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Clinical features, treatment, and outcome of juvenile dogs with meningoencephalitis of unknown etiology

Jack Galer[1] | Alexander K. Forward[1] | Jonathan Hughes[1] | Abbe Harper Crawford[2] | Sebastien Behr[3] | Giunio Bruto Cherubini[4,5] | Ine Cornelis[6] | Emilie Royaux[1]

[1]Davies Veterinary Specialists, Part of Linnaeus Veterinary Ltd, Higham Gobion, Hertfordshire, UK

[2]Royal Veterinary College, Clinical Services Division, Queen Mother Hospital for Animals, Hatfield, UK

[3]Willows Referral Services, Neurology, Highlands Road Shirley, Solihull, UK

[4]Veterinary Teaching Hospital, Mario Modenato, Department of Veterinary Sciences, University of Pisa, Pisa, Italy

[5]Dick White Referrals Ltd, Six Mile Bottom, Cambridgeshire, UK

[6]Department of Small Animal Medicine and Clinical Biology, Ghent University, Merelbeke, Belgium

Correspondence
Jack Galer, Davies Veterinary Specialists, Part of Linnaeus Veterinary Ltd, Higham Gobion, Hertfordshire, UK.
Email: jackagaler@gmail.com

Abstract

Background: The information relating to the outcome specifically for juvenile dogs with meningoencephalitis of unknown etiology (MUE) is lacking.

Objectives: To describe the clinical presentation, diagnostic findings, treatment, and outcome in a cohort of dogs with MUE <52 weeks old.

Animals: Thirty-four client-owned dogs.

Methods: Multicenter retrospective case series. Records from 5 referral centers were searched. Data was extracted from the medical records and referring veterinarians were contacted for survival data if this was not available from the record.

Results: The mean age was 31 weeks; the youngest dog was 11 weeks and 3 dogs were <16 weeks old. Altered mentation (71%), ataxia (44%), seizures (29%), and circling (26%) were the most common presenting complaints. Neuroanatomical localization was to the forebrain (38%), multifocal (35%), brainstem (18%), and cerebellum (12%). Corticosteroid monotherapy (n = 15) and corticosteroid plus cytosine arabinoside (n = 15) were used in equal proportions. Outcome data was available for 26 dogs, 8 (31%) were alive at the time of data collection with a follow-up range of 135 to 2944 days. Death or euthanasia was related to MUE in 17/18 dogs that died during the study period. Kaplan-Meier survival analysis demonstrated a median survival time for all-cause death of 84 days.

Conclusion: The prognosis for MUE in this subset of dogs was considered poor.

KEYWORDS
canine, encephalitis, immune-mediated diseases, immunology, MUO, prognosis, young

1 | INTRODUCTION

Meningoencephalitis of unknown etiology (MUE) is a term used to encompass a group of idiopathic, noninfectious, inflammatory central nervous system (CNS) disorders lacking a definitive histopathological

Abbreviations: CSF, cerebrospinal fluid; GME, granulomatous meningoencephalitis; MRI, magnetic resonance imaging; MUE, meningoencephalitis of unknown etiology; NLE, necrotizing leukoencephalitis; PCR, polymerase chain reaction; TNCC, total nucleated cell count.

diagnosis.[1,2] A diagnosis of MUE is generally made based on a combination of signalment, neurological examination findings, magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) analysis, and negative infectious disease testing. Based on a previous systematic review, recommended inclusion criteria for studies are dogs that are older than 6 months (26 weeks) with single, multiple, or diffuse intra-axial hyperintense lesions on T2-weighted (T2W) MRI; a CSF pleocytosis (total nucleated cell count [TNCC] >5 nucleated cells/L; erythrocyte count <4000 cells/L) with >50% mononuclear cells; and negative test results for infectious diseases.[2]

MUE is the most common cause of meningoencephalitis in dogs in countries where canine distemper virus infection is rare and it is generally considered to mainly affect young to middle-aged, medium to small breed toy and terrier breed dogs. However, dogs of all breeds and ages can be affected.[2,3]

