Schweizer Archiv für Tierheilkunde
K. Beckmann et al., Band 156, Heft 8, August 2014, 395–399
DOI 10.1024/0036-7281/a000612

MRI findings in a case of canine tick born meningoencephalomyelitis

K. Beckmann[1], A. Oevermann[3], L. Golini[1], F. Steffen[1], P. R. Kircher[2], I. Carrera[2]

[1]Section of Neurology, Department of Small Animals and [2]Division of Diagnostic Imaging, Vetsuisse Faculty, University of Zurich, [3]Division of Neurological Sciences, DCR-VPH, Vetsuisse Faculty, University of Berne

Summary

Tick borne encephalitis virus (TBE) is an endemic infectious agent in northeastern Switzerland causing mainly meningoencephalomyelitis in dogs. We report a canine case of tick born meningoencephalomyelitis resulting in flaccid tetraplegia and, subsequently, fatal respiratory failure. Magnetic resonance imaging (MRI) demonstrated intra-axial bilateral, symmetric, and hyperintense lesions in T2-weighted and Fluid Attenuated Inversion Recovery (FLAIR) sequences affecting thalamus, basal nuclei, cerebral white matter and ventral horns of the caudal cervical spine. These radiological findings overlap those described during flavivirus encephalitis affecting human beings. These lesions in MRI and diffusion weighted images correlated with areas of vasogenic edema detected histopathologically. In endemic regions, clinicians should be aware that bilateral, symmetrical hyperintense thalamic lesions in T2WI can be suggestive of flavivirus infection in dogs with encephalitis.

Keywords: MRI, dog, tick born meningoencephalomyelitis

MRI Befunde eines Hundes mit Frühsommermeningoencephalitis

Das Frühsommermeningoencephalitis (FSME) Virus ist endemisch in der Schweiz und verursacht Meningoencephalomyelitis beim Hund. Wir beschreiben hier einen Fall von FSME beim Hund mit Tetraparese und Atemlähmung. Die Magnetresonatztomographie zeigte intra-axiale bilateral symmetrische und hyperintense Läsionen in T2 gewichteten Sequenzen im Thalamus, den Basalkernen, der cerebralen weissen Substanz und dem Ventralhorn des Hals- Rückenmarks. Diese Bildgebungsbefunde sind vergleichbar mit Bildgebungsbefunden von humanen FSME Fällen. Die Läsionen im MRI und im Diffusionsgewichteten MRI korrelieren mit Bereichen von vasogenem Ödem in der Pathohistologie. In endemischen Gebieten sollte bei bilateral symmetrischen hyperintensen thalamischen Läsionen in T2 gewichteten Sequenzen FSME als Differentialdiagnose in Betracht gezogen werden.

Schlüsselwörter: MRI, Hund, Frühsommermeningoencephalitis

Introduction

Central European Tick Borne Encephalitis (TBE) virus is a flavivirus that is transmitted to dogs, human beings, horses, sheep (Pavlov, 1968) and goats (Zindel and Wyler, 1983) by tick bite (*Ixoides ricinus)*. Dogs are highly susceptible to TBE virus infection, but rarely symptomatic (Pfeffer and Dobler, 2011). In Switzerland several endemic areas exist (Krech, 2002) and cases of TBE in dogs have been described in the past (Tipold, 1993). Because of high seroprevalence and rapid viral clearance ante mortem diagnosis can be challenging. In people, MRI has been used to support the diagnosis and specific features for TBE infection have been reported (Alkadhi and Kollias, 2000; Horger et al., 2012). In this report we describe MRI findings in a case of TBE and their histopatological correlation.

Clinical description and neurological examination

A nine-year-old male Cocker spaniel was referred to the Small Animal Clinic, University of Zurich in April 2012 for neurological evaluation. Clinical signs consisted of anorexia, fever and progressive tetraparesis since 10 days. At physical examination, the dog was febrile (40.5 °C), obtunded, and non-ambulatory flaccid tetraparetic, with

more severe involvement of the front limbs and absent proprioception in all 4 limbs. The dog had severe hyperpigmentation of the cornea due to chronic keratoconjunctivitis sicca precluding evaluation of menace response and pupillary light reflex. Examination of the remaining cranial nerves was normal. The segmental spinal reflexes in the thoracic limbs were severely decreased, whilst reflexes in the pelvic limbs were normal. No pain was detected on palpation along the entire dorsal spinous processes of the vertebral column. Based upon these findings, a multifocal lesion was suspected with major involvement of the cervical intumescence.

