J Vet Intern Med 2009;23:527–535

Magnetic Resonance Imaging Characteristics of Necrotizing Meningoencephalitis in Pug Dogs

B. D. Young, J. M. Levine, G. T. Fosgate, A. de Lahunta, T. Flegel, K. Matiasek, A. Miller, G. Silver, N. Sharp, K. Greer, and S. J. Schatzberg

Background: The magnetic resonance imaging (MRI) characteristics of necrotizing meningoencephalitis (NME) are not well documented.

Objectives: To describe common MRI features of NME, to compare the MRI features to histopathologic findings, and to determine whether or not MRI lesions are predictive of survival time.

Animals: Eighteen Pugs with NME.

Methods: Retrospective MRI case study of Pugs identified by a search of medical records at 6 veterinary institutions. Eighteen dogs met inclusion criteria of histopathologically confirmed NME and antemortem MRI exam. MRI lesions were characterized and compared with histopathology with the kappa statistic. Survival times were compared with MRI findings by use of Mann-Whitney *U*-tests and Spearman's ρ.

Results: Twelve of 18 lesions were indistinctly marginated with mild parenchymal contrast enhancement. Prosencephalic (17/18) lesion distribution included the parietal (16/18), temporal (16/18), and occipital (16/18) lobes. There were cerebellar (4/18) and brainstem (3/18) lesions. Asymmetric lesions were present in both gray and white matter in all dogs. Falx cerebri shift was common (11/18), and 6 dogs had brain herniation. Leptomeningeal enhancement was present in 9/18 dogs. A moderate positive association was found between parenchymal contrast enhancement and both necrosis ($\kappa = 0.45$; $P = .045$) and monocytic inflammation ($\kappa = 0.48$; $P = .025$). Higher MRI lesion burden was correlated with longer time from disease onset to MRI ($P = .045$). MRI lesion burden did not correlate to survival time.

Conclusions and Clinical Importance: Asymmetric prosencephalic grey and white matter lesions with variable contrast enhancement were consistent MRI changes in Pugs with confirmed NME. While not pathognomonic for NME, these MRI characteristics should increase confidence in a presumptive diagnosis of NME in young Pugs with acute signs of neurologic disease.

Key words: Brain; Dog; Imaging; Inflammation.

Necrotizing encephalitis is an idiopathic, breed-specific intracranial disease of dogs.[1] It is diagnosed most frequently in young adult animals and it is believed to be an invariably fatal disorder. Common histologic features include nonsuppurative inflammation of the brain with extensive necrosis.[2,3] To date variations of necrotizing encephalitis have been reported in the Pug,[2,4–6] Yorkshire Terrier,[3,7–11] Maltese,[12] Pekingese,[13] French bulldog,[14] Chihuahua,[3,15] and Shih-Tzu.[12]

Two distinct patterns of lesion distribution have been identified within breeds affected by necrotizing encephalitis. The variant seen in the Pug and Maltese, often referred to as necrotizing meningoencephalitis (NME) or Pug dog encephalitis, has a strong predilection for the cerebral hemispheres with asymmetric necrosis and severe nonsuppurative inflammation of the cortical gray and subcortical white matter and the overlying meninges.[2,12,14] There often is involvement of the hippocampus and thalamus; but severe lesions of the caudal brainstem are not common in these animals. The pattern of necrotizing encephalitis seen in Yorkshire Terriers also has been described in other breeds such as the French Bulldog[3,14] and is termed necrotizing leukoencephalitis (NLE). In this form, the primary sites of involvement are the brainstem and deep white matter of the cerebrum, although extensive prosencephalic lesions occur.[11]

Abbreviations:

CT	computed tomography
GME	granulomatous meningoencephalitis
MRI	magnetic resonance imaging
NLE	necrotizing leukoencephalitis
NME	necrotizing meningoencephalitis
ROI	region of interest
TE	echo time
TR	repetition time

From the Department of Large Animal Clinical Sciences (Young), Department of Small Animal Clinical Sciences (Levine), and Department of Veterinary Integrative Biosciences (Fosgate), College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX; the Department of Biomedical Sciences, College of Veterinary Medicine, Cornell University, Ithaca, NY (de Lahunta, Miller); the Department of Small Animal Medicine, University Leipzig, Leipzig, Germany (Flegel); The Animal Health Trust, New Market, UK (Matiasek); the Neurology Department, Massachusetts Veterinary Referral Hospital, Woburn, MA (Silver); the Neurology Department, Canada West Veterinary Specialists and Critical Care Hospital, Vancouver, BC (Sharp); the School of Natural Sciences and Mathematics, Indiana University East, Richmond, IN (Greer); and the Department of Small Animal Medicine and Surgery, College of Veterinary Medicine, University of Georgia, Athens, GA (Schatzberg). *This paper was presented at the Annual Convention of the American College of Veterinary Radiology in San Antonio, TX in September 2008 by the primary author. Four of these animals were described separately in another manuscript.[25] None of these images were used in that manuscript. The data were analyzed and the manuscript was primarily written at Texas A&M University. Cases were gathered, imaged, and histopathology performed at Texas A&M University, Cornell University, the University of Leipzig, The Animal Health Trust, Massachusetts Veterinary Referral Hospital, the University of Georgia, Red Bank Animal Hospital, and Canada West Veterinary Specialists and Critical Care Hospital.*

Corresponding author: Dr Benjamin D. Young, Department of Large Animal Clinical Sciences, College of Veterinary Medicine, Texas A&M University, 4475 TAMU, College Station, TX 77843; e-mail: byoung@cvm.tamu.edu.

