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Steroid Responsive Tremor Syndrome in a Maltese Dog

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Abstract : A 4-year-old, spayed female Maltese dog was presented for evaluation of acute onset of generalized tremor, right-sided head tilt, horizontal nystagmus, and mild ataxia with 4-day duration. However, the dog was bright, alert, and responsive. The neurological examinations revealed that bilateral horizontal-, positional nystagmus, and mild ataxia. Menace responses were also absent in both eyes. Typically, moderate generalized intension tremors were noted in four limbs and the head. No abnormalities were found in hemogram, radiography, and magnetic resonance imaging (MRI). Cytologic examination of cerebrospinal fluid (CSF) revealed a mild nonsuppurative inflammation. Thus, steroid responsive tremor syndrome (SRTS) was strongly suspected because of its inflammatory and idiopathic features. The dog excellently responded to immunosuppressive doses of corticosteroid. Therefore, we definitively diagnosed the dog as SRTS based on the exclusion of other causes of the tremor, clinical signs, and response to treatment. This is a first case report of SRTS in our country and we here describe clinical and neurological features in SRTS.

Key words **:** steroid responsive tremor syndrome, generalized tremor, Maltese dog, cerebrospinal fluid, magnetic resonance imaging.

Introduction

Tremor is defined as a rhythmical involuntary oscillatory movement of antagonistic muscle groups (5). It may be classified on a number of different dimensions. The commonest classification of tremor depends on its appearance and behavioural classifications (4). It has been associated with congenital abnormal myelin formation, storage diseases, toxicity, inflammation, metabolic conditions of the central nervous system (CNS), and also appeared without a definable cause (8,9).

Steroid responsive tremor syndrome (SRTS) is a disorder characterized by generalized tremors with unknown cause. Tremors are rarely incapacitating and nearly all affected dogs respond to immunosuppressive dosages of corticosteroids (7). The most affected dog is small white dogs, particularly Maltese and West Highland white terrier, therefore the disease is often referred to as white shaker disease or little white shakers syndrome (2,7,8,10). However, it has been recognized in any sized and hair-colored dogs such as Shih tzu, Beagle, Yorkshire terrier, Australian silky terrier, Miniature Pinscher, and Miniature Dachshund dogs (2,8,9,10). Approximately one-half of dogs with SRTS do not have white coat coloring (7). The diagnosis is based on the exclusion of other causes of tremor and response to treatment. Prognosis for treatment of this disease with immunosuppressive doses of corticosteroids is excellent (7). The disease has been observed in the United States, United Kingdom, Australia, and Japan (2,9,8,10). This report firstly describes a case of SRTS in our country.

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Case

A 4-year-old, spayed female Maltese dog was presented for evaluation of acute onset of generalized tremor, right-sided head tilt, horizontal nystagmus, and mild ataxia. Clinical signs were acutely shown 4 days before the presentation and progressively increased in severity and frequency, even though supportive cares were done at the local animal hospital. There was no known trauma or exposure to a toxic agent. The dog had regularly received all of its vaccinations, heartworm prevention, and no previous medical problems.

On physical examinations, the dog was bright, alert, and responsive. However, moderate generalized tremors were noted in four limbs and the head, particularly being held with human hands for examinations. The neurological examinations revealed that bilateral horizontal-, positional nystagmus, and mild ataxia. Menace responses were also absent in both eyes. Thus, differential diagnoses were assumed as causes of tremor and central vestibular disorder, such as intoxications (mycotoxin, hexachlorophene, lead, organophosphates, carbamates, pyrethrins, pyrethroids, ivermectin, bomethaline, and theobromine) (9), myelin abnormalities

(hypo-, dys-, and demyelination), inflammation (bacterial-, mycotic-, viral-, protozoal encephalistis, and granulomatous meningoencephalitis (GME)), metabolic disorders (hepatic and uremic encephalopathy), head trauma, and idiopathic disease (SRTS). Exposure to a toxicant was ruled out based on the dog's history.

Abnormalities on the complete blood count (CBC), urine analysis, and radiographic studies were not remarkable. The serum biochemical profile revealed a mildly elevated alanine aminotransferase (ALT, 139 U/L; reference range 17 to 78 U/L) and alkaline phosphatase (ALP, 297 U/L; reference range 47 to 254 U/L). Canine distemper virus (CDV) was not detected on the serum by the reverse transcription polymerase chain reaction (RT-PCR).