To the author's knowledge only 2 studies have reported MUE in dogs <26 weeks old; both studies reported a minimum age at presentation of 16 weeks but it was not clear how many dogs were this young.[4,5] There are no studies reporting on juvenile dogs (<52 weeks old), with MUE as an individual cohort. In a study including 52 dogs of all ages with MUE, a younger age at presentation was significantly associated with an improved survival time.[6] The authors hypothesized that younger dogs might have less severe inflammation, fewer comorbidities, and that owners might be more willing to treat them long-term compared with older dogs. However, these findings have yet to be corroborated by other studies. Survival times for MUE are highly variable; a systematic review from 2010 reported a range of 1 to 1200 days and a more recent review from 2023 reported a range of 26 to 1834 days.[2,7] This study aims to describe the presentation, MRI findings, treatment, and outcomes of dogs younger than 52 weeks old with MUE.

2 | METHODS

The electronic databases of 5 referral centers were searched, 4 from the United Kingdom and 1 from Belgium, between April 1, 2012 and April 1, 2023 using the terms "meningoencephalitis," "meningoencephalitis of unknown origin" (MUO), "meningoencephalitis of unknown etiology" (MUA), "meningoencephalitis of unknown etiology" (MUE), "granulomatous meningoencephalitis" (GME), "necrotizing meningoencephalitis" (NME), "necrotizing leukoencephalitis" (NLE) and "necrotizing encephalitis" (NE). Dogs were included based on the following criteria: (a) if they were <52 weeks old at the time of presentation; (b) were examined by a board-certified neurologist or neurology resident leading to an intracranial neuroanatomical localization; (c) had focal, multifocal or diffuse T2W intra-axial lesions based on the MRI report from a board-certified radiologist; (d) had an inflammatory CSF (TNCC >5), unless it was unsafe to perform because of raised intracranial pressure; (e) had negative results for infectious disease testing (*Neospora caninum*, *Toxoplasma gondii*, and canine distemper virus) unless infectious disease testing was canceled because of early death or euthanasia. If a histopathological diagnosis was made then CSF sampling and infectious disease testing were not necessary for inclusion. Dogs were excluded if medical records were incomplete.

Information regarding the signalment, history, examination findings, results of diagnostic tests, initial treatment, and outcome were retrieved from medical records. If outcome information was not available from the records, then referring veterinarians were contacted via telephone or email to ascertain if the dog was still alive or not; if the dog was deceased then death or euthanasia was classified as "relating to MUE" or "not relating to MUE." Duration of clinical signs before diagnosis was classified as acute (≤7 days) or chronic (>7 days). Possible neuroanatomical localizations included the forebrain, brainstem, or cerebellum. If 2 or more of these areas were affected then dogs were given a multifocal neuroanatomical localization.

All dogs were anesthetized with protocols depending on the attending anesthetist's preference and magnetic resonance images were obtained with either low- or high-field scanners. Sequences varied but included a minimum of T2W sagittal and transverse, fluid attenuating inversion recovery (FLAIR), T1-weighted (T1W) images pre- and post-administration of paramagnetic contrast medium. Cases were initially included based on their MRI report but images were then reviewed independently by a board-certified radiologist (JH), board-certified neurologist (ER), and a neurology resident (JG) to ensure there was agreement with the original report and inclusion.

Data analysis was performed using a standard statistical software package (GraphPad Prism, GraphPad Software, CA). A Shapiro-Wilk test was used to assess continuous data for normality and if this test was passed then data is presented as mean with SD and if not then it is presented as median with range. Kaplan-Meir survival analysis was performed to calculate the median survival time. Survival was defined as the time from the MRI to death or euthanasia or time from MRI to data collection for those that were still alive when the study was conducted. Short-term follow-up was defined as the first 100 days following diagnosis and survival percentages were assessed at 7, 30, and 100 days as these may represent significant risk periods[8]; long-term follow-up was defined as >100 days.

3 | RESULTS

Seventy-six cases were initially identified from the database searches. After applying the inclusion and exclusion criteria 34 dogs were ultimately included in the study.