Submitted July 22, 2008; Revised November 21, 2008; Accepted January 20, 2009.

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10.1111/j.1939-1676.2009.0306.x

In a literature search of reports including either computed tomography or magnetic resonance imaging (MRI), a description of imaging findings for NME or NLE could be found in a total of 15 dogs with 3 of these descriptions involving Pugs at the time of this writing.[4,5,7–12,14,16,17] Despite the limited data available, some authors have suggested that the MRI features of NME in Pugs are relatively distinct.[18] The objectives of this paper were to describe the common MRI findings of the brain of Pugs with histopathologically confirmed NME, to examine the correlation of imaging lesions to histopathologic findings, and to determine whether or not imaging findings reflect duration of clinical signs before MRI and if they are predictive of survival time.

Materials and Methods

Data Collection and Inclusion Criteria

This study was an interinstitutional collaboration, and dogs were collected from several sources. First, dogs were selected from a larger prospective study designed to investigate NME in Pugs. Study participants were obtained between August 2002 and February 2008 with cooperation from the Pug Dog Club of America, breeders, and individual Pug owners. Information concerning the study was dispersed by 1 investigator (KG) through electronic media and through presentations. Only veterinarians were allowed to determine whether or not a Pug met inclusion criteria. The study protocols were reviewed and were approved by the animal care and use committee at Texas A&M University.

Pugs exhibiting neurological signs consistent with intracranial disease were enrolled in the study through referring veterinarians contacting 1 investigator (KG). All included animals were required to have necropsy and histopathology of the central nervous system. Pugs that were euthanized or died naturally were transported either frozen or chilled for necropsy to Texas A&M University. Samples were processed routinely for histopathology. From this larger group, only animals that had undergone antemortem MRI were selected for the study presented here.

The second source of dogs was retrospective collection of cases from 1 investigator (SS). Several collaborators (AD, TF, KM, GS, EG, NS) provided tissues and MRI images and gave permission for inclusion in the study. Cases were selected which had both MRI studies available and histologic confirmation of NME at necropsy.

Owner recognition of neurological signs, most typically seizure, was selected as the disease onset.[19] Criteria for the histologic diagnosis of NME were based on previous reports.[1,3,12] Pathologic features include gross discoloration of the cerebral cortex or subcortical white matter with loss of grey-white distinction, predominant lesion burden in the prosencephalon, necrosis with mononuclear inflammatory cell infiltration, and absence of a demonstrable infectious etiology. The cellular infiltrate type, presence of meningeal infiltration, presence of necrosis, and brain regions involved were recorded. Brain regions were defined as prosencephalon (telencephalon and diencephalon), cerebellum, and caudal brainstem (mesencephalon, ventral metencephalon [pons], and myelencephalon).

Image Analysis

For each digital or hard copy MRI sequence available, the repetition time (TR) and echo time (TE) were recorded. Two investigators, a board-certified radiologist (BY) and a board certified neurologist (JL), evaluated the images for lesions, defined as disruption of normal anatomy or change in tissue signal characteristics. Lesion location, side, symmetry, side of predominance (in asymmetric cases), and involvement of gray or white matter were recorded. Lesion signal characteristics compared with surrounding parenchyma were recorded. The presence of lesion contrast enhancement was subjectively graded as mild (faintly identifiable signal increase to surrounding tissue), moderate (easily identifiable signal increase which was not solid or uniform), and strong (easily identifiable signal increase which was solid or uniform). Meningeal enhancement was defined as an area of the meninges with greater signal intensity than nearby gray matter and normal meninges. The pattern of meningeal enhancement was classified as pachymeningeal (also named the "dural" pattern) or leptomeningeal (also named the "pial" pattern) in accordance with previous classification systems.[20] The major criterion for identifying leptomeningeal enhancement was enhancement extending into the cortical sulci. Dilation and compression of the lateral ventricles were identified subjectively.[21,22] Dilation was presumed if the ventricle appeared to be $>15\%$ of the cerebral height at the level of the interventricular foramina.[23] Compression was presumed if the ventricle appeared asymmetrically small and was abnormal in shape.[23,24]

In order to estimate the lesion burden in each animal, regions of interest (ROI) were hand drawn around lesions (noted as areas of abnormal signal increase) in every slice on the transverse plane T2-weighted series. This sequence was chosen so that perilesional edema would be included in calculation of lesion size. ROIs were drawn around the entire brain in every slice. A DICOM-compatible software program[a] was then used to calculate the number of voxels included in each ROI, providing an objective estimation of lesion and brain volumes. ROIs were drawn around the lateral ventricles, and their voxel numbers were subtracted from the total brain voxels in order to remove them from the calculation of brain parenchymal volume. For each animal, the total number of lesion voxels was divided by the number of voxels within brain parenchyma, resulting in an estimation of lesion burden as a percentage of brain parenchymal volume.

