

A Canine Case of Necrotizing Meningoencephalitis for Long-Term Observation: Clinical and MRI Findings

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ABSTRACT. A 3-year-old female pug presented with general seizure following a partial seizure. During the remaining 48 months till death, the dog showed various neurological signs such as disturbance of consciousness, myoclonus and various types of partial seizure after each occurrence of the seizure clusters, and the dog eventually exhibited inability to stand and dementia. Magnetic resonance imaging findings revealed atrophy of the brain over the course of the disease. On histopathological analysis, the dog was diagnosed with necrotizing meningoencephalitis. This case of a canine necrotizing meningoencephalitis observed over the long term is valuable.

KEY WORDS: canine, MRI, necrotizing meningoencephalitis.

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The cause of necrotizing meningoencephalitis (NM) in small-breed dogs remains unknown. Although the incidence of this disease is noted in various breeds, including Pekingese, Yorkshire Terrier, Maltese, Chihuahua, and Shi Tzu, it is very common in the pug [1–3, 5, 7–10, 12, 13]. This disease may be acute or chronic [4]. In acute cases, the onset and progression of clinical signs occur within 2 weeks. In chronic cases, the course ranges from 4 to 6 months and shows various clinical signs [4]. Since antemortem diagnosis of NM in small-breed dogs is difficult, it is confirmed histologically only after death. Characteristic findings have been reported on magnetic resonance imaging (MRI), computed tomography (CT) scanning, cerebrospinal fluid (CSF) and immunological tests, etc. However, reports on changes in clinical and MRI findings are rare [9, 11, 15, 18]. We encountered a case of NM in a dog that survived 48 months after disease onset. In this paper, we describe the changes in the clinical signs and MRI findings.

A 3-year-old female pug dog presented with general seizures following a partial seizure of the left pelvic limb for 1 month and was referred to Nihon University Animal Hospital. Prior to referral the dog had exhibited partial seizure in the left eyelid. There were no neurological and physical abnormalities at the initial examination. MRI (0.5 T, Flex-ART[®], Toshiba, Tokyo) demonstrated an area in the right parietal lobe that showed hypointensity on the T1-weighted (T1W)(TR 350 msec, TE 15 msec) images, hyperintensity on the T2-weighted (T2W) (TR 4000 msec, TE 120 msec) (Fig. 1a) and fluid attenuated inversion recovery (FLARE) images (TR 8000 msec, TE 120 msec) (Fig. 1b). Enlargement of the right ventricle was also observed. A CSF anal-

ysis revealed a cell count of 1 cell/ μ l, protein count of 20 mg/dl, a negative Pandy test and negative results for the canine distemper virus antibody. Following this, there were no episodes of seizure. However, 2 months after the initial examination, menace reaction in the left side and visual placing reaction in the left thoracic limb were absent, and a cluster of generalized seizures followed. We initiated the administration of phenobarbital (2 mg/kg PO q12h, PHE-NOBAL[®], Fujinaga Pharm Co., Ltd., Tokyo, Japan) and prednisolone (1 mg/kg q24h, Predonine[®], Bushu Pharmaceutical Ltd., Saitama, Japan). Approximately 4 months after the initial examination, partial seizures were occasionally observed in the right eyelid. Approximately 20 months after the initial examination, the dog developed myoclonus of the right limb and it showed delayed reactions to calling after clusters of generalized seizures following the partial seizure of the right eyelid. Twenty-one months after the initial examination, MRI was carried out due to the recurrence of clusters of generalized seizures. At that time, myoclonus was seen after administering general anesthesia. MRI demonstrated an enlarged right lateral ventricle and a lesion in the left cerebral cortex that showed hypointensity on the T1W images, hyperintensity on the T2W (TR 4000 msec, TE 120 msec) (Fig. 2a) and FLARE images (TR 8000 msec, TE 120 msec) (Fig. 2b). A CSF analysis demonstrated a cell count of 18 cells/ μ l, protein count of 18 mg/dl, a negative Pandy test and negative results for the canine distemper virus antibody. After the second MRI, the dog started to walk in circles. Although the dog responded to calling, it was unable to determine the direction of the call. Myoclonus was observed only while sleeping. Twenty-nine months after the initial examination, the dog developed clusters of generalized seizures and was unable to stand following the absence of proprioception in the right thoracic limb. Thirty-one months after the initial examination, the dog developed clusters of generalized seizures and was relatively unrespon-

