Received: 11 June 2021 | Revised: 15 December 2021 | Accepted: 27 January 2022

DOI: 10.1002/vrc2.310

Vet Record CaseReports

CASE REPORT

Wildlife

Diagnosis and treatment of congenital hydrocephalus in a red fox (*Vulpes vulpes)* with seizures

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Abstract

A 2-year-old male red fox (*Vulpes vulpes*) was presented for generalised tonic-clonic seizures, blindness, compulsive circling and behavioural changes that occurred since the animal was 2 months old. Neurological examination indicated a diffuse forebrain lesion. On magnetic resonance imaging of the brain, a severe dilation of both lateral ventricles was identified. Congenital hydrocephalus was suspected and the fox was treated with methylprednisolone, omeprazole and phenobarbital. Sixteen months later, the neurological signs had improved: the frequency of seizures had decreased to one seizure every 3 months and compulsive circling was less pronounced.

KEYWORDS

MRI, red fox, seizures

BACKGROUND

Hydrocephalus can be divided into two major categories. In compensatory hydrocephalus, the increase in cerebrospinal fluid (CSF) volume is secondary to loss of brain parenchyma caused by a primary disease, such as in utero viral infections.[1] Obstructive hydrocephalus is an increase in the volume of CSF caused by obstruction of flow or decreased absorption of CSF. This can be due to a malformation (developmental obstructive hydrocephalus or congenital hydrocephalus), or it can be caused by acquired conditions that disrupt normal CSF flow, mainly inflammatory and neoplastic diseases.[1]

Congenital hydrocephalus is most commonly caused by stenosis of the mesencephalic aqueduct associated with fusion of the rostral colliculi. Other causes such as presence of immotile ependymal cilia or malformation of the arachnoid villi are less frequent.[1] Clinical signs in dogs and cats are usually present at birth, although they might appear during the first months of life. The most common neurological signs usually reflect forebrain dysfunction and include behavioural changes, blindness, circling, altered mental status and seizures.[2]

The gold standard for the diagnosis of hydrocephalus is magnetic resonance imaging (MRI).[3] MRI findings allow differentiating hydrocephalus from incidental ventriculomegaly. The main MRI findings include a ventricle/brain index >0.6, elevation of the corpus callosum, dorsoventral flattening of the interthalamic adhesion, periventricular oedema, dilation of the olfactory recesses, thinning of the cortical sulci and/or subarachnoid space and disruption of the internal capsule adjacent to the caudate nucleus.[4]

Congenital hydrocephalus can be treated medically with drugs that decrease CSF production, such as furosemide, acetazolamide, omeprazole and/or prednisone. Surgical treatment consists of placement of a ventriculoperitoneal shunt (VPS).[2]

To the authors' knowledge, congenital hydrocephalus diagnosed by MRI and causing seizures has not been reported in foxes. The purpose of this case report is to describe the neurological signs, MRI findings, treatment and outcome in a fox with congenital hydrocephalus.

CASE PRESENTATION

A 2-year-old male red fox (*Vulpes vulpes*) was presented for generalised tonic-clonic seizures (GTCS) that lasted 1 minute and occurred every 10 days. The owner reported constant blindness and behavioural changes that included compulsive circling. Clinical signs had been present since the animal was 2 months old, when it was rescued by the owners. Physical examination was unremarkable, with normal head shape and no open fontanelles palpable.

On neurological examination, the animal was obtunded, disoriented and walked in circles to the right side. Paresis was not observed, but postural reactions were delayed in all four limbs. Cranial nerve examination revealed absent vision and menace response bilaterally with normal pupillary

light reflexes, and absent response to stimulation of the nasal mucosa on both sides. A diffuse forebrain lesion was suspected, and the main differential diagnoses included anomaly, metabolic disease, cranioencephalic trauma (old) and inflammatory/infectious diseases.