Statistical Analysis

Data were summarized for all dogs by descriptive statistics. Agreement of lesion recognition and location between the 2 MRI evaluators was quantified by the kappa statistic. Estimation of the kappa statistic and its corresponding 95% confidence intervals were performed independently for evaluation of MRI and histopathologic lesions in available software.[b] Survival times (calculated as both time from MRI imaging to death and as time from onset of clinical signs to death) were compared based on signalment and MRI findings. The time from the onset of clinical signs to MRI imaging was also compared with signalment and MRI findings. Investigated predictors of survival included sex, age (<2 versus ≥ 2 years), MRI lesion descriptions, and lesion severity as measured by the lesion burden (ratio above median versus not). Mann-Whitney *U*-tests were used to compare medians of survival data between groups. Spearman's rho (ρ) was used to assess the correlation between survival and lesion severity (lesion burden ratio). Statistical analyses excluding the estimation of the kappa statistic were performed in commercially available software.[c] All statistical results were interpreted at the 5% level of significance.

Results

Eighteen Pugs met the inclusion criteria for this study. There were 3 intact males, 6 castrated males, 5 intact females, and 4 spayed females. The median age was 18 months (range, 8 months–7 years). The median time from onset of clinical signs to MRI was 4 days (range, 1–107 days) and the median survival time from onset of clinical signs was 18 days (range, 1–253 days). All dogs

had histologic confirmation of nonsuppurative inflammation of the brain diagnostic for NME. The findings in 4 of these dogs also have been described separately.[25]

Images were acquired with magnets ranging from 0.5 to 1.5 T. All dogs had T1-weighted (TR = 366–816, TE = 10–25) and T2-weighted images (TR = 2,000–5,500, TE = 85–128); and 17 dogs had fluid-attenuated inversion recovery (FLAIR) images (TR = 5,000–10,004, TE = 93–137). Postcontrast T1-weigted images were available for all 18 dogs, but contrast agent and dose were not recorded for most dogs.

Seventeen of 18 dogs had MRI lesions in the prosencephalon, all of which were asymmetrically distributed and included at least 1 telencephalic lesion. Four of these dogs also had diencephalic MRI lesions. The parietal (16/18), temporal (16/18), and occipital (16/18) lobes were affected most commonly (Fig 1). Frontal (10/18), olfactory (7/18), and pyriform (9/18) lobe lesions were common but less frequently seen. Four of 18 dogs had MRI lesions in the cerebellum and 3/18 in the caudal brainstem. In 1 of these dogs, the only MRI lesion identified was in the caudal brainstem. Lesions were identified within both cortical gray and white matter in all dogs. Eleven dogs had a deviation of the falx cerebri from midline with the direction of shift always away from the hemisphere with the higher lesion burden (Fig 2). Falx cerebri shift was not associated predictably with ventricular changes, being away from compressed ventricles (4), away from dilated ventricles (4), toward a compressed ventricle (1), toward a dilated ventricle (1), and seen without any ventricular size abnormalities (1). In 2 dogs with ventricular compression, no falx cerebri shift was present. Six dogs had dilation of 1 lateral ventricle, 5 of which were contralateral to the higher lesion burden, 1 being ipsilateral. Nine dogs had 1 lateral ventricle, which appeared compressed subjectively, 7 of which were ipsilateral to the highest lesion burden (Fig 1), 2 being contralateral. One dog had herniation of the cerebellar vermis through the foramen magnum and 5 dogs had a caudal transtentorial herniation of the cerebrum as evidenced by compression of the mesencephalon by the temporal or occipital lobes[26] (Fig 1).

All MRI lesions were isointense or mildly hypointense on T1-weighted images and hyperintense on T2-weighted and FLAIR images. The majority of MRI lesions in all dogs appeared as poorly defined regions of signal change and anatomical disruption. Ten dogs had sharply defined lesions of high signal intensity on T2-weighting. The sharp lesion demarcation nearly always corresponded to a gray-white matter junction. Two of these dogs had a corresponding sharply defined hypointense lesion on T1-weighting (Fig 3). In the remainder of dogs, the corre-

