



Magnetic Resonance Imaging and Histopathological Findings as Diagnostic Tools for Detection of Canine Distemper Virus Infection in Dogs

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ABSTRACT

Background: The canine distemper virus (CDV) causes a persistent infection within the central nervous system, resulting in a progressive, multifocal demyelinating disease. Magnetic resonance imaging (MRI) and brain histopathology are important correlates for evaluating disease progression in canine distemper. This study aims to assess magnetic resonance imaging and histopathological findings of canine distemper virus infection in dogs.

Methods: This study included 82 dogs with a nervous form of CD virus, confirmed by reverse transcriptase polymerase chain reaction (RT-PCR), at the College of Veterinary Sciences and Animal Husbandry, Central Agricultural University, Selesih, Aizawl, Mizoram, between March 2022 and July 2025. Dogs with clinically positive canine distemper virus infection were subjected to magnetic resonance imaging of the brain under general anaesthesia and histo-pathological examinations.

Result: The MRI findings of the T1W axial image showed hypointense signal in the right temporal lobe with a corresponding area showing hyperintense signal on T2W with loss of gray-white matter differentiation in CD-infected dogs. Gross pathology of the brain showed haemorrhages on the meninges and histopathological examination revealed spongiosis and degenerative ischemic changes in the cerebellar hemisphere, microgliosis and loss of neurons in the cerebrum in all the examined dogs.

Key words: Canine distemper virus, Dogs, Histo-pathology, MRI.

INTRODUCTION

Canine distemper (CD) is a highly contagious viral disease of dogs caused by canine distemper virus (CDV), which belongs to the family Paramyxoviridae and genus Morbilli virus. Canine distemper virus (CDV) infection is characterised by a systemic and nervous form as well as virus persistence in selected organs, including the central nervous system and lymphoid tissue. Canine distemper virus (CDV) is responsible for high morbidity and mortality in young dogs worldwide. Canine distemper is most likely to affect dogs when they are crowded, stressed, immunologically susceptible and directly or indirectly exposed to infected wildlife (Schumaker *et al.*, 2012). Dogs that do not receive routine vaccinations according to established guidelines are at high risk (Dodds, 2021) and dogs from shelters and dog rescue organisations are particularly vulnerable (Willi *et al.*, 2015). In dogs, CDV can result in subclinical infection, gastrointestinal signs and/or respiratory signs, frequently with central nervous system (CNS) involvement (Freire *et al.*, 2025). The course and outcome of the disease and the type of neuropathological presentation are directly related to the virus strain and host factors such as age and the immunocompetence of the affected animal (Ranjithkumar and Dey, 2021). Multifocal demyelination of white and grey matter (Mahajan *et al.*, 2018) is a characteristic lesion in the neurological form of the disease in dogs and can be attributed to of the excessive

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production and accumulation of free radicals during viraemia (Vandevelde and Zurbriggen, 2005). Once neurologic signs become evident, the prognosis is commensurately poor and euthanasia is frequently justified (Ranjithkumar and Dey, 2021).

The identification of pathological changes is the gold standard for therapeutic interventions of the disease but has intrinsic limitations owing to the limited availability of autopsy and biopsy tissue. Hence, MRI has gained a leading role in the assessment of CDV infection in dogs because it allows doctors to obtain an ante mortem picture of the degree of CNS involvement. A number of correlative pathological and MRI studies have helped to define *in vivo* pathological substrates of CDV in CNS lesions and normal-appearing white matter. These studies have identified many of aspects of pathophysiology that were previously neglected, including grey matter involvement and vascular pathology. The prominent histopathological hallmark of canine distemper virus infection is demyelination. MRI can be a valuable tool for diagnosing canine distemper in dogs, particularly in detecting brain lesions associated with the disease. MRI findings, such as hyperintense lesions in the cerebellum and brainstem and loss of contrast between grey and white matter can correlate with demyelination, a key characteristic of acute canine distemper virus infection (Bathen-Noethen *et al.*, 2008). MRI and histopathology findings show a strong correlation, particularly in the brain, where both techniques reveal demyelination, a key characteristic of the disease. In this paper, we describe regions in which pathological and MRI assessment have provided concordant findings and regions with discrepancies for which additional research is needed and discuss emerging pathological and MRI findings that might together enhance the understanding of disease pathophysiology and help to identify reliable *in vivo* markers to monitor different pathological aspects of canine distemper virus infection in dogs.