Haematology revealed lymphopenia, while serum biochemistry was normal. Electrodiagnostic was performed under general anaesthesia. Electromyography confirmed the clinical localization detecting wide spread fibrillation potentials and positive sharp waves in appendicular musculature with the thoracic limbs displaying much denser pathological discharges than the pelvic limbs. Motor nerve conduction velocity of the ulnar nerve was severely reduced (proximal portion: 3,8 m/s; distal portion: 8,2 m/s Ref: 49,4–86,9 m/s). Motor nerve conduction velocity of the sciatic nerve was only mildly reduced (55 m/s Ref: 75,2 –115,0 m/s). F-wave ratio of the ulnar nerve (stimulated at the elbow) was elevated (1,2 Ref: 0,66 +/−0,12).

Imaging findings

Thoracic radiographs and abdominal ultrasound were unremarkable. MRI of the cervical spine including the brachial plexus was performed with the dog in general anaesthesia and dorsal recumbency with a 3 Tesla system (Philips Ingenia), with dStream HeadNeckSpine Coil Solution (Philips AG, 8027 Zurich, Switzerland). This study included FSE (Fast Spin Echo) T2-weighted sequences (T2W) in transverse, dorsal and sagittal planes; FSE T1-weighted sequences (T1W) in transverse plane before and after intravenous administration 0.1 mmol/kg of gadopentetate dimeglumine (Magnevist, Bayer HealthCare Pharmaceuticals); and SPIR (SPectral Inversion Recovery) in dorsal plane. At this time, the study did not reveal any abnormalities affecting the spinal cord, nerve roots, vertebral bodies and paravertebral soft tissues.

Cerebro spinal fluid (CSF) analysis

A cisternal CSF tap was collected at the end of the MRI investigation. A lymphocytic pleocytosis with elevated total protein was found (66 cells, 180 mg/dl total protein). Serology of *Toxoplasma gondii*, *Neospora canis* and *Encephalitozoon cuniculi* was negative. In contrast, the tick born encephalitis virus – Enzyme-linked Immunosorbent Assay (Labor Alomed, D-78304 Radolfzell/Bodensee) from cerebrospinal fluid was positive (100 U/L, reference: < 5 UI).

Clinical outcome and MRI follow-up

Despite intensive physiotherapy and supportive care, the flaccid paresis progressed over the nexed 10 days until involving the neck muscle and, subsequently, the dog developed respiratory failure. A follow up MRI was performed 10 days after the first MRI. This study included the same sequences as the previous study for the cervical spine region, and FSE-T2W, FLAIR (Fluid Attenuation Inversion recovery, T2-weighted), FSE-T1W in the 3 orthogonal planes and diffusion-weighted (DWI) sequences in the transverse plane were added for examining the brain. Bilateral and symmetric intra-axial lesions, affecting the thalamus (with well-defined, rather round shaped), as well as the cerebral white matter and basal nuclei were observed. These lesions were hyperintense in T2W and FLAIR sequences compared to white matter (Fig. 1), and

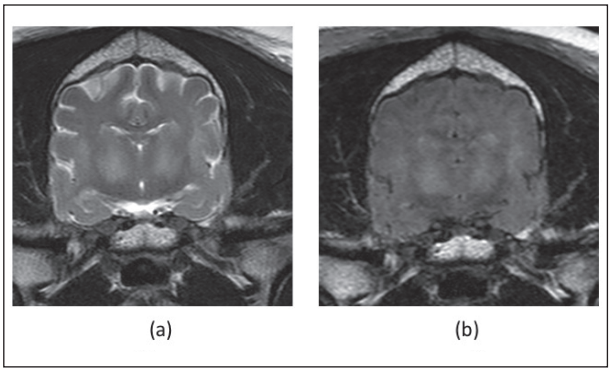

Figure 1: T2-weighted transverse (a) and FLAIR transverse (b) images of the brain at the level of the thalamus. Bilateral and symmetric hyperintense lesions are seen affecting the thalamic region. Note the lack of mass effect.