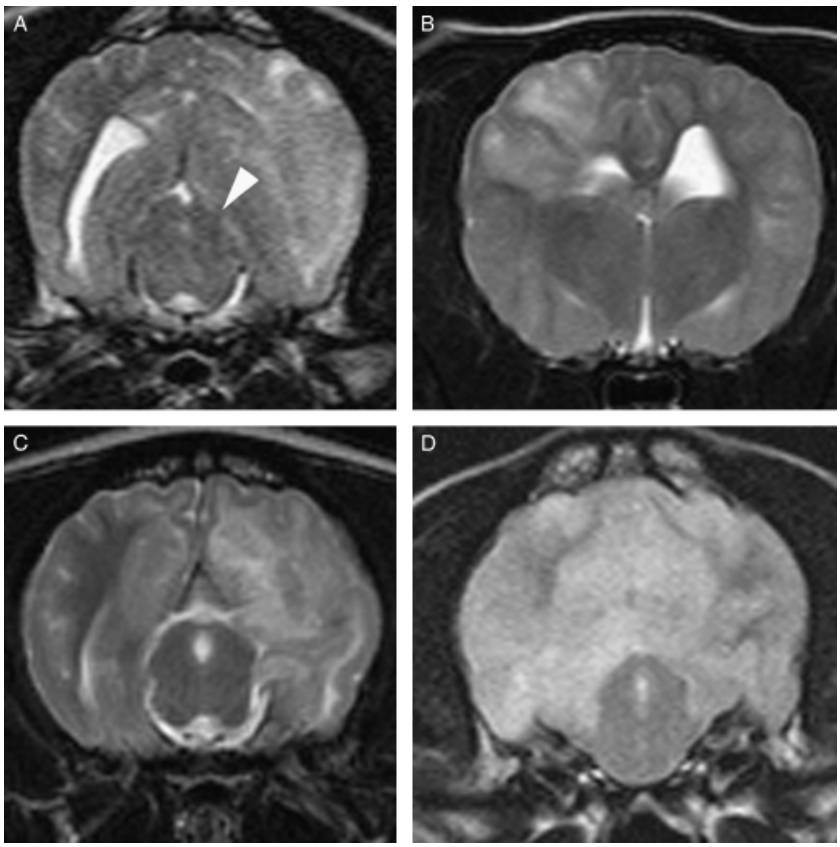

Fig 1. Transverse T2-weighted images made at the level of the thalamus to the mesencephalon in 4 Pugs with necrotizing meningoencephalitis. Asymmetric hyperintense lesions are present within the cortical gray and subcortical white matter of the parietal, temporal, and occipital lobes. Note compression of the lateral ventricle on the side with the higher lesion burden (**A** and **B**) and compression of the mesencephalon by the occipital lobe (A–D) indicating transtentorial herniation (arrowhead). 101×101 mm (316×316 DPI).

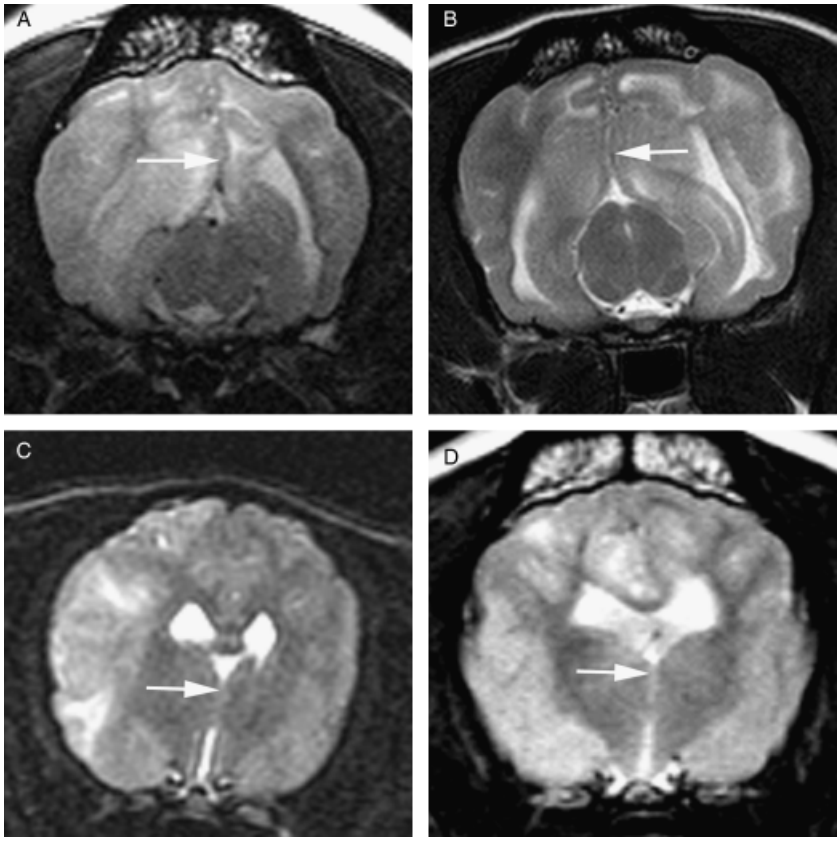

Fig 2. Transverse T2-weighted images made at the level of the thalamus to the mesencephalon in 4 different Pugs with necrotizing meningoencephalitis. There is a shift of midline (arrows) both at the falx ceribri (**A** and **B**) and interthalamic adhesion (**C** and **D**). The shift is away from the hemisphere with the higher lesion burden in all cases 117×117 mm (300×300 DPI).

sponding site on T1-weighted sequences was mildly hypointense and without defined lesion borders. After contrast administration lesion enhancement was variable. In the slight majority of dogs (12/18) lesion contrast enhancement was present and it was always mild or moderate (Fig 4). No areas of strong contrast enhancement or peripheral rim enhancement were noted. Nine of 18 dogs had meningeal enhancement, which always involved the leptomeninges (Fig 5).

