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A Comparison Study of Magnetic Resonance Imaging Findings and Neurological Signs in Canine Brain Diseases

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Abstract : The object of this study was to compare magnetic resonance imaging (MRI) findings and neurological signs in canine brain diseases. Brain diseases can cause severe neurological deficits and may be life-threatening. The antemortem diagnosis of the brain diseases is difficult for the clinician, since definitive diagnosis is based upon histopathological confirmation. Brain diseases are often associated with specific clinical signs, signalment, progression, and location. Accurate lesion localization through neurological examination and MRI findings is helpful for developing a differential diagnosis. A retrospective study was performed to compare the neurological examination of dogs with suspected brain disease to the MRI findings. Based on this study, neurological examination is a reliable way to localize most brain lesions. Postural reaction deficits do not provide sufficient information to localize lesions. Additionally, not all brain lesions present clinical signs and inflammatory lesions may cause no detectable abnormalities on MRI. Therefore, in clinical practice, a combination of neurological examination and MRI findings recommended for accurate brain lesion localization.

Key words **:** dog, brain diesease, magnetic resonance imaging, neurological examination, lesion localization.

Introduction

Functionally, the brain is divided into three regions: the forebrain, brainstem, and cerebellum, and each division has distinctive functions (16). The forebrain includes the cerebrum and diencephalon. Abnormalities of the forebrain are associated with seizures, depression, behavioral changes, head pressing, circling, blindness, and contralateral postural reaction or sensory deficits. The brainstem consists of the midbrain, pons, and medulla. Midbrain abnormalities can result in stupor/coma, cranial nerve deficits, contralateral or ipsilateral postural reaction deficits, vestibular dysfunction, and abnormal respiratory or cardiovascular function. Neurologic signs of cerebellar dysfunction includes cerebellar ataxia, incoordination, intention tremor, and vestibular dysfunction (12,13).

There are many diseases that can affect the brain and they can be classified using the DAMNIT-V acronyms. With this acronym, D = Degenerative; A = Anomalous; M = Metabolic; N = Neoplastic, Nutritional; I = Inflammatory, Infectious, Idiopathic; T = Traumatic, Toxic; V = Vascular. Each condition has a characteristic signalment, onset, progression, and distribution within the brain. Inflammatory diseases most commonly affect the entire brain (4,13), while primary brain tumors are more localized, and are commonly observed in older dogs (5,14).

The neurological examination is essential to localize brain lesions. The neurological examination consists of evaluation of mental status and behavior; examination of gait, postural reactions, cranial nerves, and spinal reflexes; and pain perception. Proper lesion localization based on signalment and history is necessary to develop a differential diagnosis, and can facilitate the selection of appropriate ancillary diagnostic tests, including the complete blood count, serum biochemistry, urinalysis, contrast radiographic studies, advanced imaging, cerebrospinal fluid (CSF) analysis, or electrodiagnostic examination (4).

Magnetic resonance imaging (MRI) is a widely used, noninvasive method of examining the brain. Brain MRI, using multiplanar imaging, provides excellent resolution and soft tissue contrast, and has the ability to differentiate abnormal from normal tissue (10). Routine high field MRI used to detect brain lesions has a sensitivity of 94.4% and a specificity of 95.5% (19).

The purpose of this retrospective study was to compare neurological signs and the MRI findings in canine brain disease. In addition, the author evaluated the usefulness of the neurological examination for localizing brain lesions.