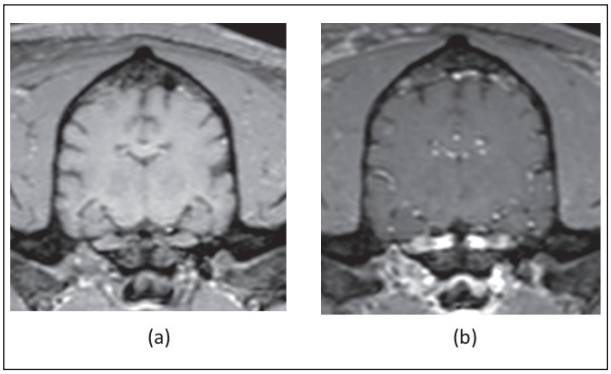

Figure 2: Pre-contrast T1-weighted (a) and post-contrast T1-weighted (b) transverse images at the same level as Figure 1. The lesions are slightly isointense in T1W when compared to gray matter (a). No evidence of contrast enhancement is seen (b).

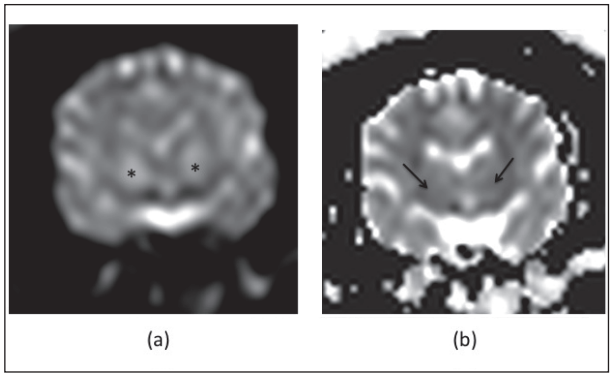

Figure 3: DW image (a) and ADC map (b) of the brain at the same level as Figure 1. The thalamic lesions are hyperintense in DW (asterisks), while they are isointense in the ADC map, when compared to white matter. These findings indicate a non-restrictive pattern.

slightly hypointense in T1W without contrast uptake (Fig. 2). The lesions did not show mass effect. The lesions were of high signal intensity when compared to gray matter in DWI and rather isointense in the apparent diffusion coefficient (ADC) map (Fig. 3). The remaining intra and extra-axial structures of cranial cavity were normal. Subtle hyperintense T2W lesions compared to normal spinal cord grey matter were seen affecting the ventral horns of the gray matter at the level of C7 spinal segment, which were not present in the first MRI examination. These lesions were bilateral and symmetrical.

Pathological examination

After the follow up MRI study the dog was humanely euthanized due to poor prognosis and a complete necropsy was performed. No abnormalities were detected on macroscopical examination. Brain, spinal cord and tissue samples from the peripheral nerves were fixed by immersion in 4 % neutral buffered formaldehyde. Representative tissue samples were processed, embedded in paraffin, sectioned at 5 µm and stained with haematoxylin and eosin (HE). Histologically, there was diffuse vacuolization of the brain most prominent in the basal nuclei, internal capsule, cerebral white matter, thalamus (Fig. 4) and midbrain, matching with T2WI and FLAIR hyperintense signals on the second MRI. Additionally, mild to moderate multifocal neuronal and axonal degeneration/necrosis associated with the activation of microglia and presence of glial nodules (neuronophagia) was observed in the spinal cord (mainly affecting the ventral horns), brainstem, lateral vestibular nucleus, thalamus, red nucleus, basal nuclei and cerebral cortex. Multifocal gliosis and axonal degeneration was also present in the white matter. These lesions were accompanied by multifocal and mild lymphoplasmacytic and histiocytic perivascular infiltrates and meningitis. Central nerve roots showed multifocal Wallerian type degeneration with digestion chamber containing axonal and myelin fragments, myelinophages and schwan cell proliferation. In summary, histological findings were consistent with a viral infection of brain and spinal cord complicated by a vasogenic edema in the brain. Immunohistochemistry for tick born encephalitis virus showed mild granular positivity in axons and in glial cells of the cerebral cortex and spinal cord.