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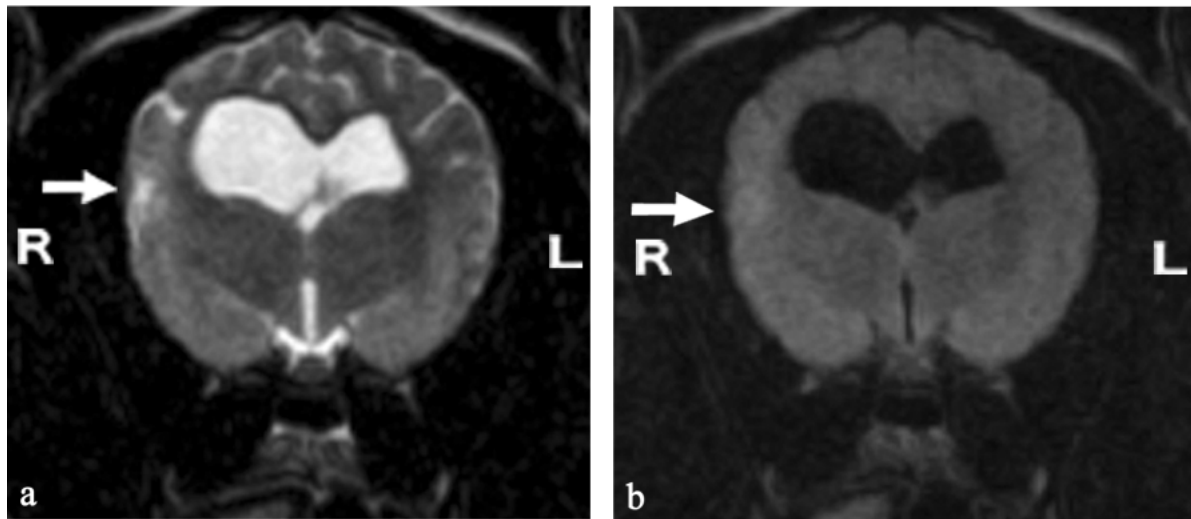


Fig. 1. (a) T2-weighted transverse image and (b) FLARE image in the initial examination. A lesion showing hyperintensity was noted in the right cerebrum (arrow). The right ventricle was enlarged.

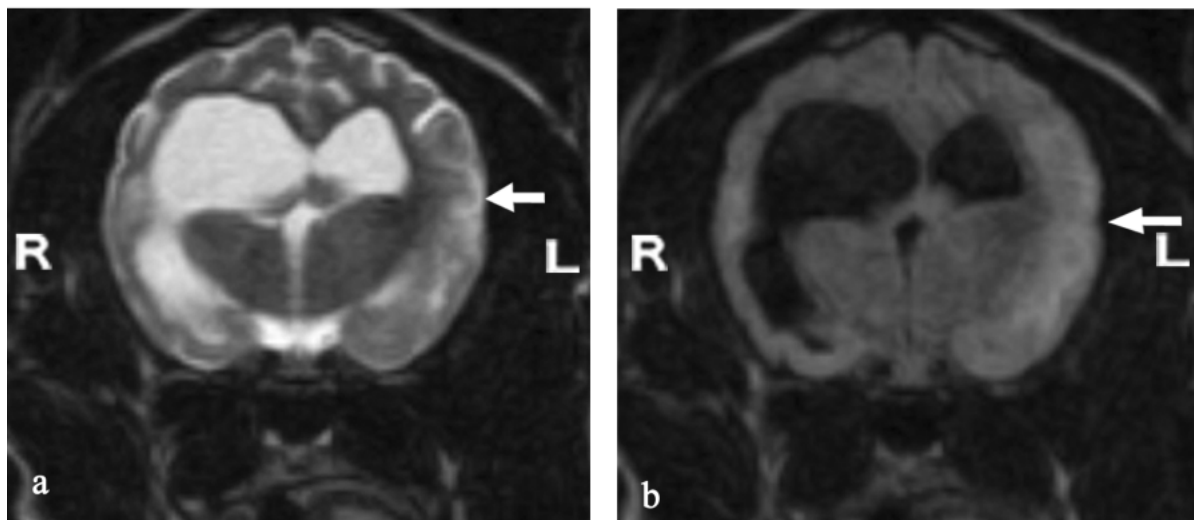


Fig. 2. (a) T2-weighted transverse image and (b) FLARE image 21 months after the initial examination. A lesion showing hyperintensity was noted in the left cerebrum (arrow). The right ventricle was more enlarged than in Fig. 1.

