J Vet Clin 24(3) : 406-409 (2007)

Journal of Veterinary Clinics
www.ksvc.or.kr

Granulomatous Meningoencephalitis in an Old Dog ; magnetic resonance imaging and immunohistopathologic findings

Dong-In Jung, Jong-Hyun Yoo, Byeong-Teck Kang, Chul Park, Su-Hyun Gu, Ju-Won Kim, Hyo-won Jeon, So-Young Lee, Eung-Je Woo***, Jung-Hyang Sur* and Hee-Myung Park[1]**

*Department of Veterinary Internal Medicine and *Veterinary Pathology, College of Veterinary Medicine, Konkuk University, Seoul 143-701, Korea, **BK21 Program of Inteegrative Network Systems for Veterinarians in Basic Science, Industrial Animals and Preventive Medicines, Konkuk University, Seoul 143-701, Korea ***College of Electronics and Information, Kyunghee University, Yongin 446-701, Korea*

(Accepted: July 2, 2007)

Abstract : A 12-year-old female mixed Chihuahua dog was referred because of acute blindness and progressive tetraparesis. Mutifocal lesions in the cerebrum were noted on brain magnetic resonance images and cerebrospinal fluid analysis showed monocytic pleocytosis. Based on these results, granulomatous meningoencephalitis (GME) was strongly suspected. Cerebral lesions were definitely diagnosed as GME based on histopathological findings and positive results of immunohistological stains of brain with T-cell marker (CD3). This report describes the clinical findings, diagnostic imaging characteristics, and immunohistopathologic features of GME in an old dog. In addition, this case demonstrates that clinical signs of GME were mediated by perivascular infiltration of T lymphocytes and identification of causes in T cell-mediated inflammation should be further studied.

Key words **:** dog, granulomatous meningoencephalitis (GME), magnetic resonance imaging (MRI), immunohistopathology.

Introduction

Granulomatous meningoencephalitis (GME) is an idiopathic inflammatory disease of the central nervous system (CNS) of dogs (1,3). GME appears to have a worldwide distribution and represents from 5% to 25% of all CNS disorders in dogs (1). Females, toy and terrier breeds may be overrepresented for GME, however, both sexes and all breeds can be affected (3). GME usually has an abrupt onset and an inexorably progressive course, and if left untreated, it is usually fatal (3,6). Three morphologic forms of GME have been described: disseminated, focal, and ocular (3,6). Clinical signs reflect the arrangement and location of the CNS lesions and may include, but are not limited to, blindness, seizures, vestibulo-cerebellar and spinal cord signs (6). GME is often fatal if not treated with aggressive immunosuppression (3,6).

Case Report

A 12-year-old intact female Chihuahua with body weight of 3.8 kg was presented due to a 1-month history of ataxia and acute blindness. One month prior to this evaluation, clinical signs were first observed by owner and worsened progressively. On physical examinations, submandibular, axillary, inguinal, and popliteal lymph nodes were mildly enlarged. Postural reactions of four limbs were severely reduced and cranial nerve deficits included bilaterally decreased menace response and pupillary light reflex (PLR). The results of fundic examination and other ophthalmologic examinations were normal.

Based on the neurological examination, clinical signs were likely due to intracranial lesion.

The results of a complete blood count (CBC), serum chemistry profiles, and thoracic radiographs were not remarkable.

To rule out the intracranial cause of lesions, we then performed a brain magnetic resonance imaging (MRI) scan. T1- and T2-weighted images, postcontrast T1-weighted images and fluid attenuated inversion recovery (FLAIR) images were obtained. Analysis of the images revealed multifocal lesions on cerebrum (Fig 1A, B, C and D). Multiple, ill-defined hypersignal intensed lesions were noted in the bilateral white matter area including cortical portion on T2-weighted and FLAIR images (Fig 1C and D). These lesions appeared hypointense on T1-weighted images and well enhanced after intravenous administration of gadolinium-diethylenetriamine pentaacetic acid (Omniscan; Nycomed) (0.1 mmol/kg, IV). Prior to cerebrospinal fluid (CSF) collection, we used 15% mannitol (Daehan pharma, Korea) (1 g/kg CRI for 30 minutes) to decrease intracranial pressure and collected CSF from cerebellomedullary cistern. Results of CSF analysis indicated increased nucleated cell count of 7 cells/μl (reference range, 0 to 5 cells/μl) and protein concentration of 45 mg/dl (reference range, <25