3.1 | Signalment

The mean age was 31 weeks (SD ± 12 weeks, *R*: 11-50). Twelve dogs (35%) were <26 weeks old at presentation and 3 dogs (9%) were <16 weeks old. Median weight was 5.3 kg (*R*: 1-21.1). There were similar proportions of males and females with 18 and 16, respectively. One female was neutered and the remainder were entire. Crossbreed dogs were most common in this study (n = 8) followed by Pug (n = 4),

Chihuahua (n = 3), Maltese Terrier (n = 3), Jack Russel Terrier (n = 3), Beagle (n = 2), French bulldog (n = 2), and 1 each of the following breeds: Miniature Pinscher, English Bulldog, Dachshund, Labrador, Japanese chin, Wheaten Terrier, Cocker Spaniel, Golden Retriever, and Irish Terrier. Four of the crossbreeds were poodle crosses and 1 was not stated as a specific cross, the remaining 3 were crosses of Lhasa Apso, Dachshund, and Shih Tzu.

3.2 | Presentation

Presentation was acute in 23/34 (68%) and chronic in 11/34 (32%). The most common presenting complaints were abnormal mentation 24/34 (71%), ataxia 15/34 (44%), seizures 10/34 (29%), and circling 9/35 (26%). The majority of dogs (56%) had received no medications before presentation. Most commonly prescribed medications were non-steroidal anti-inflammatory drugs (21%), antibiotics (21%), and anti-seizure medications (18%). Two dogs (6%) had received corticosteroids 24 hours before presentation, at doses of 0.07 and 0.23 mg/kg. The general physical examination was unremarkable in 27/34 (79%) dogs and pyrexia was identified in 2/34 (6%). Neurological examination findings and neuroanatomical localizations are summarized in Table 1.

3.3 | Diagnostic findings

All but 1 of the dogs had hematology and serum biochemistry performed. Neutrophils (RI 2.9-13.6) were low in 2 dogs, 2.3 and 2.7 $\times$ 10^9/L, and increased in 5 dogs, ranging from 14.5 to 19.9 $\times$ 10^9/L. Hematology and biochemistry results were otherwise normal or showed mild non-clinically relevant changes. Plasma ammonia level was measured in 12/34 (35%) and a bile acid stimulation was performed in 7/34 (21%), all of these were normal. Thoracic radiographs were performed in 2 dogs (6%) to screen for aspiration pneumonia and 2 dogs (6%) had cervical radiographs to evaluate for atlanto-axial instability. An abdominal ultrasonographic examination was performed in 3 dogs (9%); 2 for screening for a portosystemic shunt and 1 for gastrointestinal ulceration.

The lesions identified on MRI are summarized in Table 2. CSF was collected via a cerebellomedullary cisternal puncture in 26/34 (74%) dogs and was deemed to be unsafe because of suspected raised intracranial pressure in the remainder. CSF protein concentration was raised in 19/20 dogs in which protein analysis was performed, with a median of 64 mg/dL (*R*: 10-207). The median CSF TNCC was 119.5/μL (*R*: 8-1077). Cytological analysis revealed a mononuclear pleocytosis in 20/26 (77%), neutrophilic pleocytosis in 4/26 (15%), and mixed pleocytosis in 2/26 (8%). *Neospora caninum* was tested for in 31/34 (91%) dogs (via serology for 17 and CSF PCR for 14), *Toxoplasma gondii* was tested for in 28/34 (82%) dogs (via serology for 16 and CSF PCR for 12), and canine distemper virus CSF PCR was performed in 18/34 (53%) dogs; all were negative. A histopathological diagnosis was reached in 2 dogs; 1 case was confirmed as GME via post-mortem examination and 1 as NME via a surgical brain biopsy.

TABLE 1 Summary of neurological examination findings.

Neurological deficits (most common)	
Abnormal mentation	24/34 (71%)
Postural reaction deficits	24/34 (71%)
Menace response deficits	23/34 (68%)
Bilateral	14
Unilateral	9
Ataxia	18/34 (53%)
Vestibular	10
Proprioceptive	8
Cranial nerve deficits other than menace	16/34 (47%)
Circling	15/34 (44%)
Head turn	8/34 (24%)
Head tilt	7/34 (21%)
Neck pain	6/34 (18%)
Neuroanatomical localization	
Forebrain	13/34 (38%)
Multifocal	12/34 (35%)
Brainstem	6/34 (18%)
Cerebellum	4/34 (12%)

TABLE 2 Summary of MRI findings.