Materials and Methods

Animals

A retrospective review of records, from November 2008

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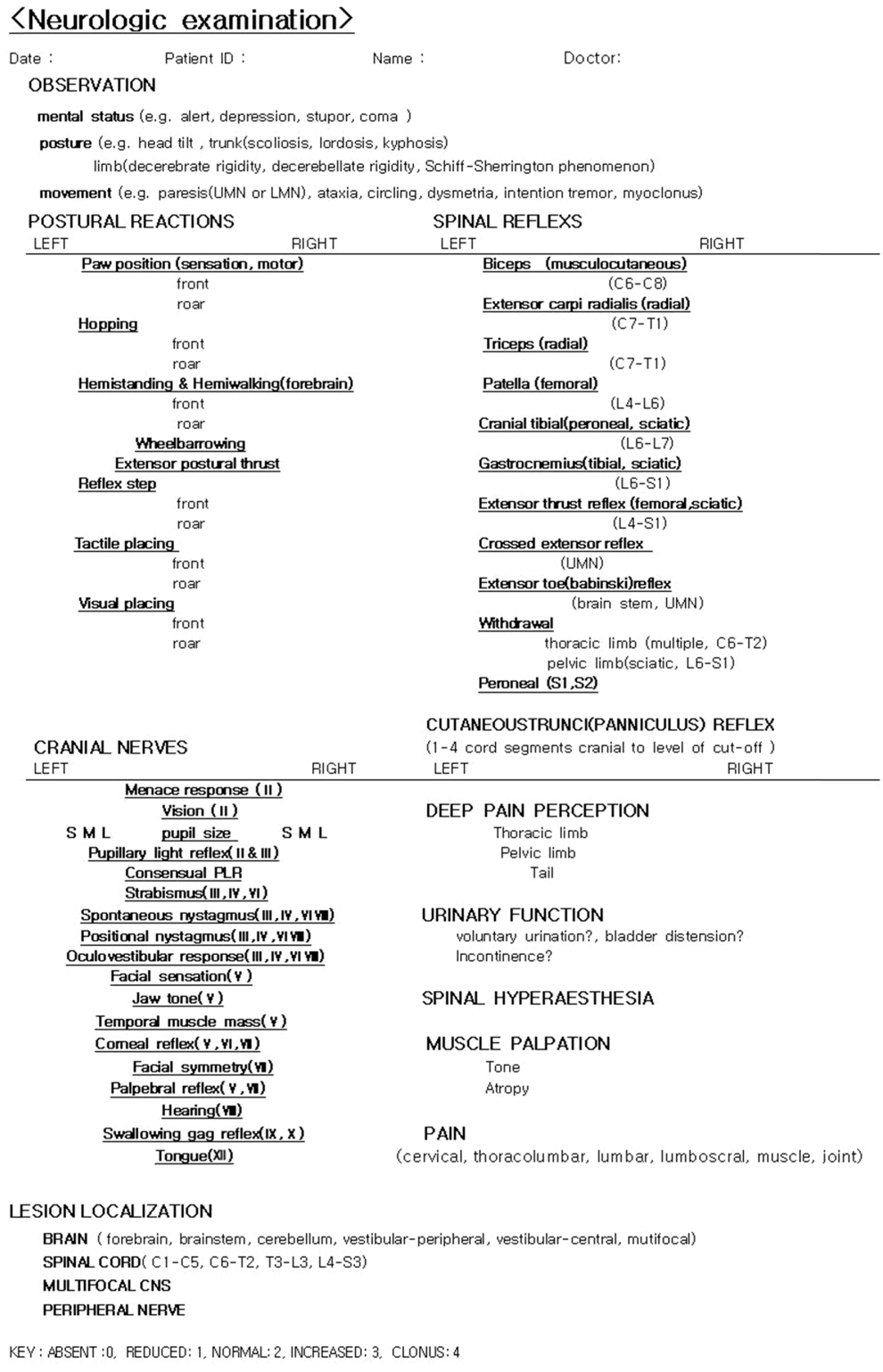

Fig 1. Procedures of neurological examination used in Gyeongsang National University Veterinary Medical Teaching Hospital.

through October 2017, at the Gyeongsang National University Veterinary Medical Teaching Hospital, was performed to compare the neurological examination of dogs with suspected brain disease to the MRI findings. The records of 40 dogs, of various genders, ages, and breeds, were evaluated.

Exclusion criteria included: a diagnosis of primary epilepsy or spinal cord disease, and prior treatment with immunosuppressive drugs, corticosteroids, or antiepileptic drug.

Lesion localization of the brain

All animals were subjected to detailed neurological examination using Gyeongsang National University Veterinary Medical Teaching Hospital neurological examination procedures. The examination included: observation; evaluation of postural reactions, cranial nerve function, spinal reflexes, urinary function, and muscle tone; and a sensory evaluation (Fig 1).

Based on the neurologic examination, lesions were local-

ized to the forebrain, brainstem, cerebellum, or were considered multifocal.