sive to the environment and showed an increased sleeping tendency. Although we suggested euthanasia to the owner because of this, the owner refused. Thirty-five months after the initial examination, the increased sleeping tendency and response to the environment improved slightly; however, the dog could not stand despite the improvement. Thereafter, partial seizures and a single general seizure were occasionally observed but not in clusters. Forty-six months after the initial examination, the dog developed clusters of generalized seizures, and myoclonus in the left lip. Two months later, MRI was carried out because nystagmus and head tilt were observed. However, the dog died without recovery from anesthesia. The MRI revealed hypointensity on the T1W images (TR 375 msec, TE 15 msec) (Fig. 3a) and

hyperintensity on the T2W (TR 4000 msec, TE 120 msec) (Fig. 3b), FLARE images (TR 8000 msec, TE 120 msec) (Fig. 3c) in most regions of the cerebral cortex and the left thalamus. Moreover, the cortex was thin and the ventricles, enlarged (Fig. 3a,b,c). A macropathological examination demonstrated cortical congestion and necrosis. A histopathological examination revealed necrosis extending into the meninges, congestion, infiltration of monocytes (lymphocytes, plasma cells and macrophages) and perivascular cuffing of monocytes in the cerebrum (Fig. 4). Macrophages that had engulfed myelin were also observed. Based on the pathological findings, the dog was diagnosed with NM.

It has been reported that chronic NM induces general and/or partial seizure during the first stage without any other

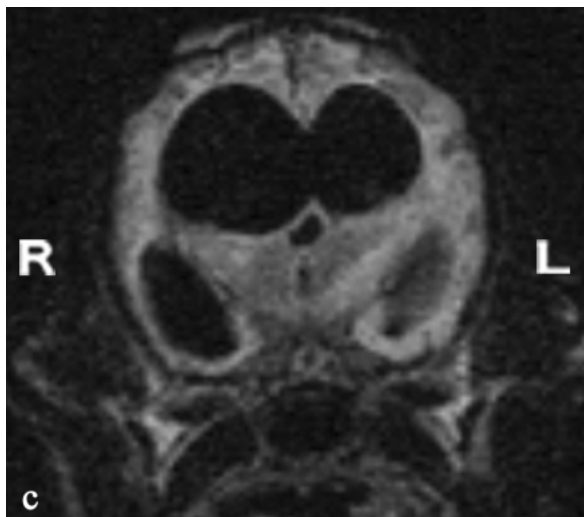
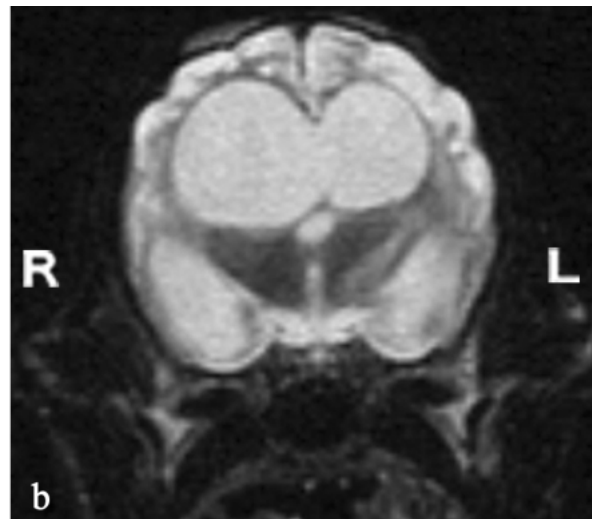
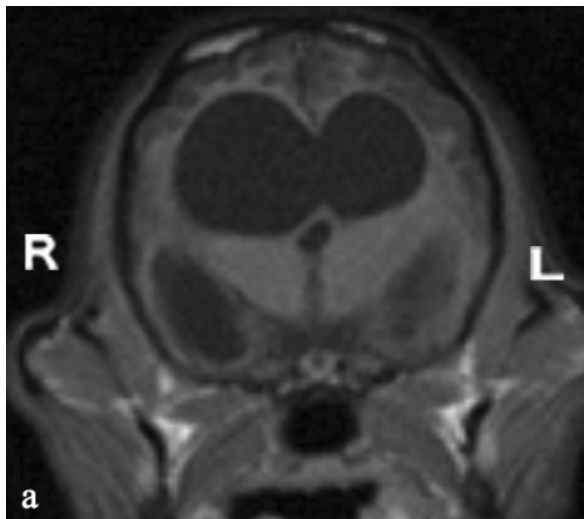


Fig. 3. T1- (a) and T2- (b) weighted transverse images and FLARE image (c) 48 months after the initial examination. Almost all regions of the cerebral cortex, and a lesion located in the left thalamus, showed hypointensity on the T1-weighted image and hyperintensity on the T2-weighted image. Severe enlargement of the ventricles and thinning of the cerebrum were noted.