Lesion distribution	
Multifocal	21/34 (62%)
Focal	11/34 (32%)
Diffuse	2/34 (6%)
Lesion location	
Cerebrum	28/34 (82%)
Thalamus	19/34 (56%)
Midbrain	15/34 (44%)
Pons	13/34 (38%)
Medulla oblongata	12/34 (35%)
Cerebellum	12/34 (35%)
Gray matter	27/34 (79%)
White matter	25/34 (74%)
Contrast enhancement of lesion(s)	25/34 (74%)
Presence of herniation (all types)	13/34 (38%)

3.4 | Treatment

Corticosteroid monotherapy was used in 15/34 (44%) dogs and corticosteroid with cytosine arabinoside (cytarabine) was used in 15/34 (44%) dogs. All dogs received dexamethasone (0.1-0.4 mg/kg IV Q24h) while hospitalized before transitioning to oral corticosteroid if they survived to discharge. Other immunosuppressive treatments in combination with corticosteroids included ciclosporin (n = 2), cytarabine with ciclosporin (n = 1), and lomustine with cytarabine (n = 1). For those that survived to discharge the median starting dose of oral

prednisolone was 2 mg/kg/24 h (*R*: 0.83-3.48); 18 dogs were treated with doses of ≥2 mg/kg/24 h, 8 dogs received doses of 1 to 1.99 mg/kg/24 h and 1 dog received a dose of <1 mg/kg/24 h. This dog was started on 0.83 mg/kg Q24h PO while awaiting the results of infectious disease testing and showed resolution of clinical signs within 1 month and the dose was then gradually tapered. Two dogs were discharged with dexamethasone at doses of 0.2 mg/kg/24 h and 0.08 mg/kg/24 h PO. Corticosteroids were tapered at clinician's discretion with a median duration between dosage reductions of 3 weeks (*R*: 1-8). Timing for starting cytarabine was variable with 12 dogs receiving it during hospitalization and the remaining 5 after discharge. Total doses of 200 mg/m^2 were given in all 17 dogs. Ten dogs received cytarabine intravenously, as an infusion over 8 hours ($n = 8$) or as an infusion over 24 hours (n = 2); 5 dogs received subcutaneous injections of 50 mg/m^2 every 12 hours for 4 doses; the route of administration was not stated in 2 dogs. Seven dogs continued to receive a tapering course of cytarabine via subcutaneous injections. Ciclosporin was prescribed at a dose of 5 mg/kg SID PO. The 1 dog that received lomustine received a single dose of 10 mg (18.5 mg/m^2) while hospitalized but no further doses after discharge. Anti-seizure medications were prescribed for 15/34 (44%) dogs. Ten dogs (29%) presented with seizures and an additional 3 (9%) developed them while hospitalized; 2 dogs were treated with anti-seizure medications despite not having exhibited seizure activity, reasons for this were not stated in the clinical record. Six dogs received phenobarbital, 5 dogs received levetiracetam, and 4 dogs received both phenobarbital and levetiracetam. Seven dogs received clindamycin until tests for *Toxoplasma gondii* and *Neospora caninum* were confirmed to be negative.