INVESTIGATIONS

Complete blood cell count (CBC) and serum biochemistry showed a mild neutrophilic leukocytosis (white blood cell count 15.1×10^9/L; reference range: 2.5×10^9 to 11.2×10^9/L) and segmented neutrophilia (14.2×10^9/L; reference range: 0.55×10^9 to 7.31×10^9/L), which were attributed to an ulcerative dermatitis in the left forelimb. Serum biochemistry showed elevated creatine kinase (CK 2851.2 UI/L; reference range: 37–891 UI/L), which could be caused by the tonic-clonic seizure suffered before hospital admission. Thoracic radiographs were performed to as a part of the preanaesthetic protocol to assess lung parenchyma and cardiac silhouette. Results were unremarkable.

MRI was performed with a 0.4 T unit (Hitachi, Aperto Lucent). Dorsal, transverse and sagittal plane T2-weighted images (T2W; TR = 5832 ms, TE = 100 ms), transverse fluid-attenuated inversion recovery (T2-FLAIR; TR = 10,396 ms, TE = 90 ms, TI = 1800 ms) and transverse and sagittal T1-weighted images (T1W; TR = 757 ms, TE = 13 ms) before and after intravenous administration of paramagnetic contrast media (gadopentetate dimeglumine, 0.1 mmol/kg bodyweight [Magnevist; Bayer, Spain]) were obtained.

MRI revealed severe dilation of both lateral ventricles in all the segments (rostral and temporal horns and central portions), absence of septum pellucidum, and irregular edges and thinning of the cerebral cortex, as well as dilation of the left olfactory recess. The severe ventricular enlargement caused elevation of the corpus callosum, bilateral disruption of the internal capsule between the lentiform and caudate nuclei and dorsoventral flattening of the interthalamic adhesion. In the left frontal lobe, there was a poorly defined lesion of finger-like appearance that communicated with the left lateral ventricle. This lesion was isointense to CSF on T2W, hypointense on T1W and showed suppression of fluid signal on T2-FLAIR images. No contrast enhancement (CE) was observed on T1W images after contrast administration. MRI findings were consistent with congenital hydrocephalus and a left frontal porencephaly (Figure 1). Analysis of the CSF collected from the cerebellomedullary cistern showed no abnormalities.

DIFFERENTIAL DIAGNOSIS

Considering the young age of the fox and the nonprogressive nature of the neurological signs, our main differential diagnosis was congenital hydrocephalus. Acquired hydrocephalus secondary to inflammatory or infectious diseases or neoplasm was also considered. However, the nonprogressive course of the signs and the unremarkable CSF analysis made inflammatory or infectious diseases unlikely. Neoplasia was excluded after MRI.

LEARNING POINTS/TAKE-HOME MESSAGES

- Congenital hydrocephalus should be considered as a differential diagnosis in young foxes with diffuse forebrain neurological signs.
- Medical management of congenital hydrocephalus with methylprednisolone and omeprazole was associated with clinical improvement in this case.
- Despite lack of a therapeutic range for serum phenobarbital concentration in foxes, in this case, a good response to treatment with phenobarbital was achieved when serum phenobarbital concentration reached therapeutic range for dogs.
- Pharmacokinetic studies to determine the serum phenobarbital therapeutic range could be important to manage epilepsy in foxes.

TREATMENT

The fox was discharged on an anti-inflammatory dose of methylprednisolone (Urbason 4 mg; Sanofi, Spain) (0.5 mg/kg PO every 24 hours), omeprazole (Omeprazol 10 mg; Normon, Spain) (1 mg/kg PO every 24 hours) and phenobarbital (Luminaletas 15 mg; Kern Pharma, Spain) (2 mg/kg PO every 12 hours). On recheck examination 3 weeks after, the methylprednisolone dose was tapered (0.5 mg/kg PO every 48 hours) and omeprazole was stopped. On the 3-month recheck, the methylprednisolone dose was recommended to be tapered to 0.25 mg/kg every 48 hours, but the owners refused to do it. On the 16-month recheck, the fox was on the same methylprednisolone dose (0.5 mg/kg PO every 48 hours), phenobarbital (5.6 mg/kg PO every 12 hours) and S-adenosylmethionine, silybin, vitamin E and selenium (Hepatosil 100/10; Pharmadiet, Spain) (one tablet PO every 24 hours) were added because hepatic enzymes were increased on serum biochemistry (ALKP 267.7 UI/L; reference range: 20–156 UI/L; ALT 302.2 UI/L; reference range: 39–102 UI/L). A bile acid assay was recommended, but the owners refused.