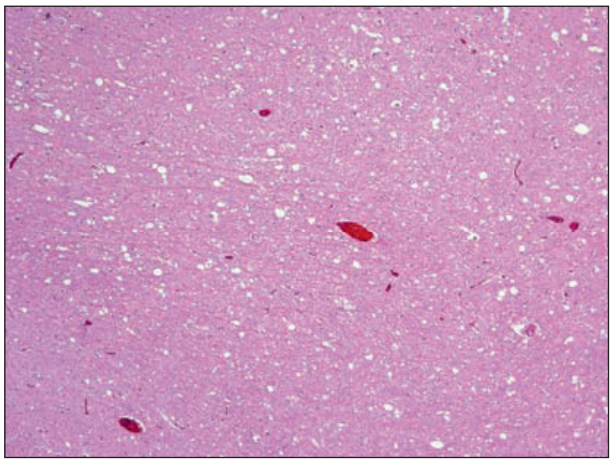

Figure 4: Thalamic lesion and diffuse vacuolization consistent with edema (H&E 100×).

Discussion

The dog here described showed a biphasic clinical course as it is usually described in human TBE with a first phase of influenza-like symptoms, followed by a short remission (1–3 days) and an abrupt transition to meningitis or, in more severe cases, meningoencephalitis, myelitis and/or radiculitis. Motor neuron deficits like in the present case have been described in 37 % of dogs with TBE (Leschnik et al., 2002). However, tick borne encephalitis – antibodies have been detected in both clinically healthy dogs and those with central nervous system inflammatory diseases (Reiner, 2002). In this case necropsy was consistent with viral encephalitis and immunohistochemistry showed a mild positive reaction for tick borne encephalitis virus. The mild reaction can be explained by rapid seropositivity of CSF and consecutive virus clearance (Weissenbock et al., 1998).

The signal changes visible on MRI correlate well to those reported in people with tick borne encephalitis infection (Alkadhi and Kollias, 2000; Horger et al., 2012). The most common affected area in people is the thalamus, but also basal nuclei, brain stem, cerebellum and caudate nuclei (Alkadhi and Kollias, 2000; Horger et al., 2012). TBE has predilection for the anterior (motor) horn, where the lesions are also bilateral and symmetric (Bender et al., 2005; Horger et al., 2012), again consistent with the findings seen in the patient reported here. However, only in

20 % of cases MRI reveals abnormalities in people affected with TBE (Kaiser, 1999; Bender et al., 2005). A delay in time from the onset of neurological signs and detectable MRI abnormalities has been suggested (Alkadhi and Kollias, 2000). This applies most likely to the case herein reported, where lesions in the spinal cord were not seen in the first magnet resonance imaging study.

These signal intensity changes matched with the histopathologically detectable vasogenic edema. This was further confirmed by DWI, where the lesions were hyperintense in DWI and isointense in the ADC map, a non-restrictive pattern; which may be compatible with edema or inflammation. DWI can distinguish between cytotoxic, vasogenic and interstitial edema, since cytotoxic edema shows a clear restrictive pattern. These findings are also in agreement with those reported in people (Marjelund et al., 2004; Horger et al., 2012).

The pathogenesis of the lesions caused by the TBE virus in humans is not clear: infiltration of inflammatory cells are believed to be responsible for the structural changes (Alkadhi and Kollias, 2000), but histopathological conformation in humans is lacking. Vasogenic edema as it is seen in our patient would also correlate with the imaging findings in humans.

Differential diagnosis of bilateral symmetric lesions include metabolic or nutritional, degenerative diseases, and toxicities. Metabolic and nutritional diseases that are described to cause bilateral symmetrical lesions of the brain are osmotic myelinolysis (O'Brien et all., 1994)., hepatic encephalopathy (Torisu et al., 2005) and thiamine deficiency (Garosi et al., 2003).

Subacute necrotizing polioencephalopathy of Alaskan Huskies (Brenner et al., 2000;) or L-2-hydroxyglutaric aciduria in Staffordshire terrier (Abramson et al., 2003) and Yorkshire Terriers (Baiker et all., 2009) are examples of degenerative disorders associated with symmetric lesions of either gray or white matter of the nervous system. Clinical findings, bloodwork and CSF examination were suggestive for a inflamatory CNS disease making meningoencephalomyelitis of autoimmune or infectious origin most important clinical differential diagnosis; however, they tend to have more asymmetric distribution.

In conclusion, in cases of encephalitis living in endemic areas or coming back from endemic ones where MRI reveals bilateral symmetric lesions, particularly affecting thalamus and ventral horn of the spinal cord, the possibility of flaviviurs infection, such as TBE, should be considered as an important differential to the known degenerative and metabolic nutritional diseases that are presented with such imaging features.