Image analysis

All MR images were performed with a 0.4T scanner (APERTO, Hitachi Medical Corporation, Tokyo, Japan) by veterinary imaging specialists. Dogs were scanned under general anesthesia in sternal recumbency. The images were obtained in the sagittal and transverse planes by using T1-weighted (T1W), T2-weighted (T2W) and T2 fluid attenuated inversion recovery (T2-FLAIR) sequence. Slices were 2-3 mm thick. Postcontrast sequences were acquired after intravenous administration of gadodiamide. Based on MR images, lesions were classified anatomically to forebrain, brainstem and cerebellum. Multifocal lesions or those with mass effect impacting multiple areas were classified into more than one brain region.

Classification

In seven dogs (17.5%), the diagnosis was confirmed by postmortem examination, including histopathology and immunohistochemistry. In the remaining 33 dogs (82.5%), signalment, history, neurological examination, clinicopathological findings, CSF analysis, diagnostic imaging, and response to treatment were used to determine the diagnosis.

Dogs were classified according to the DAMNIT-V classification system based on their diagnosis.

Results

Baseline characteristics of the dogs

Forty dogs with various neurological signs were included in the study. There were 16 males (10 neutered) and 24 females (11 neutered). Median age was 7.3 years (SD, 4.4 years; range 1-17 years) and the median body weight was 4.8 kg (SD, 4.5 kg; range, 1.4-25 kg). Breeds represented in this study were: Maltese (n = 15); Shih tzu (n = 6); Chihuahua (n = 4); mixed (n = 4); Yorkshire terrier (n = 3); Poodle (n = 2); French bulldog (n = 1); Jindo dog (n = 1); Miniature pinscher (n = 1); Pomeranian (n = 1); Pug (n = 1); Schnauzer (n = 1). In inflammatory brain diseases, the most frequently observed breed was the Maltese (n = 11, 36.7%). The Maltese was the most frequently observed breed with neoplastic brain diseases (n = 4, 44.4%).

Neurological signs in dogs with different brain diseases

Based on clinical examination, nine dogs (22.5%) were diagnosed with neoplastic brain disease; 30 dogs (75%) had inflammatory brain disease, and 1 dog (2.5%) had vascular disease. In the neoplastic group, the median age was 9.8 ± 3.7 years (range, 2-14 years) and the most common clinical sign was seizures (55.6%). In inflammatory group, the median age was 6.3 ± 4.2 years (range, 1-17 years) and the most common clinical sign was ataxia (25%), followed by seizures (23.3%). Only one dog had vascular disease, and this dog presented with seizures (Table 1).

Table 1. Neurological signs in dogs with different brain diseases

Classification	N = 40 (%)	Age at Presentation (years)	Chief Neurological Sign
Neoplastic	9/40 (22.5%)	9.78 ± 3.7 (range 2-14)	Ataxia (22.2%) Head tilt (22.2%) Seizure (55.6%)
Inflammatory	30/40 (75%)	6.33 ± 4.2 (range 1-17)	Ataxia (25%) Behavior change (1.7%) Blindness (1.7%) Cervical pain (1.7%) Circling (5%) Facial palsy (1.7%) Head tilt (8.3%) Head turn (6.7%) Nystagmus (5%) Paresis (16.6%) Seizure (23.3%) Tremor (3.3%)
Vascular	1/40 (2.5%)	15	Seizure (100%)

Table 2. MRI findings and categories of brain diseases

MRI findings	Neoplastic	Inflammatory	Vascular
Forebrain	3/9 (33.3%)	17/30 (56.7%)	1/1 (100%)
Brainstem	-	4/30 (13.3%)	-
Cerebellum	2/9 (22.2%)	-	-
More than 1 brain region	4/9 (44.4%)	9/30 (30%)	-

MRI findings and categories of brain diseases

In the neoplastic group, lesions that caused mass effect and affected more than one brain region by mass effect or secondary pathologic changes like edema were frequently observed (4/9, 44.4%). In the inflammatory group, the most frequently affected location was the forebrain (17/30, 56.7%). Multifocal lesions which affect more than one brain region were identified in dogs with inflammatory brain disease (9/30, 30%) (Table 2).