There was substantial interobserver agreement for detecting MRI lesions in the cerebellum and brainstem (κ = 0.60, 95% CI = 0.14, 1.0, $P \leq .01$). There appeared to be substantial agreement for detection of prosencephalic lesions, however, because of the small sample size and a zero marginal total, it was not possible to estimate the kappa statistic. Histopathologic evidence of inflammatory involvement was present in both gray and white matter in 16/18 dogs. Meningeal involvement was present in all dogs. Lymphocytic inflammation was a component of the histologic infiltrate in all dogs. The associations of other inflammatory cell types and necrosis with MRI findings are summarized in Table 1. The associations of both signalment and MRI findings with time from lesion onset to MRI, survival time after MRI, and survival time from onset of clinical signs are summarized in Table 2. There was a tendency for female dogs to have shorter survival time after MRI (P = .063). There was a moderate positive correlation between lesion burden and time from onset of clinical signs to MRI (correlation coefficient ρ = 0.491; P = .045). There was no significant correlation between lesion burden and survival time after MRI (ρ = −0.148; P = .571) or survival time from onset of clinical signs (ρ = 0.65, P = .804). There was no difference in survival time after MRI in dogs with lesion burden above the median (1 day) compared with dogs with less lesion burden (13 days; P = .370).

Discussion

Brain lesions were identified with MRI in all 18 dogs with NME and interobserver agreement was high. Lesions were identified most easily on T2-weighted and FLAIR images. The finding of a predominance of lesions in the cortical gray and subcortical white matter of the cerebral hemispheres was similar to the findings of previous studies of NME.[2,5,6] It is noteworthy that 1 dog had lesions present only in the caudal brainstem, which is atypical topography for NME. This finding suggests that an absence of prosencephalic lesions should not be used to exclude NME as a differential diagnosis in Pugs. NME had similar findings to GME including midline shift and mass effect and parenchymal contrast enhancement. The presence of cystic lesions was uncommon.

The frequent finding of midline shift is similar to previous reports of NME in Pugs and NLE in Yorkshire Terriers, for which the midline shift has been proposed to

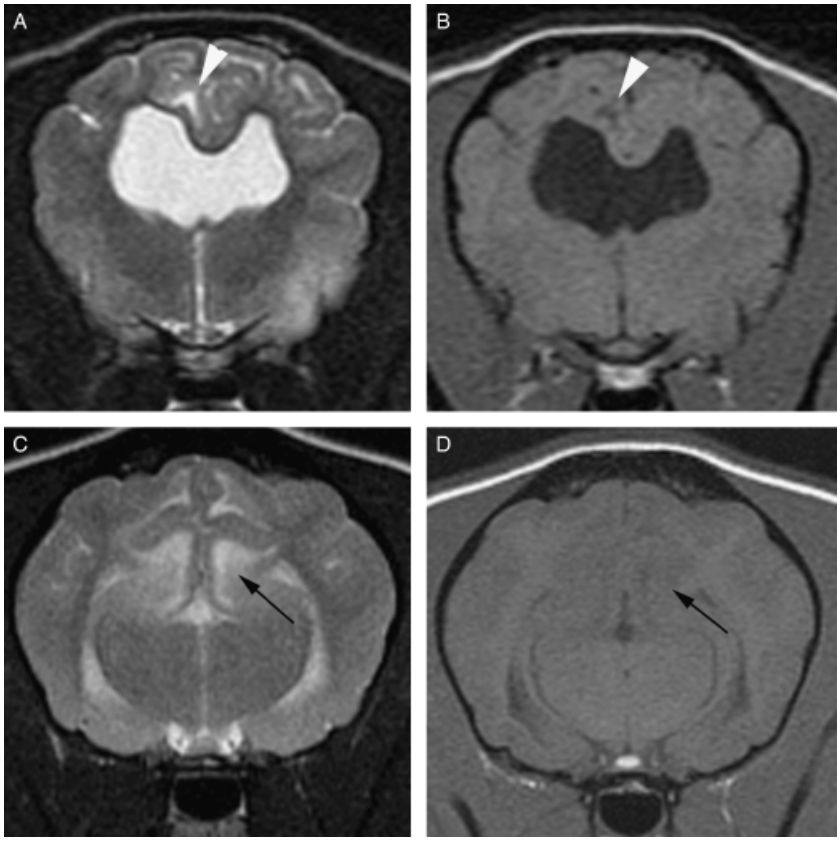

Fig 3. Transverse images made at the level of the thalamus in 2 different Pugs with necrotizing meningoencephalitis. One dog has a sharply margined lesion in both T2-weighted (**A**) and T1-weighted precontrast (**B**) images indicating a cavitary lesion (white arrowheads). The other has sharply defined lesions on T2 weighting (**C**) and only undefined hypointensity on T1-weighted precontrast (**D**) indicating edema following white matter tracts (black arrows). 101×101 mm (337×337 DPI).

be secondary to a combination of atrophy on the smaller hemisphere and the presence of edema within the larger hemisphere.[5,8] Interestingly the midline shift was not associated predictably with change in ventricular volume. The appearance of a mass effect, previously defined as deviation of the falx cerebri from midline or compression of a lateral ventricle,[23] was present in the majority of dogs (14/18) and was not associated with infiltrative cell type or necrosis. Mass effect may have been responsible for brain herniation identified in 6 dogs. It is noteworthy that this was a common observation, as a previous report cited that a ''midline shift due to a focal mass effect'' had been reported in granulomatous meningoencephalitis (GME) but not in NLE in the Yorkshire Terrier.[11] Based on our observations, NME in the Pug cannot be differentiated from GME according to the presence or lack of a midline shift or mass effect.