3.5 | Outcome

Adequate detail about short-term (≤100 days) outcome was available from the clinical records of 30/34 dogs. Five dogs (15%) did not survive to hospital discharge. Two dogs were euthanized because of lack of clinical improvement, 1 was euthanized after failure of return of spontaneous ventilation following a respiratory arrest, 1 did not recover from general anesthesia following the MRI scan and 1 dog died secondary to seizures and raised intracranial pressure. Six dogs died or were euthanized within the first 7 days following diagnosis (80% surviving), a further 5 dogs up to day 30 (63% surviving), and 3 dogs up to day 100 (53% surviving). Suspected relapses were noted in the records of 10/29 (29%) dogs that survived to discharge. None of these were confirmed with repeated MRI and CSF analysis. One dog had an increase in seizure frequency and 1 dog developed new seizures, the remainder had deterioration or recurrence of neurological deficits. Median time from discharge to relapse for these dogs was 69 days with a range of 7 to 720 days. Two dogs were reported to have relapsed twice, 1 dog at 92 days and then 720 days, and the other dog at 73 days and then 110 days. Ten relapses occurred during treatment and 2 after cessation of treatment. At the time of data collection long term (>100 days) outcome information was available for 16 dogs, 8 were still alive with a median follow-up of 752 days (*R*: 135-2944), 4 dogs died or were euthanized beyond 100 days, and 4 were lost to follow up at varying times beyond this point. One dog in our study was euthanized because of a complication attributed to immunosuppressive therapy which was a septic non-healing wound on the leg and then aspiration pneumonia; this dog was receiving corticosteroids as a monotherapy. MUA was stated as the cause of death or euthanasia in 17/18 dogs. One dog died because of respiratory compromise 839 days after presentation and was reported to be neurologically normal, but the dog had a suspected relapse 4 months before this and been restarted on prednisolone and cytarabine. Seizures were stated as the specific reason for death or euthanasia in 7/18 (39%). Median survival time for all-cause death was 84 days (*R*: 0.08-2944 days; Figure 1).

4 | DISCUSSION

This study reports on dogs younger than 16 weeks old with MUE. The clinical presentation, diagnostic findings, and treatment choices were similar to that reported for dogs of all ages although this could be biased by inclusion criteria. The median survival time was poor compared with studies including dogs of all ages so this provides useful information for vets to provide to owners with regards to prognosis in this subset of dogs.

Three dogs were <16 weeks old at presentation. MUE typically affects small breed dogs though any breed can be affected. Those represented in our study were comparable with the breed distributions in previous reports.[2,9-11] Four dogs (12%) would be considered large breeds when reaching their expected adult weight which is a lower proportion compared to the 25% reported by Cornelis et al. (2016, p. 3). Crossbreeds were the most commonly represented though the majority of there were crosses of breeds typically affected by MUE. Dogs with NE typically present at a younger age compared to those with GME; Pugs, Chihuahua's, and Maltese terriers are predisposed to this form of MUA which may be an explanation as

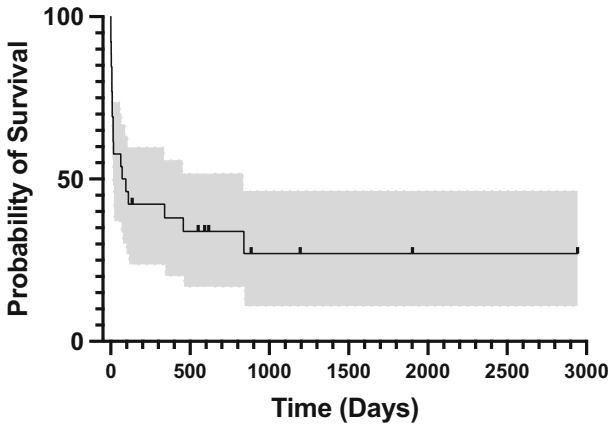

FIGURE 1 Kaplan-Meier survival curve with 95% confidence bands for all-cause death for juvenile dogs with MUE. The small bars represent censored observations.

to why these breeds made up a significant portion of our cohort.[2] There was an equal number of males and females in our study. Granger et al reported a higher female-to-male ratio in a systematic review but recent large cohort studies reported equal proportions of males and females.[5,10] The presenting signs, neuroanatomical localizations, and CSF findings in our study were also comparable with the findings in 2 of the largest cohort studies on dogs with MUE to date.[5,10]