Comparison between brain lesion localization by neurological signs and MRI

Lesion localization according to neurological signs, and MRI findings are shown in Table 3. All dogs that presented with typical neurological signs of forebrain disease, including behavioral changes (n = 1), wide circling (n = 3), head turn (n = 6), and seizures (n = 21), the MRI identified lesions in the forebrain. In dogs that presented with depressed mentation (n = 7), the MRI identified lesions in the forebrain or brainstem, where the ascending reticular activating system exists. In all dogs with typical central vestibular signs, in-

Table 3. Comparison between brain lesion localization by neurological signs and MRI

Clinical signs	Lesion localization	MRI Findings	Number
Behavior change	F	F + B	1
Wide Circling (Lt.)	F (Lt.)	F (Lt.)	1
		F (Lt., Rt.)	1
Wide Circling (Rt.)	F (Rt.)	F (Rt.)	1
Head turn (Lt.)	F (Lt.)	F (Lt.)	3
		F (Lt., Rt.)	1
		F (Lt., Rt.) + B	1
Head turn (Rt.)	F (Rt.)	F (Lt., Rt.) + B	1
Seizure	F	F	15
		F + B	6
Depression	F, B	F	5
		B	1
		F + C	1
Head tilt (Lt.)	B (Lt.), C (Rt.)	B (Lt.)	1
		B (Lt., Rt.)	1
		C (Lt., Rt.)	1
		F + B (Lt.)	1
		B (Lt.) + C (Lt.)	1
Head tilt (Rt.)	B (Rt.), C (Lt.)	B (Rt.) + C (Rt.)	1
		F + B (Rt.)	2
Falling (Lt.)	B (Lt.), C (Rt.)	B (Lt.)	1
Leaning (Lt.)	B (Lt.), C (Rt.)	F + B (Lt.)	1
Nystagmus	B, C	B	2
		C	1
		F + B	6
		B + C	1
Dysmetria	C	F + B	1
		F + C	1
Menace response deficit	F, B, C CN (2,7)	F	4
		F + B	4
		F + C	1
Mydriasis	B CN (2,3)	B + C	1
PLR deficit	F, B CN (2,3)	F	1
		B	1
		F + B	2
Strabismus	B, C CN (3,4,6,8)	F	1
		F + B	1
Facial palsy	F, B CN (5,7)	F	1
		F + B	1
		B + C	1
Palpebral reflex deficit	B CN (5,7)	B + C	1

F, forebrain; B, brainstem; C, cerebellum; CN, cranial nerve

cluding head tilt (n = 8), falling (n = 1), leaning (n = 1), and nystagmus (n = 10), the MRI identified lesion in brainstem or cerebellum. Two dogs presented with dysmetria, which is typically due to a cerebellar abnormality. However, on MRI, one dog with dysmetria had forebrain and brainstem lesions, but not cerebellar lesions. The second dog with dysmetria had a cerebellar lesion. Cranial nerve deficits identified included: lack of menace response (n = 9), mydriasis (n = 1), defects in the pupillary light reflex (PLR) (n = 4), strabismus (n = 2), facial palsy (n = 3), and palpebral reflex deficit (n = 1). Except for one case with strabismus, the MRI findings were consistent with the clinical lesion localization.

Table 4. Agreement between neurological examination and MRI findings

Agreement / Disagreement	N = 34 (%)
Complete agreement	29/34 (85.3%)
Partial agreement	3/34 (8.8%)
Disagreement	2/34 (5.9%)

Agreement between neurological examination and MRI findings

Lesion localization was performed based on the history and neurological examination. In six of the 40 dogs (15%), postural reaction deficits were the only clinical sign, and specific lesion localization could not be clinically identified. In the remaining dogs, lesion localization and MRI findings were consistent in 32 of the 34 dogs (94.1%). Of these 32 dogs, 29 had complete agreement (85.3%) and three had partial agreement (8.8%) between the clinical and MRI localization (Table 4).

Discussion

The antemortem diagnosis of the brain diseases is challenging for the clinician, since definitive diagnosis is based upon histopathological confirmation (15). Since, brain diseases are often associated with specific clinical signs, signalment, progression, and location, understanding that characteristics is helpful for antemortem diagnosis (4).