The lateral ventricular size was subjectively abnormal in most dogs (14/18). Presumably the ventricular compression seen in some of the dogs is due to a space occupying effect from edema and inflammatory cell infiltration. Lateral ventricular dilation has been reported previously as a common feature of NME[3–5,7–10,12,14] and this has been suggested to be due to hydrocephalus ex vacuo secondary to white matter loss.[4,8,10] Previous studies have cited high percentages of ventriculomegaly and ventricular asymmetry in normal dogs as well as variation in lateral ventricular volume between breeds.[21,23,27,28] To our knowledge no study has defined the normal ventricular volume in Pugs. Although change in ventricular size was a common feature in the current study of NME, the contribution of normal variation to this asymmetry is unknown.

Description of contrast enhancement in the 3 previous reports of MRI findings in Pugs is either vague or not included.[4,5,17] The mild and variable contrast enhancement present in most of the dogs in the current study is consistent with previous reports of necrotizing encephalitis in other breeds.[8,9,11,14] Our results also agree with previous findings that contrast enhancement in NME is variable and not predictive of survival time.[11] A moderate positive association was found between MRI parenchymal contrast enhancement and the histologic presence of both necrosis ($\kappa = 0.45$; $P = 0.045$) and monocytic inflammation ($\kappa = 0.48$; $P = 0.025$). It has been suggested previously that cavitary lesions, characterized by sharply demarcated T1 hypointensity and T2 hyperintensity without contrast enhancement, are highly indicative of necrotizing encephalitis and can be used to make a presumptive diagnosis.[14,16] However, only 2 dogs in this study had lesions fitting this description. Eight dogs had no sharply defined lesions. In the 10 dogs with sharply

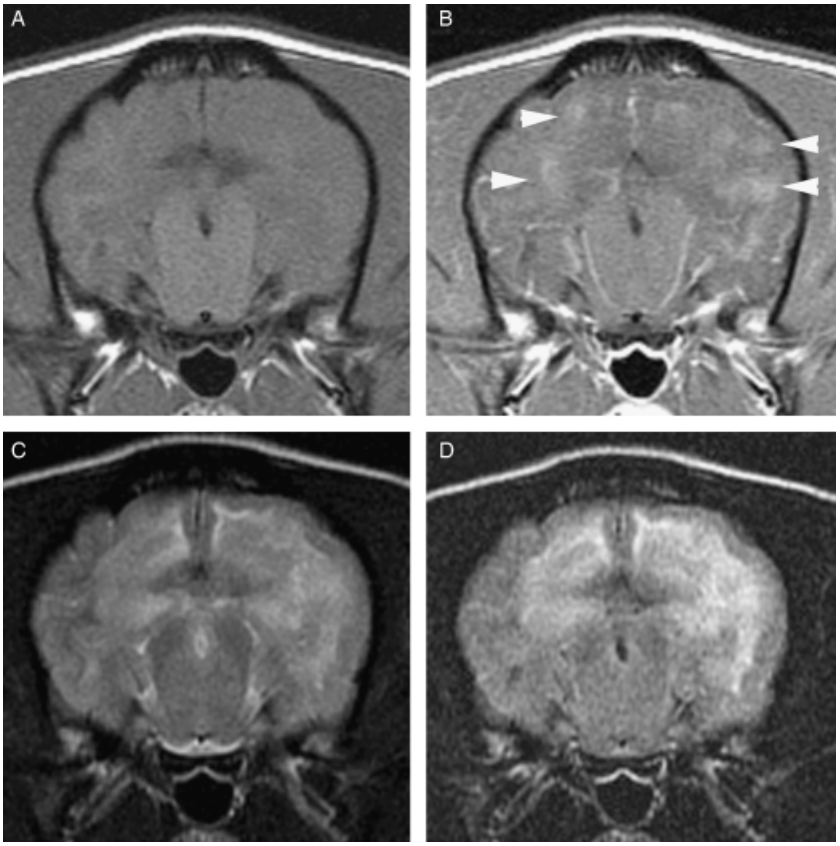

Fig 4. Transverse T1-weighted pre (**A**) and postcontrast (**B**), T2-weighted (**C**), and fluid-attenuated inversion recovery (FLAIR) (**D**) images made at the level of the mesencephalon in a Pug with necrotizing meningoencephalitis. The cerebral lesions are asymmetrically bilateral, isointense on precontrast T1 (A) and hyperintense on T2 and FLAIR (C and D) weighting. Note the mild to moderate enhancement (arrowheads) on postcontrast T1 images (B). 131×131 mm (300×300 DPI).

defined hyperintense lesions on T2-weighting, the majority (8/10) had undefined or diffusely hypointense lesions at the same site on T1-weighted sequences. In addition, the majority of sharply defined lesion margins on T2-weighting occurred at gray-white matter junctions, which may indicate edema extending along the white matter tracts. These findings suggest that the identification of cystic lesions should not be a prerequisite for a presumptive MRI diagnosis of NME in Pugs and may, in fact, be uncommon.