MATERIALS AND METHODS

Place of work/location

The study was conducted in the Veterinary Clinical Complex, College of Veterinary Sciences and Animal Husbandry, Central Agricultural University, Selesih, Mizoram and Veterinary Polyclinic Hospital, Khatla, Aizawl and various private pet clinics of Aizawl, Mizoram state (Fig 1).

Ethics statement

This research was conducted under the approval of the Institutional Animal Ethics Committee, College of Veterinary Sciences and Animal Husbandry, Central Agricultural University, Selesih, Aizawl, Mizoram (1476/GO/Re/SL/11/CPCSEA, CVSC/CAU/IAEC/21-22/P-35).

Selection of animals

This study included 82 dogs that tested positive via rapid diagnostic kit and RT-PCR and were brought for treatment

with nervous symptoms to the Veterinary Clinical Complex, Veterinary Polyclinic in Khatla and private veterinary clinics in Aizawl, Mizoram. All the dogs died during the treatment period and a post-mortem with histology examination of the brain was carried out.

Screening by rapid CDV antigen test kit

All the suspected cases were screened by a commercially available Canine CDV rapid antigen detection kit (Bionote, cat. No. RG1103DD, Gyeonggi-do), Korea, as per the manufacturer's instructions.

Magnetic resonance imaging (MRI) examination

Anatomical MRI was performed (Ingenia Prodiva CS 1.5 Tesla, Philips) under general anaesthesia. Anaesthesia was initiated with diazepam (Diazepam®; Ratiopharm) and propofol (Narcofol®; cp-Pharma) and maintained using isoflurane and oxygen (Isofluran®; Baxter). Transverse, sagittal and dorsal plane images were obtained in T1 (time to repeat (TR) = 330 ms and time to echo (TE) = 12 ms) and T2 (TR = 3458 ms and TE = 96 ms) sequences in an extremity coil.

Necropsy and histopathological examination

Post-mortem and histopathological examinations were carried out according to standard procedures described by Luna (1968) and Bancroft and Gamble (2008) to determine the etiological factors. Tissue fragments of myocardium, lung, pancreas, liver, bladder, kidney and brain tissues that presented macroscopic alterations were collected. The fragments were fixed in 10% buffered formalin for 48 hours and routinely processed for the preparation of histological slides stained with Hematoxylin and Eosin (HE) (Tolosa *et al.*, 2003). The sections were examined and photographed under a light microscope.

RESULTS AND DISCUSSION

Canine distemper antigen was detected from the study animals. Out of the total 200 dogs, the antigen was detected from 41% (82/200) of the dogs sampled. No reliable information could be obtained on the vaccination status of

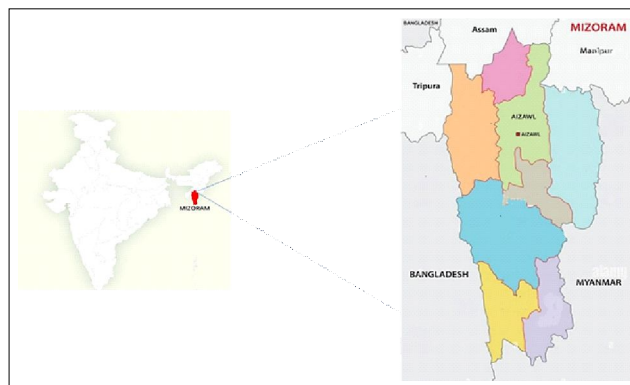


Fig 1: Red box in the Mizoram map indicates the study area.

the vaccinated cases (completed or single dose), as either the animals were abandoned at the clinic or the animal owners were not informed. Based on anamnesis and clinical findings, all the cases (100%) had nervous system infection alone with the involvement of respiratory and digestive systems. In these cases, hyperkeratosis had also developed on the footpad and tip of the nose. During the treatment period, all the animals died.