In this study, inflammatory, neoplastic, and vascular diseases were identified. Inflammatory disease was most common, identified in 75% of cases. All dogs with inflammatory brain disease were given a preliminary diagnosis of meningoencephalitis of unknown etiology (MUE). In dogs, MUE is a common, idiopathic, noninfectious, inflammatory disease of the central nervous system that occurs primarily in dogs 3 to 7 years of age and is associated with multifocal to diffuse lesions. In contrast, granulomatous meningoencephalitis (GME) can cause focal lesions (3,6,8,11,15). The mean age of dogs with inflammatory brain disease in this study was 6.33 years and multifocal lesions were identified in 25% of cases.

Inflammatory diseases present highly variable clinical signs that correlate with the affected regions. In GME, seizures, vestibulocerebellar signs, and cervical hyperesthesia have been most often reported. In necrotizing encephalitis (NE), seizures are most frequently reported (3,15). In this study, various clinical signs were identified and the most common sign of inflammatory brain diseases was ataxia, followed by seizures.

Neoplastic brain diseases commonly affect older dogs (> 5 years of age) and present with seizures (1,5,7,14,17). Our study is in agreement with previous reports, and the mean age of dogs with neoplastic brain disease was 9.78 years and the most common sign was seizures. Typically, neoplastic brain diseases feature focal lesions, but multifocal lesions can be seen in metastatic neoplasia (9). A mass effect results in the secondary pathologic changes that can be observed in neoplastic brain disease (2). Due to the mass effect, 44.4% of dogs with neoplastic disease were classified with disease in more than one brain region. This finding emphasizes that focal neoplastic disease with mass effect may present with neurological signs suggestive of multifocal lesions (14).

Specific lesion localization could not be performed in dogs presenting with only postural reaction deficits. Postural reactions involve complex pathways and the entire nervous system (13). Though postural reaction deficits may be subtle neurological abnormalities, it is not possible to specifically localize the affected regions by postural reaction deficits alone.

Lesion localization is based on history, neurological signs, and the neurological examination. A single localized lesion should explain all of the abnormal clinical signs; if it does not, multifocal or diffuse lesions should be considered (13). In this study, the concordance rate of clinical brain lesion localization and the MRI findings was 94.1%. There was complete agreement in 85.3% of dogs, while 8.8% had additional lesions. This suggests that not every lesion presents with clinical signs, and it may be more difficult to exactly localize the brain lesion.

Brain lesion localization and MRI findings were inconsistent in two dogs. One dog presented with strabismus, and the MRI did not identify a lesion in the brainstem or vestibular apparatus. Generally, strabismus is associated with the lesions affecting cranial nerve 3, 4, 6, or the vestibular apparatus (10,18). Although the exact mechanism is uncertain, there is a report that forebrain lesion may induce the strabismus (13). This dog may have had strabismus due to forebrain lesion. The other dog presented with left-sided head tilt, hypermetria, loss of balance, and postural reaction deficits in right forelimb. These signs suggested paradoxical vestibular syndrome. However, MRI findings identified brainstem and forebrain lesions adjacent to the cerebellum, but no lesions of the cerebellum. In previous reports, approximately 25% dogs with an inflammatory change in the CSF had normal brain MRI findings (9). In this dog, we considered that cerebellar inflammation, which was not detectable on MRI, was responsible for the cerebellar defects.

Comparison of the neurological examination with brain lesions identified on MRI has not been previously reported. This study shows that assessment of clinical signs and a thorough neurological examination is an accurate way to localize a brain lesion. A thorough and accurate neurological examination may be useful where advanced imaging diagnostics are not available. However, it may be difficult to clinically localize lesions in patients with only postural reaction deficits, and the MRI may be nondiagnostic in patients with mild inflammation or early disease. Therefore, to localize the lesion of the brain, one should consider both the neurological examination and MRI.

There are several limitations to this study. First, the population of each disease is insufficient for statistical analysis. Further studies with a larger number of dogs with brain and spinal cord diseases would provide more accurate results. Second, the majority of dogs had a preliminary diagnosis, and histopathological evaluation was not performed in all dogs.

The present study reports a comparison of MRI findings, neurological signs, and brain lesion localization. Neurological examination is a reliable way to localize most brain lesions. Postural reaction deficits do not provide sufficient information to localize lesions. Additionally, not all brain lesions present clinical signs and inflammatory lesions may cause no detectable abnormalities on MRI. Therefore, in clinical practice, a combination of neurological examination and MRI findings recommended for accurate brain lesion localization.

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