Mild meningeal contrast enhancement was present in half of the dogs. In each dog the pattern was most sug-

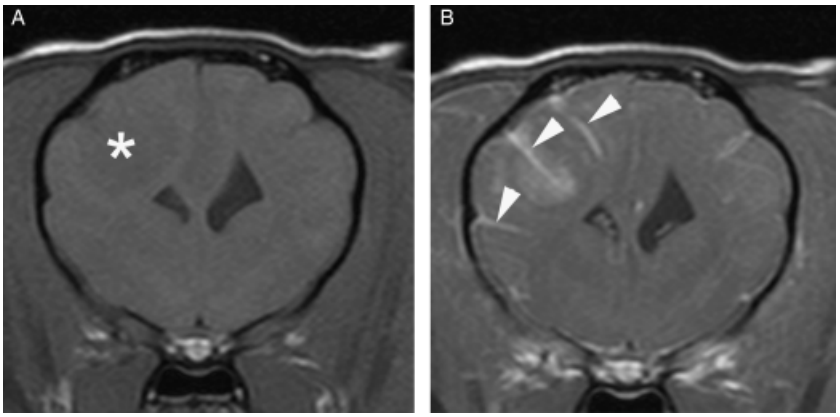

Fig 5. Transverse T1-weighted pre (**A**) and postcontrast (**B**) images made at the level of the caudate nucleus in a Pug with necrotizing meningoencephalitis. The cerebral lesion is slightly hypointense on precontrast images (*). Following contrast administration, there is leptomeningeal enhancement extending into the cerebral sulci (arrowheads). Mild parenchymal contrast enhancement of the lesion is also present. 134×66 mm (300×300 DPI).

Table 1. Agreement between MRI findings and histological lesions for 18 Pugs with NME.

MRI Finding	Histological Finding	Percent Agreement (n)	κ (95% CI)	*P* Value
Parenchymal enhancement	Necrosis	78 (18)	0.45 (0.34, 1.0)	.045
	Neutrophilic inflammation	56 (16)	0.20 (−0.20, 0.60)	.330
	Monocytic inflammation	81 (16)	0.48 (0.06, 0.90)	.025
Meningeal enhancement	Necrosis	56 (18)	0.05 (−0.35, 0.46)	.800
	Neutrophilic inflammation	50 (16)	0 (−0.48, 0.48)	1.0
	Monocytic inflammation	63 (16)	0.25 (−0.07, 0.57)	.131
Herniation	Necrosis	33 (18)	−0.13 (−0.43, 0.18)	1.0
	Neutrophilic inflammation	50 (16)	−0.14 (−0.61, 0.33)	1.0
	Monocytic inflammation	38 (16)	0.09 (−0.11, 0.30)	.383
Mass effect	Necrosis	67 (18)	0.18 (−0.26, 0.63)	.423
	Neutrophilic inflammation	38 (16)	−0.18 (−0.61, 0.25)	1.0
	Monocytic inflammation	75 (16)	0.38 (0, 0.77)	.051
Lesion size greater than median	Necrosis	47 (17)	−0.03 (−0.42, 0.36)	1.0
	Neutrophilic inflammation	33 (15)	−0.36 (−0.85, 0.12)	1.0
	Monocytic inflammation	47 (15)	−0.02 (−0.34, 0.31)	1.0

CI, confidence interval; MRI, magnetic resonance imaging; NME, necrotizing meningoencephalitis.

gestive of leptomeningeal enhancement as characterized by enhancement extension into the cerebral sulci.[20] Leptomeningitis has been reported as an important characteristic of NME in Pugs.[2] The majority of meningeal cellular infiltrates in NME have been identified histologically in the cerebral sulci and longitudinal fissure.[2] Previous reports have cautioned against over interpreting MRI contrast enhancement of the longitudinal fissure, as this might result from contrast pooling in the dorsal sagittal sinus.[20] In the dogs presented here, meningeal contrast enhancement was most identifiable adjacent to the parietal, temporal, and occipital lobes, which suggests that this is a characteristic of an abnormal finding, the absence of meningeal enhancement does not rule out meningitis[29] or inflammatory CSF.[30] Half of the dogs in our study had no meningeal changes on MRI despite histologic conformation of meningeal infiltrate in all dogs. Future studies of NME might benefit from inclusion of specialized MRI sequences, such as diffusion-weighted imaging, which has been shown to be more sensitive for the identification of subtle meningeal changes.[31] While meningeal enhancement has been described in a dog with GME,[20] a previous study of GME found no meningeal enhancement[32] suggesting this could be a characteristic of distinction between NME and GME.

The lesion burden in these dogs was calculated to investigate the prognostic value of MRI in Pugs with NME. This methodology was modeled, in part, on the

Table 2. Descriptive statistics and comparison of survival time based on signalment and MRI lesions in 18 dogs with confirmed NME.