References

Abramson C. J., Platt S. R., Jakobs C., Verhoeven N. M., Dennis R., Garosi L., Shelton G. D.: L-2-Hydroxyglutaric aciduria in Staffordshire Bull Terriers. J Vet. Intern. Med. 2003, 17: 551–556.

Alkadhi H., Kollias S. S.: MRI in tick-borne encephalitis. Neuroradiology 2000, 42: 753–755.

Baiker K., Hofmann S., Fischer A., Godde T., Medl S., Schmahl W., Bauer M. F., Matiasek K.: Leigh-like subacute necrotising encephalopathy in Yorkshire Terriers: neuropathological characterisation, respiratory chain activities and mitochondrial DNA. Acta Neuropathol. 2009, 118: 697–709.

Bender A., Schulte-Altedorneburg G., Walther E. U., Pfister H. W.: Severe tick borne encephalitis with simultaneous brain stem, bithalamic, and spinal cord involvement documented by MRI. J. Neurol. Neurosurg. Psychiatry 2005, 76: 135–137.

Brenner O., Wakshlag J. J., Summers B. A., De Lahunta A.: Alaskan Husky encephalopathy – a canine neurodegenerative disorder resembling subacute necrotizing encephalomyelopathy (Leigh syndrome). Acta Neuropathol. 2000, 100: 50–62.

Garosi L. S., Dennis R., Platt S. R., Corletto F., De Lahunta A., Jakobs C.: Thiamine deficiency in a dog: clinical, clinicopathologic, and magnetic resonance imaging findings. J. Vet. Intern. Med. 2003, 17: 719–723.

Horger M., Beck R., Fenchel M., Ernemann U., Nagele T., Brodoefel H., Heckl S.: Imaging findings in tick-borne encephalitis with differential diagnostic considerations. AJR. Am. J. Roentgenol. 2012, 199: 420–427.

Kaiser R.: The clinical and epidemiological profile of tick-borne encephalitis in southern Germany 1994–98: a prospective study of 656 patients. Brain 1999, 122: 2067–2078.

Krech T.: TBE foci in Switzerland. Int. J. of Med. Microbiology 2002, 291, Suppl.33: 30–33.

Leschnik M. W., Kirtz G. C., Thalhammer J. G.: Tick-borne encephalitis (TBE) in dogs. Int. J. of Med. Microbiology 2002, 291, Suppl. 33: 66–69.

Marjelund S., Tikkakoski T., Tuisku S., Raisanen S.: Magnetic resonance imaging findings and outcome in severe tick-borne encephalitis. Report of four cases and review of the literature. Acta Radiol. 2004, 45: 88–94.

O'Brien D. P., Kroll R. A., Johnson G. C., Covert S. J., Nelson M. J.: Myelinolysis after correction of hyponatremia in two dogs. J. Vet. Intern. Med. 1994, 8: 40–48.

Pavlov P.: Studies on tickborne encephalites of sheep and their natural foci in Bulgaria. Zentralbl. Bakteriol. Orig. 1968, 206: 360–367.

Pfeffer M., Dobler G.: Tick-borne encephalitis virus in dogs – is this an issue? Parasit. Vectors 2011, 4: 59.

Reiner B. G. S., Steffen F., Djuric N., Schindler T., Müller W., Fischer A.: Prevalence of TBE in serum and CSF of dogs with inflammatory and non-inflammatory CNS disease. Int. J. Med. Microbiol. 2002, Suppl. 33: 234.

Tipold A. F. R., Holzmann H.: Zentraleuropäische Zeckenenzephalitis beim Hund Kleintierpraxis 1993: 619–628.

Torisu S., Washizu M., Hasegawa D., Orima H.: Brain magnetic resonance imaging characteristics in dogs and cats with congenital portosystemic shunts. Vet. Radiol. Ultrasound 2005, 46: 447–451.

Wakshlag J. J., De Lahunta A.: Hereditary encephalomyelopathy and polyneuropathy in an Alaskan husky. J. Small Anim. Pract. 2009, 50: 670–674.

Zindel W., Wyler R.: Tick-borne encephalitis in a goat in lower Pratigau. Schweiz. Arch. Tierheilk. 1983, 125: 383–386.

Corresponding author

Katrin Beckmann
Clinic for Small Animal Surgery
Vetsuisse Faculty, University of Zurich
Winterthurerstrasse 260
8057 Zurich
Switzerland
kbeckmann@vetclinics.uzh.ch

Received: 4 November 2013
Accepted: 26 February 2014