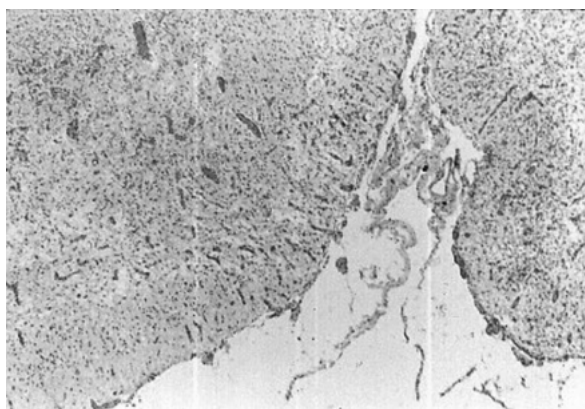


Fig. 4. A histopathological examination revealed necrosis extending into the meninges and congestion in the cerebrum (hematoxylin-eosin staining $\times 100$).

neurological signs during the interictal period [16]. However, it has also been reported that progressively deteriorating NM cases show various neurological signs such as

forebrain dysfunction, lethargy, ataxia, circling and blindness [16]. In the present case, partial seizure of the left eyelid or generalized seizure following the partial seizure was observed. Thereafter, partial seizure occurred in the right eyelid and the pelvic limb, and this was followed by generalized seizure. The MRI findings also showed changes accompanying the neurological course. These changes in the MRI findings and clinical signs show that the NM lesions progressed over time (Table 1).

It has been reported that myoclonus is usually noted in cases of distemper virus encephalomyelitis as well as in other forms of encephalomyelitis [17]. However, there are no previous reports of NM in which myoclonus was noted. Myoclonus is considered to be induced by pacemaker activity in the injured nerve cell [4]. This dog developed myoclonus and the region experiencing myoclonus changed over the disease course (the eyelid, pelvic limb, thoracic limb, lip). We consider that the changes indicated disease progression in the dog.

In this dog, in addition to seizure, neurological signs (circling, absence of menace reaction, deficit of proprioception,

Table 1. MRI findings of a Pug with necrotizing meningoencephalitis

Time of MRI	Lesion	T1-weighted image	T2-weighted image	FLARE	
First	Right lateral lobe	Hypo-intensity	Hyper-intensity	Hyper-intensity	Enlargement of the right lateral ventricle
21 months	Left lateral lobe	Hypo-intensity	Hyper-intensity	Hyper-intensity	Severe enlargement of the right lateral ventricle
48 months	Cerebral cortex	Hypo-intensity	Hyper-intensity	Hypo-intensity	Severe enlargement of the both lateral ventricle

increased sleeping tendency, etc.) were observed after a cluster of generalized seizures. It is known that chronic and/or static seizures lead to lesions in the brain [6]. Moreover, it has been reported that the lesion site of NM may include the hippocampus, thalamus, cortex and cerebellum [6]. Although the seizures of primary inflammatory diseases may promote necrosis or extend it to other regions, it has been reported that there was no evidence of necrosis extending to the white matter being caused by seizures in NM [3]. It has been reported that NM causes lesions in the cerebrum and the brain stem in Yorkshire terriers; however, in the pug, it has been restricted to the cerebrum [14]. In the present case, the findings of the third MRI revealed that the lesion in the left thalamus showed hyperintensity on the T2W images. Although this lesion might have been caused by seizures, it was also attributable to inflammation based on the result of the histopathological examination. The findings of the third MRI revealed remarkable thinning of the cerebrum. On the second MRI, the left cerebrum, which showed an abnormal signal on the first MRI, showed slight thinning. We suspect that the thinning of the cerebrum was due to atrophy following inflammation.

We investigated the clinical signs and MRI findings of a dog with NM, which survived 48 months after disease onset. This report has described the changes in the neurological signs and MRI findings of a chronic NM case, providing useful information for veterinary clinicians.

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