[1]Corresponding author.
E-mail : parkhee@konkuk.ac.kr

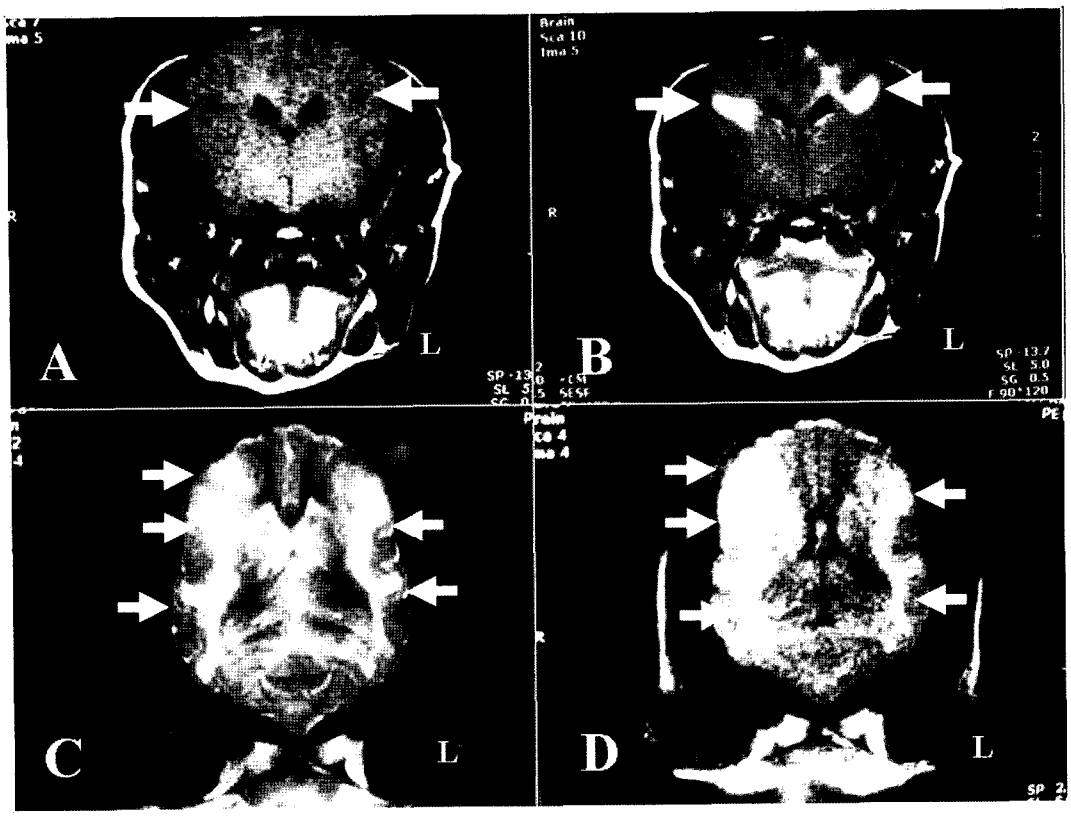

Fig 1. Magnetic resonance images of this case. A : Transverse T1-weighted image. Multifocal lesions showed hyposignal intensity (arrows). B : Post-contrast transverse T1-weighed image of same level with the panel A. The same lesions were enhanced and showed hypersignal intensities (arrows). C : Dorsal T2-weighted images. Multifocal lesions showed hypersignal intensity (arrows). D : FLAIR images of same level with the panel A an C, respectively. Multiple, ill-defined hypersignal intensed lesions were noted (arrows).

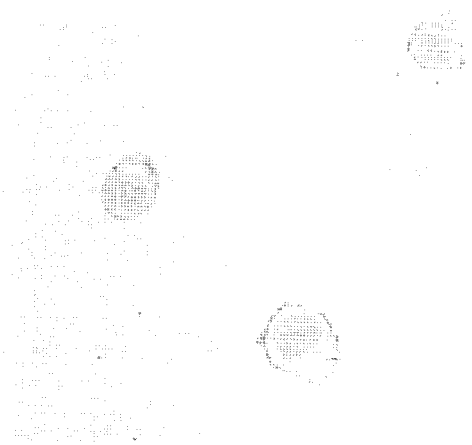

Fig 2. CSF cytology of this case. Monocytoid cells were predominated (Diff-quik stain× 1000).

