondary to blood-brain barrier breakdown given the patient's vaccination history. Blood contamination may have further been supported by screening for CPV antigens, which typically are not present in CSF, but was not performed.

Optimal treatment for intracranial bacterial infection has not been established and should ideally be guided by culture and sensitivity testing. Amoxicillin-clavulanic acid is a common empirical agent (Rawson et al. 2023). A recent systematic review reported the best evidence for the use of enrofloxacin, benzylpenicillin or ampicillin (Hertzsch & Richter 2022). The use of corticosteroids remains controversial, however a recent systematic review reported fewer lasting neurological deficits without an elevated risk for adverse effects in human patients treated with short courses of anti-inflammatory doses of corticosteroids (Brouwer et al. 2010).

Conclusion

This case report describes the unusual presentation of a dog with suspected bacterial ventriculitis, which represented a unique category of intracranial infection. The available literature comprises case reports in which most of the dogs died or were euthanised and seizures were an uncommon presenting complaint in these reports. However, bacterial ventriculitis should be considered as a rare differential diagnosis for seizures in dogs. MRI findings consistent with ventriculitis can be used to make a provisional diagnosis of ventriculitis pending CSF analysis and may facilitate rapid initiation of treatment given the grave prognosis.

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Conflict of interest

The authors declare that they have no conflicts of interest that are directly or indirectly related to the research.

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Costs related to initial diagnostic testing and treatment were paid for by the dog's owner. Costs of the post-mortem examination, histopathology and bacterial culture were paid for by Panorama Veterinary Clinic and Specialist Centre.

Ethical approval

Ethics approval was obtained from the University of Pretoria, Faculty of Veterinary Science Research Ethics Committee (Ref: REC154-23).

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