Negative results for infectious disease testing was an inclusion criteria for our study, in the absence of a histopathological diagnosis. *Neospora caninum* was excluded in all but 1 dog which had a histopathological diagnosis of GME and 2 dogs that had the test canceled because of early death or euthanasia; we cannot definitively rule out that these dogs had *Neospora caninum* but excluding them based on a lack of testing would have introduced a selection biased in favor of less severely affected dogs. *Toxoplasma gondii* was not tested for in 18% of the dogs in our study. However, the prevalence of active infection in dogs with encephalitis in the United Kingdom is reported to be extremely low at 0.25% so it was felt to be unlikely that cases with *Toxoplasma gondii* were included erroneously.[12] Canine distemper virus was tested for in 53% of dogs; a canine distemper virus PCR was run in 83% of dogs <26 weeks old and in 36% of those older than 26 weeks old. Post-vaccinal distemper encephalitis has been reported in 2 border collies at 5 and 27 days post-vaccination and both dogs were euthanized within 4 days.[13] Distemper encephalitis is associated with a poor prognosis and dogs are typically euthanized soon after the presentation because of seizures that are poorly responsive to medications.[13,14] A 19-week-old Chihuahua in our study presented 32 days after vaccination with seizures, obtundation, and tetraparesis and was not tested for distemper; this case was treated with dexamethasone, cytarabine, and diazepam which resulted in cessation of the seizures, but the dog failed to improve otherwise and was euthanized within 3 days. A post-vaccinal encephalitis cannot be excluded in this dog but was felt to be unlikely based on the dogs' signalment and clinical course. All other dogs in our study that were presented within or around 1 month after vaccination had a negative distemper PCR. Suspected tick-borne meningoencephalomyelitis has recently been reported in a small number of dogs in the United Kingdom but remains a very rare presentation.[15] Tick-borne encephalitis is more prevalent in northern Europe but to our knowledge, no reports have emerged of this causing neurological signs in dogs in Belgium.[16,17] Fungal encephalitis was reported in 3/1140 dogs with inflammatory central nervous system disease in a large study of dogs in England and remains a very rare presentation.[18] Testing for tick-borne encephalitis virus and fungal infections was not required for inclusion in this study so we cannot exclude that dogs that showed a poor response to immunosuppressive treatment had either of these as an underlying infectious cause for their encephalitis. Clinicians should be cognizant of the relative prevalence of infectious diseases within their geographical location and exclude these as an underlying cause of encephalitis.

Corticosteroid monotherapy and corticosteroid with adjunctive cytarabine were used in equal proportions for the treatment of the dogs in this study. Neutropenia is a documented side effect of cytarabine treatment and immunosuppressive doses of corticosteroids can increase the risk of developing infections so in combination these could pose an increased risk of microbiological infections in juvenile dogs.[19-21] Only 1 dog in our study was reported to have developed a significant microbial infection, resulting in euthanasia, whilst receiving corticosteroids; however, because of incomplete follow-up information complications may have been underestimated.

Survival was used as the main outcome measure in this study which may be flawed as it does not account for dogs that have significant ongoing neurological deficits that may be affecting quality of life. Recently a neurodisability scale has been proposed for dogs with MUE which aims to assess outcomes in more detail.[22] As this was a retrospective study there were very few instances where follow up neurological examinations were recorded and as such, it was not possible to retrospectively apply such a disability scale.

Relapse rate can also be considered as an outcome measure and 29% of dogs surviving to discharge in our study were suspected to have had a relapse based on a recurrence or deterioration in clinical signs. One dog in our study had a repeat MRI performed 600 days after diagnosis and 6 months after cessation of prednisolone because of poorly controlled seizures; MRI scan and CSF analysis were unremarkable and the dog was successfully managed with alterations in the anti-seizure medication protocol so this was not classified as a relapse. Two of the 10 relapse cases were restarted on immunosuppressive medications because of the worsening of seizures in 1 dog and development of new seizures in the other. As repeat investigations were not performed it was conceivable that these dogs developed epilepsy and were not genuine relapses of MUE. Detailed long-term follow-up was missing for a large proportion of the dogs in our study and so it is possible that the relapse rate was underestimated. Relapse rates have been inconsistently reported in studies on MUE but percentages vary from 10% to 65% with variation based on the timing of follow-up, treatment choice, and whether animals were still receiving treatment or not.[10,23,24]