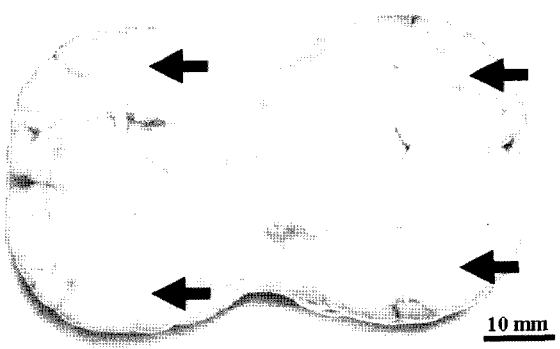

Fig 3. Necropsy finding of this case. Transverse section of the brain. Multifocal lesions were found in white matter (arrows).

mg/dl). Cytologic examination of the CSF revealed a population of monocytoid cells (Fig 2). To rule out canine distemper virus (CDV) infection and toxoplasmosis, CDV antigen (RT-PCR) and toxoplasma IgG/IgM (Neodin vet lab., Seoul, Korea) were examined and all results were negative on CSF. In addition, bacterial and fungal cultures were performed on CSF and both results were all negative. Based on results of all examinations obtained above, we tentatively diagnosed this case as GME.

Management with prednisolone (Prednisolone; Korea Pharma) (1 mg/kg, PO, q 12 hours) was initiated and clinical signs

Fig 4. Immunohistopathological findings of this case (in cerebral cortex white matter). Perivascular lymphocytes infiltration were indicated. The lymphocytes accumulated around the vessel was well differentiated small lymphocytes. A, Cerebrum: Immunohistopathological stain for B-cell antigen (CD 79a) was negative. (×200, anti CD 79a stain). B, Cerebrum : Immunohistopathological stain for T-cell antigen (CD3) was positive (×200, anti CD 3 stain).

improved gradually. And then prednisolone dosage was increased (2 mg/kg, PO, q 12 hours). However, the client declined to further therapy 1 month after therapy because clinical signs did not fully disappear. Thus, the patient was euthanized and we performed necropsy according to client's consent.

On necropsy findings, multifocal lesions were found on cerebral cortex white matter which is consistent finding of MRI (Fig 3). Results of histopathological examination showed that numerous lymphocytes were infiltrated in lesions. Perivascular lymphocytes infiltrations were also indicated on brain histopathology. The lymphocytes accumulated around the vessel were well differentiated small lymphocytes (Fig 4). Immunohistological stain of brain for T-cell antigen (CD3) was positive (Fig 4B) and for B-cell antigen (CD 79a) was negative (Fig 4A). This case was definitely diagnosed as GME in old dog according to the results of immunohistopathological examinations.

Discussion

GME can affect any breed of dog of any age and either sex (1,3,4). However, young to middle-aged (median age of 5 yr) female dogs of small breeds appear to be predisposed (3). GME is not common CNS disease in old dogs. However, the present case was a 12-year-old intact female Chihuahua dog.

Multifocal GME is characterized by acute onset and rapid progression of CNS dysfunction (1,2,4,5,8). Immunosuppressive glucocorticoid therapy is the standard therapy for GME. However, the prognosis for definitively diagnosed cases of GME is poor until recently. In a recent report (3), the median survival time for dogs with multifocal GME was 14 days. Although this case was euthanized after 1 month, clinical signs were improved gradually with prednisolone therapy.

Leptomeningeal involvement may result in mild to severe mononuclear pleocytosis and a total protein elevation in CSF; however, these findings are not unique to GME (6). The CSF from dogs with GME is occasionally normal (6). The CSF of this case indicated mild mononuclear pleocytosis. Computed tomography (CT) or MRI may reveal lesions confined to the CNS white matter, but such changes are not pathognomonic for the diagnosis (3,6). The present case revealed multifocal hyperintensed lesions in cerebral cortex (white matter) on T2-weighted MR images, FLAIR images and enhanced T1-weighted MR images.

Definitive diagnosis necessitates brain biopsy or post-mortem examination. As such, the antemortem diagnosis of GME is typically presumptive. A definitive diagnosis of GME is based upon characteristic histopathologic features of affected brain parenchyma (1,3,7). In other words, since a definitive diagnosis GME is typically based upon a necropsy report, mortality statistics for this disease may be biased toward the most severe cases. For this reason, aggressive immunosuppressive therapy of the suspected GME is highly recommended (3).