			Time: Onset to MRI (days)		Survival from MRI (days)		Survival from Onset (days)	
Variable	Level	n	Median (range)	*P* Value	Median (range)	*P* Value	Median (range)	*P* Value
Sex	Female	9	6.0 (1, 28)	.863	1.0 (0, 242)	.063	7.0 (1, 253)	.136
	Male	9	4.0 (1, 107)		18.0 (1, 77)		35.0 (3, 127)	
Age	<2 yrs	11	6.0 (1, 76)	.211	1.0 (0, 242)	.425	11.0 (1, 253)	.791
	≥2 yrs	7	2.0 (1, 107)		13.0 (1, 77)		21.0 (3, 109)	
Cerebellar lesions	Yes	4	8.0 (2, 76)	.277	1.5 (0, 51)	.505	9.0 (3, 127)	.798
	No	14	4.0 (1, 107)		7.5 (0, 242)		21.0 (1, 253)	
Caudal brainstem lesions	Yes	3	2.0 (1, 9)	.360	2.0 (1, 34)	1.0	11.0 (3, 35)	.654
	No	15	4.0 (1, 107)		2.0 (0, 242)		21.0 (1, 253)	
Lesions outside prosencephalon	Yes	5	7.0 (1, 76)	.849	2.0 (0, 51)	.849	11.0 (3, 127)	1.0
	No	13	4.0 (1, 107)		2.0 (0, 242)		21.0 (1, 253)	
Mass effect	Yes	12	4.0 (2, 107)	.291	1.5 (1, 242)	.494	25.0 (3, 253)	.437
	No	6	4.0 (1, 9)		7.5 (0, 34)		13.0 (1, 35)	
Herniation	Yes	6	5.5 (2, 107)	.335	10.0 (0, 58)	.750	41.5 (3, 127)	.335
	No	12	4.0 (1, 28)		1.5 (0, 242)		13.0 (1, 253)	
Lesion burden above median	Yes	8	6.5 (2, 107)	.200	1.0 (0, 77)	.370	14.0 (3, 109)	1.0
	No	9	3.0 (1, 76)		13.0 (0, 58)		15.0 (1, 127)	
MRI parenchymal enhancement	Yes	14	4.0 (2, 107)	.233	2.0 (1, 242)	.382	18.0 (3, 253)	.505
	No	4	3.5 (1, 7)		7.5 (0, 34)		14.0 (1, 35)	
Neutrophilic inflammation	Yes	6	2.0 (3, 127)	.469	1.0 (0, 13)	.371	22.0 (1, 253)	.792
	No	10	5.0 (1, 107)		1.5 (0, 77)		14.0 (3, 127)	

MRI, magnetic resonance imaging; NME, necrotizing meningoencephalitis.

current role of MRI in establishing prognosis and its use as a biological marker of disease severity in people with multiple sclerosis .[33,34] For the purposes of this study, lesion burden as a percentage of brain volume was considered to be the most effective way to standardize measurements given the variability of brain size. The volume of the lateral ventricles was subtracted from total brain volume with the intention of estimating the lesion burden of brain parenchyma. This methodology may have underestimated the true effect of the disease in dogs with significant ventriculomegaly secondary to white matter loss. However, as stated above, the normal variability of ventricular size in dogs prevents the ability to account for this factor. Another possible source of error in this method may result from the fact that slice thickness and interslice gap were not uniform between MRI studies. A lack of standardization of these 2 variables could have affected the accuracy of volume estimation. No difference was found in median survival time after MRI when a greater MRI lesion burden was present (1 day if the lesion burden was above the median compared with 13 days if not; $P = .370$). The median survival time from onset of clinical signs was short (18 days) indicating a very poor prognosis. The possible role for MRI in establishing prognosis in Pugs with NME remains undetermined. Future investigation in this area would be beneficial in the continued study of this disease.

Determining the relative specificity of MRI findings in NME is likely to be useful, but the design of this study excluded other intracranial diseases, and therefore the accuracy of MRI for NME diagnosis remains unknown. The hypointense T1 and hyperintense T2 signal changes associated with NME are characteristic of many intracranial disorders, but cannot differentiate between neoplastic and nonneoplastic lesions.[35] For example, cavitary lesions recognized on MRI have been shown to be present in various other diseases, including neoplasia.[35] Mass effect and contrast enhancement have been reported to be associated most commonly with neoplastic diseases,[35] and yet were observed frequently in this group of Pugs with NME. Multifocal cortical gray and white matter distribution with predominance in white matter, variable contrast enhancement, prosencephalic predilection, perilesional edema, and irregular lesion margins were common features described here, but importantly are frequent MRI features of GME.[32] Only meningeal enhancement, mass effect, and ventricular dilation were features frequently seen in these cases of NME that are not commonly associated with GME.[32] A future study comparing the findings of NME, GME, and neoplasia is necessary to determine the predictive value of these findings.

Several MRI features were common to NME in Pugs. While none were determined to be specific for NME, the presence of these findings in a young Pug with acute onset of neurologic signs should increase the confidence in a presumptive diagnosis of NME. MRI lesion burden may be of assistance in determining the duration of NME and potentially in assessing prognosis. Future studies are needed to pursue these considerations.

Footnotes

[a] MRIcro, Chris Rorden, University of South Carolina, Columbia, SC
[b] Epi Info, version 6.04, CDC, Atlanta, GA
[c] SPSS, version 15.0, SPSS Inc, Chicago, IL

Acknowledgments

The authors thank Eric N. Glass (Red Bank Veterinary Hospital, Red Bank, NJ) and Brian Porter (Texas A&M University, College Station, TX) for providing case materials, and Lindsay Boozer (University of Georgia, Athens, GA) for supportive assistance. This project was funded in part by the American Kennel Club Canine Health Foundation, grant #640, Dr Kimberly A. Greer (PI).

No grants or other support have been provided for this paper.

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