The median survival time of 84 days was considered to be poor when compared with a recent review article which evaluated 15 studies including dogs of all ages.[7] One study reported a median survival time of 26 days, the other 14 reported median survival times higher than that of our study, ranging from 250 to 1834 days with various treatment protocols.[7,23] Several time points have been suggested as potential at-risk periods. A retrospective study including 116 dogs with MUE reported 26% died within the first 7 days.[5] A prospective study investigating treatments for MUE found that 30% died within the first 30 days of treatment and all but 1 dog survived more than 12 months beyond this time point.[25] Another study reported 56% of dogs died within the first 3 months and beyond this time point no dogs died within an 18 month follow-up period.[23] A more recent retrospective study investigating prognostic indicators at these specific time points reported survival percentages at 7, 30, and 100 days as 90%, 77%, and 69%, respectively.[8] Percentages in our study were 80%, 60%, and 53% for the same time periods. Oliphant et al found that a younger age at presentation was significantly associated with

longer survival time. The median ages in the 2 groups (those with midline shift and those without) in this study were 4.1 and 6.4 years with the youngest being 39 weeks.[6] To the author's knowledge a younger age at presentation has not been found to influence survival in other studies and our results suggest that juvenile dogs have a shorter survival time.

Our study has several limitations, largely because of being retrospective and including multiple centers. Treatment protocols were nonstandardized and at the discretion of the clinician in charge of the case. Choice of treatment and dosing may have affected outcome though to date no consensus has been reached on the optimal treatment regime for MUE.[7] There was a lack of histopathological diagnoses so we cannot exclude that cases with an infectious or neoplastic etiology were included erroneously and these could have been the dogs that had a worse outcome. Long-term outcome data was not available for all cases and only limited information was obtained about survival. We did not include a control group of "non-juvenile" dogs for statistical comparison which may be seen as a limitation.

In conclusion, juvenile dogs with MUE appear to have similar signalment, diagnostic findings and outcomes compared with dogs of more typical ages with this disease. Despite the rare presentation, MUE should remain a differential diagnosis in juvenile dogs presenting at an age of <16 weeks. The median survival of juvenile dogs was low compared to studies including dogs of all ages but it is challenging to make direct comparisons to other studies because of the lack of standardization in treatment protocols and follow-up.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Approved by the Royal College of Veterinary Surgeons ethical review panel, reference 2022-080-Galer.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

ORCID

Jack Galer https://orcid.org/0000-0002-7620-3635
Abbe Harper Crawford https://orcid.org/0000-0003-2176-5873
Emilie Royaux https://orcid.org/0009-0004-8463-3063