MRI findings

T1W axial image showed an ill-defined, focal hypointense signal in the right temporal lobe with a corresponding area and T2W axial image showed a hyperintense signal with loss of grey-white matter differentiation (Fig 2A and 2B). T1W axial image at the level of the cerebellum showed a hypointense signal in the left cerebellar hemisphere. The

corresponding T2W images showed hyperintense signal in the affected area (Fig 3A and 3B). The findings showed an abnormal T2 hyperintense signal in the cerebellum. T1W axial image at the level of the cerebellum showed hypointense signal (Fig 4A and 4B). MRI scan was performed 3-5 days after the last episode of seizure and abnormal findings were confirmed in all the scans. Abnormal T1/T2 signal lesions/areas were observed in both the temporal lobes and cerebellum of the affected dogs. The lesions were distributed asymmetrically, involving both cortical grey and subcortical white matter and these lesions were observed in all the imaging planes. The primarily affected part in the forebrain was the temporal lobe (Fig 2A and 2B) and the cerebellum in dogs (Fig 3A and 3B). All lesions were hypointense in T1-weighted images and hyperintense in T2-weighted images relative to unaffected brain parenchyma.

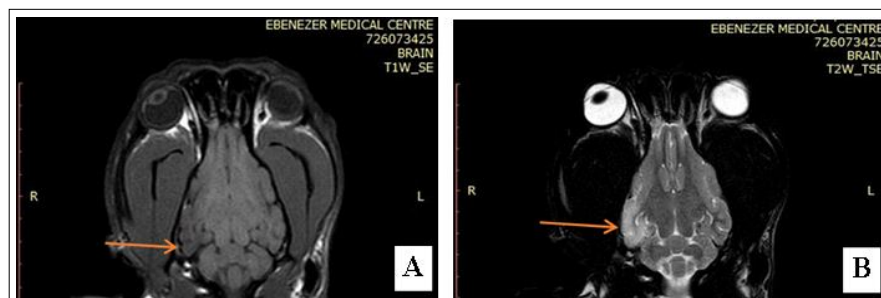


Fig 2: TIW (A) axial image shows focal, ill-defined, hypointense signal (arrow) in the right temporal lobe with corresponding area showing hyperintense signal (arrow) on T2W (B) with loss of gray-white matter differentiation.

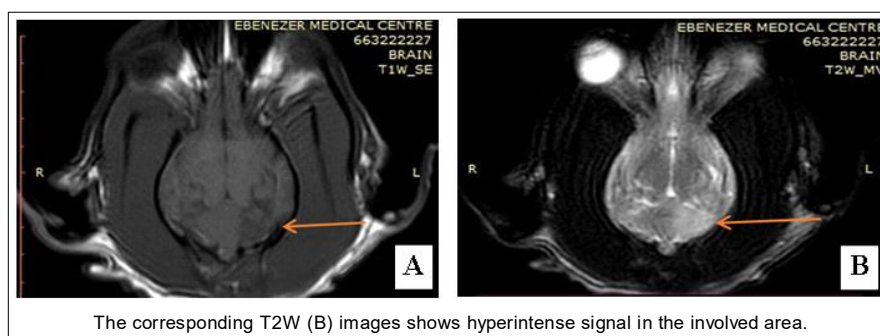


Fig 3: TIW (A) axial image at the level of the cerebellum shows ill-defined, focal hypointense signal in the left cerebellar hemispheres.