OUTCOME AND FOLLOW-UP

On recheck examination 3 weeks after discharge, the neurological signs had improved: mental status was alert and the compulsive circling was less pronounced. The absent postural reactions, blindness, loss of bilateral menace response and absent response to stimulation of the nasal mucosa on both sides remained unchanged for the 16-month follow-up period. The intensity of seizures also improved: the fox experienced only focal seizures (facial twitching) and no more GTCS. However, the frequency of seizures was unchanged. Phenobarbital serum concentration (9.1 mg/L) was below the normal therapeutic range in dogs (15–40 mg/L), thus the phenobarbital dosage was increased to 5.6 mg/kg PO every 12 hours. Phenobarbital serum concentration was then checked 3 weeks later and it had increased to 20.8 mg/L. Seizure frequency had also decreased to one every month and the duration and

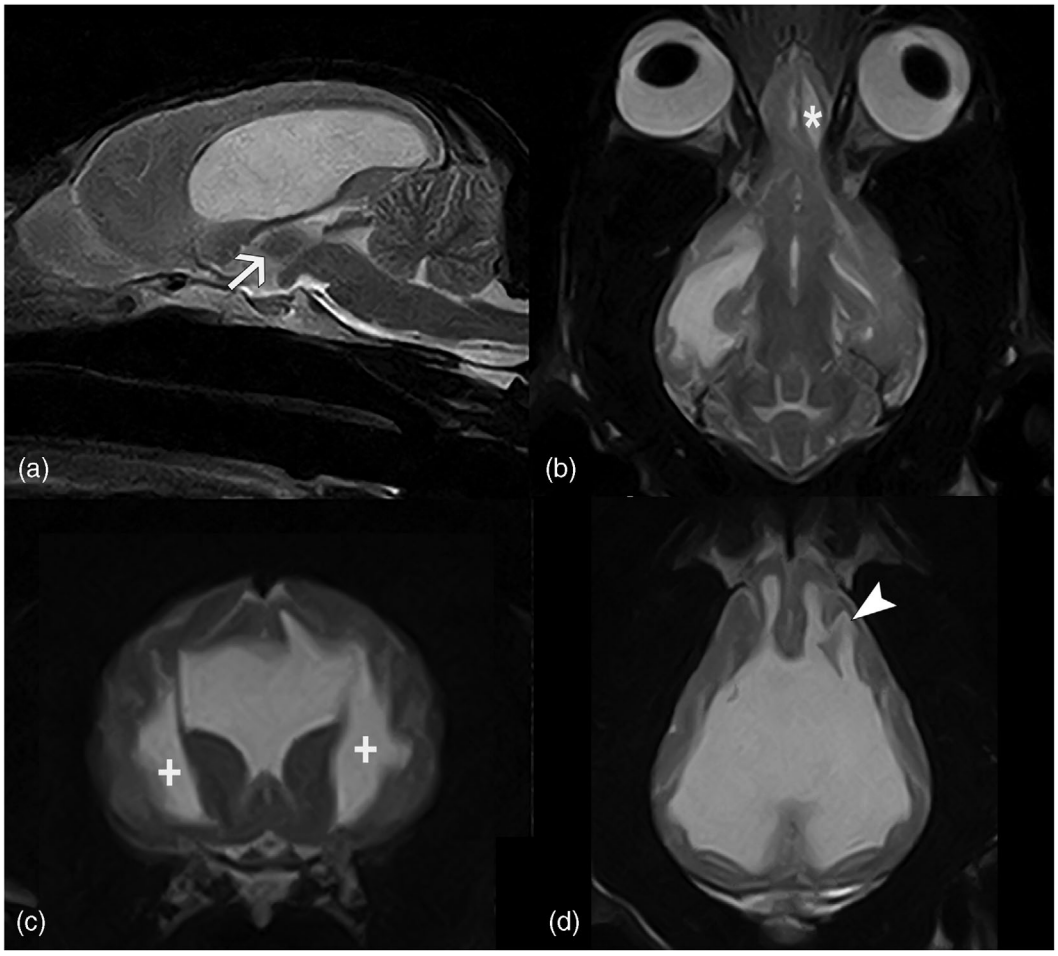

FIGURE 1 Magnetic resonance images of the brain of the red fox (*Vulpes vulpes*). Midsagittal T2-weighted (a) image showing dorsoventral flattening of the interthalamic adhesion (arrow), dilation of the lateral ventricles and elevation of the corpus callosum. Dorsal T2-weighted (b) image showing a dilation of the left olfactory recess (asterisk). Transverse T2-weighted (c) image at the level of the caudate nucleus showing bilateral disruption of the internal capsule (plus). Dorsal T2-weighted (d) image showing dilation of the lateral ventricles and the left frontal porencephaly (white arrowhead)