REFERENCES

1. Adamo PF, Rylander H, Adams WM. Ciclosporin use in multi-drug therapy for meningoencephalomyelitis of unknown aetiology in dogs. *J Small Anim Pract*. 2007;48(9):486-496.
2. Granger N, Smith PM, Jeffery ND. Clinical findings and treatment of non-infectious meningoencephalomyelitis in dogs: a systematic review of 457 published cases from 1962 to 2008. *Vet J*. 2010; 184(3):290-297.
3. Cornelis I, Volk H, De Decker S. Clinical presentation, diagnostic findings and long-term survival in large breed dogs with meningoencephalitis of unknown aetiology. *Vet Rec*. 2016;179(6):147.
4. Levine JM, Fosgate GT, Porter B, Schatzberg SJ, Greer K. Epidemiology of necrotizing meningoencephalitis in Pug dogs. *J Vet Intern Med*. 2008;22(4):961-968.
5. Cornelis I, Volk HA, Van Ham L, et al. Prognostic factors for 1-week survival in dogs diagnosed with meningoencephalitis of unknown aetiology. *Vet J*. 2016;214:91-95.
6. Oliphant BJ, Barnes Heller HL, White JM. Retrospective study evaluating associations between midline brain shift on magnetic resonance imaging and survival in dogs diagnosed with meningoencephalitis of unknown etiology. *Vet Radiol Ultrasound*. 2017;58(1):38-43.
7. Jeffery N, Granger N. New insights into the treatment of meningoencephalomyelitis of unknown origin since 2009: a review of 671 cases. *Front Vet Sci*. 2023;10.
8. Lawn RW, Harcourt-Brown TR. Risk factors for early death or euthanasia within 100 days of diagnosis in dogs with meningoencephalitis of unknown origin. *Vet J*. 2022;287:105884.
9. Brady SL, Woodward AP, le Chevoir M. Survival time and relapse in dogs with meningoencephalomyelitis of unknown origin treated with prednisolone and ciclosporin: a retrospective study. *Aust Vet J*. 2020; 98(10):491-498.
10. Paušová TK, Tomek A, Šrenk P, Belašková S. Clinical presentation, diagnostic findings, and long-term survival time in 182 dogs with meningoencephalitis of unknown origin from Central Europe that were administered glucocorticosteroid monotherapy. *Top Companion Anim Med*. 2021;44:100539.
11. Song JH, Yu DH, Lee HC, et al. Evaluation of treatment with a combination of mycophenolate mofetil and prednisolone in dogs with meningoencephalomyelitis of unknown etiology: a retrospective study of 86 cases (2009-2017). *BMC Vet Res*. 2020;16(1):192.
12. Coelho AM, Cherubini G, De Stefani A, et al. Serological prevalence of toxoplasmosis and neosporosis in dogs diagnosed with suspected meningoencephalitis in the UK. *J Small Anim Pract*. 2019;60(1):44-50.
13. Fairley RA, Knesl O, Pesavento PA, Elias BC. Post-vaccinal distemper encephalitis in two border collie cross littermates. *N Z Vet J*. 2015; 63(2):117-120.
14. Galán A, Gamito A, Carletti BE, et al. Uncommon acute neurologic presentation of canine distemper in 4 adult dogs. *Can Vet J*. 2014; 55(4):373-378.
15. Gonzalo-Nadal V, Kohl A, Rocchi M, et al. Suspected tick-borne flavivirus meningoencephalomyelitis in dogs from the UK: six cases (2021). *J Small Anim Pract*. 2024;65(2):132-143.
16. Kleeb C, Golini L, Beckmann K, Torgerson P, Steffen F. Canine tick-borne encephalitis: clinical features, survival rate and neurological sequelae: a retrospective study of 54 cases (1999–2016). *Front Vet Sci*. 2021;8:8.
17. Pfeffer M, Dobler G. Tick-borne encephalitis virus in dogs – is this an issue? *Parasit Vectors*. 2011;4:59.
18. Gonçalves R, De Decker S, Walmsley G, et al. Inflammatory disease affecting the central nervous system in dogs: a retrospective study in England (2010-2019). *Front Vet Sci*. 2021;8:819945.
19. Cardillo L, Piegari G, Iovane V, et al. Lifestyle as risk factor for infectious causes of death in young dogs: a retrospective study in southern Italy (2015-2017). *Vet Med Int*. 2020;2020:6207297.
20. Viviano KR. Glucocorticoids, cyclosporine, azathioprine, chlorambucil, and mycophenolate in dogs and cats: clinical uses, pharmacology, and side effects. *Vet Clin North Am Small Anim Pract*. 2022;52(3):797-817.
21. Guillen A, Finotello R, Wynne P, et al. Toxicity of cytarabine constant rate infusion in dogs with high-grade non-Hodgkin lymphoma with

bone marrow or central nervous system involvement. *Aust Vet J*. 2020;98(3):69-78.
22. Gonçalves R, Maddox TW, Phillipps S, et al. Development of a reliable clinical assessment tool for meningoencephalitis in dogs: the neurodisability scale. *J Vet Intern Med*. 2023;37(3):1111-1118.
23. Lowrie M, Smith PM, Garosi L. Meningoencephalitis of unknown origin: investigation of prognostic factors and outcome using a standard treatment protocol. *Vet Rec*. 2013;172:527.
24. Stee K, Broeckx BJG, Targett M, Gomes SA, Lowrie M. Cytosine arabinoside constant rate infusion without subsequent subcutaneous injections for the treatment of dogs with meningoencephalomyelitis of unknown origin. *Vet Rec*. 2020;187(11):e98.
25. Smith PM, Stalin CE, Shaw D, Granger N, Jeffery ND. Comparison of 2 regimens for the treatment of meningoencephalomyelitis of unknown etiology. *J Vet Intern Med*. 2009;23(3):520-526.

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