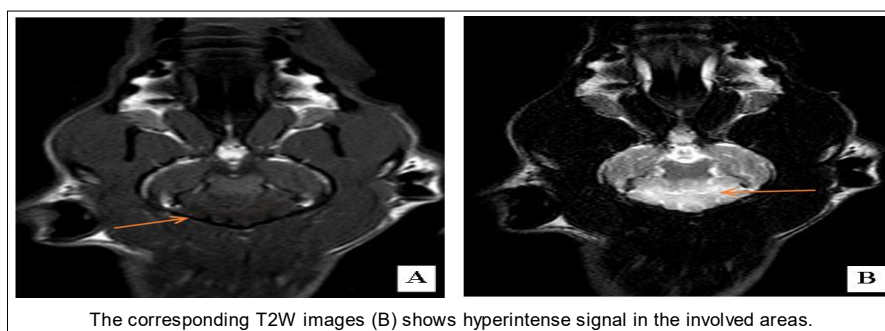


Fig 4: TIW axial image (A) at the level of the cerebellum, diffuse, ill-defined, hypointense signal is seen in both cerebellar hemispheres.

Gross pathology and histopathology

Gross pathology of the brain showed haemorrhages on the meninges of the brain (Fig 5). Histopathological examination revealed spongiosis, demyelination and degenerative ischemic changes in the cerebellar hemisphere of all examined dogs (Fig 6A). The cerebrum showed microgliosis and neuronal loss (Fig 6B), while the white matter exhibited degenerating neurons and hemorrhages (Fig 6C). Extensive microgliosis and astrogliosis were also evident in the white matter (Fig 6D).

Canine distemper, one of the most fatal diseases in dogs, remains an important viral disease in the veterinary field. To provide timely medical treatment that preserves the life of the infected dog (especially if neurological signs are present), it is essential to have an easy-to-use assay that can rapidly and accurately detect CDV. To the best of the authors' knowledge, although neurological involvement is a critical aspect of canine distemper, no previous studies have particularly investigated its neurological form using MRI in India.



Fig 5: Brain showing haemorrhages on the meninges (arrow).

Both pathological and MRI data suggest that CNS lesions evolve differently during early versus chronic disease phases and, within each phase, different types and stages of demyelinating activity are evident pathologically. In this study, histopathology showed lesions in the cerebrum, cerebellum and white matter, with the lesions characterised by spongiosis and degenerative ischemic changes in the cerebellar hemisphere, microgliosis and loss of neurons in the cerebrum and degenerating neurons and haemorrhages in the white matter in all the examined dogs. Extensive microgliosis and astrogliosis were seen in the white matters which are consistent with the inflammatory response typical of the chronic phase of the disease (Destri *et al.*, 2020). Neurological signs are common in animals with CDV and were observed both clinically and pathologically in this study. Intranuclear eosinophilic inclusion bodies observed in the astrocytes localized to the demyelinated areas. The microscopic findings of the nervous system agreed with the results of previous studies (Klemens *et al.*, 2019; Çomaklı *et al.*, 2020). Consistent with the findings of CDV, MRI in these diseases is also characterised by hyperintense lesions in T2-weighted images (Mariani *et al.*, 2001). The presence of hypointense lesions on T1W images, particularly when correlated with T2W hyperintensities, can be a significant indicator of CDV-related neurological disease in dogs. These findings can help veterinarians diagnose and assess the severity of the infection and guide treatment decisions. Regarding the MRI appearance, the authors suspect that the T2W hyperintense lesions represent areas of increased water content due to demyelination and that contrast enhancement is secondary to a perivascular inflammatory infiltrate.