intensity of epileptic seizures were reduced. Sixteen months later, the animal remained stable, experiencing one focal seizure every 3 months. Phenobarbital serum concentration was 21.6 mg/L. The owners reported that the mental status and behaviour had improved substantially after initiating treatment, and the compulsive circling has stopped at home.

DISCUSSION

Congenital hydrocephalus is a relatively common disease in fox cubs abandoned by the vixen due to abnormal behaviour. In these animals, congenital hydrocephalus is suspected to be caused by infection with the Ljungan virus.[5] A case of hydrocephalus associated with encephalitis diagnosed at postmortem examination was described in a fox by Mandara et al. in 2007.[6] In the case presented here, congenital hydrocephalus was suspected because of the nonprogressive course of clinical signs, consistent MRI findings and normal CSF analysis.

Neurological deficits in dogs with hydrocephalus usually reflect a forebrain disorder and include abnormal behaviour, obtundation, blindness, circling and seizures,[2] although the relationship between seizures and hydrocephalus has recently been questioned.[7] The fox presented here showed consistent clinical signs.

The main MRI findings such as dilation of the olfactory recesses, elevation of the corpus callosum, disruption of the internal capsule adjacent to the caudate nucleus and dorsoventral flattening of the interthalamic adhesion were indicative of increased intraventricular pressure.[4,8] The presence of porencephalic cavities in dogs with severe internal hydrocephalus was reported to be due to loss of parenchyma that was filled by CSF.[9]

A standardised decision-making protocol for treatment of this condition does not exist in foxes. In dogs, there are two options: medical or surgical treatment.

Medical management with prednisone was chosen because it has been demonstrated to be effective in dogs.[10] Omeprazole was also prescribed to reduce CSF production, although its efficacy in dogs is controversial.[11] Other drugs such as acetazolamide combined with furosemide were not prescribed because of the side effects and lack of demonstrated efficacy.[12] In the present case, an improvement was observed in mental status and behaviour. The rest of the signs such as blindness and proprioceptive deficits remained and were thought to be permanent chronic signs secondary to irreversible brain lesions. Prednisone should be tapered to the lowest possible dosage that can control clinical signs or discontinued if possible.[13] In this case, tapering was not performed because the owners refused to do so.

Surgical management of hydrocephalus by placing a ventriculoperitoneal shunt is controversial. In the present case, it could have been indicated by the MRI findings,[14] but the potential secondary complications described in dogs (shunt obstruction, shunt infection, pain and others),[15] financial concerns, plus the partial response to medical treatment and the presence of chronic signs did not support this option.[2]

Anticonvulsant treatment with phenobarbital was also started. There was only one case described in a fox with seizures caused by Lafora disease that was unsuccessfully treated with phenobarbital.[16] Phenobarbital serum concentration was monitored despite lack of a therapeutic range in foxes. The therapeutic range for dogs was used as reference. Seizure intensity was reduced and the interictal period was prolonged when the phenobarbital serum concentration was within the therapeutic range for dogs (15–40 mg/L).[17]

FUNDING INFORMATION

The authors received no specific funding for this work.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

ETHICS STATEMENT

The authors confirm that legal and ethical requirements have been met with regards to the humane treatment of animals. Management throughout was performed with appropriate informed consent from the client. No home office license or ethical review committee approval was required.

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How to cite this article: Raposo M, Añor S, Verdés J, Soler V, Martorell J. Diagnosis and treatment of congenital hydrocephalus in a red fox (*Vulpes vulpes)* with seizures. Vet Rec Case Rep. 2022;e310. https://doi.org/10.1002/vrc2.310