Typical histopathological lesions associated with GME include the concentric proliferation of inflammatory cells around blood vessels, predominantly of CNS white matter. In this case, perivascular lymphocytes infiltrations were observed and lymphocytes accumulated around the vessel was well differentiated small lymphocytes.

Although the underlying cause of this disease remains to be unclear, there is evidence that GME represents an autoimmune disorder, specially a delayed-type (T-cell mediated) hypersensitivity reaction (3). The predominate accumulation of CD3 positive lymphocytes (T-cell) on cerebral parenchyma were detected on immunohistopathologic findings in this case. These immunohistopathologic results were evident that CNS inflammation in the present case was GME, which is consistent with the previous reports (3,7).

In conclusion, this report describes the clinical findings, diagnostic imaging characteristics, and immunohistopathologic features of GME in an old dog. In addition, most affected dogs with GME are young to middle aged. however, this case

report demonstrates that old dog could be affected and GME was mediated by T-cell inflammation of cerebral parenchyma.

Acknowledgement

This work was supported by the SRC/ERC program of MOST/KOSEF (R11-2002-103)

References

1. Adamo FP, O'Brien RT. Use of cyclosporine to treat granulomatous meningoencephalitis in three dogs. J Am Vet Med Assoc 2004; 225: 1211-1216.
2. Braund KG, Vandevelde M, Walker TL, Redding RW. Granulomatous meningoencephalitis in six dogs. J Am Vet Med Assoc 1978; 172: 1195-1200.
3. Dewey CW. Encephalopathies. In : A Practical Guide of to Canine and Feline neurology, 1st ed. Iowa: Blackwell. 2003: 157-160.
4. Gnirs K. Ciclosporin treatment of suspected granulomatous meningoencephalomyelitis in three dogs. J Small Anim Pract 2006; 47: 201-206.
5. Sarfaty D, Carrillo JM, Greenlee PG. Differential diagnosis of granulomatous meningoencephalomyelitis, distemper, and suppurative meningoencephalitis in the dog. J Am Vet Med Assoc 1986; 188: 387-392.
6. Schatzberg SJ. An update on granulomatous meningoencephalitis, necrotizing meningoencephalitis and necrotizing leukoencephalitis. In Proceedings of 23nd ACVIM 2005; 351-353.
7. Susuki M, Uchida K, Morozumi M, Hasegawa T, Yanai T, Nakayama H and Tateyama S. A comparative pathology study on canine necrotizing meningoencephalitis and granulomatous meningoencephalomyelitis. J Vet Med Sci 2003; 65: 1233-1239.
8. William B. Thomas. Inflammatory diseases of the central nervous system in dogs. Clinical techniques in small animal practice 1998; 13: 167-178.

노령견에서 병발한 육아종성 뇌수막염 증례 보고; 자기 공명 영상 및 면역조직병리학 소견

정동인 · 유종현 · 강병택 · 박철 · 구수현 · 김주원 · 전효원 · 이소영 · 우응제*** · 서정향* · 박희명[1]**

건국대학교 수의과대학 수의내과학 교실, *건국대학교 수의과대학 수의병리학 교실
**건국대학교 BK21 수의기초 · 산업동물 · 예결예방의학 통합네트워크 연구인력양성 사업단
***경희대학교 전자정보대학 동서의료 공학과

요 약 : 12년령의 암컷 치와와 믹스견이 급성 시력 상실과 진행성 사지마비 증상으로 내원하였다. 두부 자기공명 영상 촬영 결과 뇌에서 다발성 병변이 확인되었고 뇌척수액 검사 결과에서는 단핵구 증가 소견이 나타났다. 이러한 결과들을 토대로 육아종성 뇌수막염이 강력하게 의심되었다. 뇌의 병변은 조직 병리 검사를 통해 최종적으로 육아종성 뇌수막염으로 진단되었고 면역 조직 염색 상에서 T-cell 항원에 양성을 나타내었다. 본 증례 보고는 노령견에서 육아종성 뇌수막염의 임상적인 증상, 진단 영상의 특징, 그리고 면역조직병리학적인 소견 등을 나타내고 있다. 또한 본 증례 보고는 뇌혈관 주위의 T 림프구 침착에 기인한 육아종성 뇌수막염의 임상 증상들에 관해 서술하고 있으며 T세포 매개 염증의 원인 규명에 관한 고찰이 더 필요하다.

주요어 : 개, 육아종성 뇌수막염, 자기 공명 영상, 면역조직병리