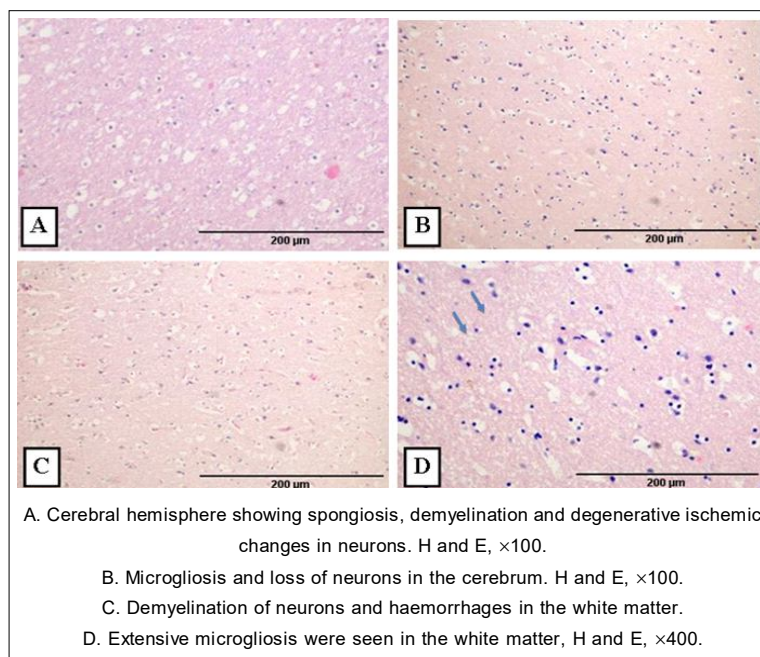


Fig 6: Histopathological findings of the brain of canina distemper-infected dogs.

Distemper is the only acquired demyelinating disease reported in dogs and has been used as a model for demyelinating human diseases such as multiple sclerosis, neuromyelitis optica spectrum disorder, acute disseminated encephalomyelitis and myelin oligodendrocyte glycoprotein encephalomyelitis (Miki, 2019). MRI characteristics of demyelinating disorders in human beings have been reported as having different appearances, with the most common being ovoid T2W hyperintense lesions (Miki, 2019) similar to the ones observed in the present study. This may be due to the disappearance of the myelin sheath and subsequent replacement with water, causing hyperintensity in T2W sequences and T2W hyperintense lesions represent areas of increased water content due to demyelination and contrast enhancement is secondary to a perivascular inflammatory infiltrate. Hyperintense lesions in the cerebrum, cerebellum or brainstem were found in the brains of all dogs in T2-weighted images. However, histopathological examination also revealed demyelination in the cerebellum and the brainstem, respectively, in the temporal lobe of the affected dogs. As all the dogs in the present study had generalised seizures in the last four days before MRI, the hyperintense appearance of the brain lesions in these dogs could be due to acute, possibly cytotoxic, postictal oedema (Bathen-Noethen *et al.*, 2008). Another possible explanation for an increased signal in T2-weighted images is the presence of other diamagnetic materials other than water, such as oxyhaemoglobin, copper, gold or proteinaceous cysts (Bagley *et al.*, 2000).

CONCLUSION

In the present study, all dogs with histopathologically confirmed acute CDV lesions showed abnormal findings in MRI in terms of hyperintense lesions in T2-weighted images. Correlation of MRI and histopathological findings of demyelination in the affected areas of brain stem and cerebellum seems to be a sensitive tool for antemortem diagnosis of the extent of demyelinating lesions arising out of CDV infection or viral antigen load, although specificity is limited. In conclusion, CDV meningomyelitis can appear in MRI as ill-defined, T2W hyperintense and affecting both grey and white matter, which are suspected to be secondary to demyelination and inflammatory response.

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Disclaimers

The views and conclusions expressed in this article are solely those of the authors and do not necessarily represent the views of their affiliated institutions. The authors are

responsible for the accuracy and completeness of the information provided, but do not accept any liability for any direct or indirect losses resulting from the use of this content.

Informed consent

All animal procedures for experiments were approved by the Committee on Experimental Animal Care and Handling and techniques for animal care were approved by the University of Animal Care Committee (CVSC/CAU/IAEC/20-22/P-13).

Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this article. No funding or sponsorship influenced the design of the study, data collection, analysis, decision to publish, or preparation of the manuscript.

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