Since central neurological disease was suspected, magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) analysis were performed. MRI of the brain was obtained using a 0.2 Tesla magnet (E-Scan®, ESAOTE, Italy) in transverse, sagittal, and dorsal T1- (pre and postcontrast) and T2-weighted images. No abnormalities were found in MRI. Results of CSF analysis were shown in Table 1. Cytologic examination of CSF revealed a mild nonsuppurative inflammation (mononuclear pleocytosis) (Fig 1). Bacterial and fungal cultures were all negative. In addition, Toxoplasma antibody titer was no remarkable. Central vestibular disease, metabolic disease, and trauma were excluded, based on the hemogram, CSF analysis, radiographic and MR examinations. Myelin abnormalities were also unlikely because generalized tremors of such cases are likely to present within weeks of birth and often resolve within months (3). Thus, it was tentatively diagnosed as SRTS which has the inflammatory and idiopathic categories of tremor.

Initially, the dog was treated with immunosuppressive doses of corticosteroid (prednisolone, 2 mg/kg body weight, PO, BID) on the first day of admission. The tremor was mildly improved on the third day and completely disappeared from all of the body on the fifth day. Since sixth day, tremor had not been relapsed and prednisolone had been gradually tapered over 3 months. According to the excellent and persistent response to corticosteroid, SRTS was definitively diagnosed.

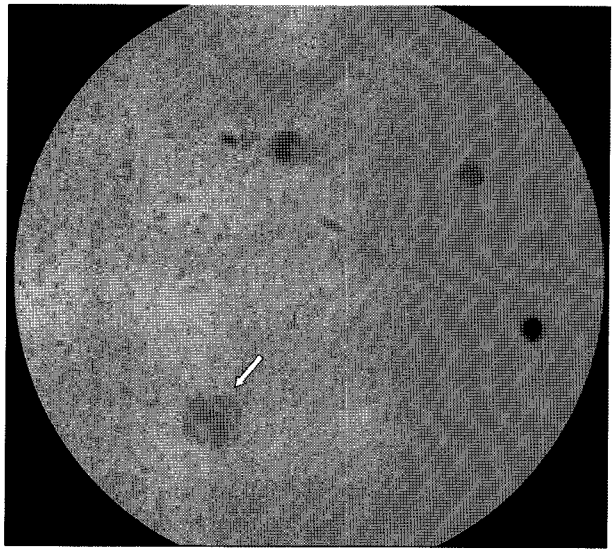

Fig 1. Cytologic examination of CSF. Mild nonsuppurative inflammation (mononuclear pleocytosis) was founded. Two small lymphocytes and one large mononuclear cell (arrow) were shown. (Diff-Quick; ×250)

Discussion

Generally, most dogs with SRTS were young (less than 5 years old) and small to medium sized (less than 15 kg) (7,9). The prevailing clinical signs are generalized intention tremor, decreased menace responses, head tilt, nystagmus, opsoclonus, paraparesis, tetraparesis, and ataxia (6,7,9). In this case, the dog was also young (4 years old), small sized (1.2 kg), and had white hair color. However, head tilt, paraparesis, and tetraparesis were not shown.

Based on the results of CSF analyses or a history of toxin exposure, Wagner (9) grouped the causes of generalized tremors into inflammatory, noninflammatory, and idiopathic. In inflammatory group, CSF analysis revealed mixed or mononuclear inflammation. In that study, half of the dogs with SRTS were determined to have inflammatory CNS disease. Therefore, Wagner (9) reported that similarities in signalment, duration of signs prior to examination, and response to treatment indicate that dogs in the inflammatory and idio-

Table 1. Results of CSF analysis

Examinations	Results	Reference range
White blood cell/μl	12	<5
Cytologic examination (% of cell type)	L: 76 / LM: 24	Predominantly L
Red blood cell/μl	0	0
Protein concentration (mg/dl)	15	<25
Bacterial culture	negative	-
Fungal culture	negative	-
CDV (RT-PCR and IgG titer)	negative	-
Toxoplasma antibody (IgG titer)	negative	-

L=lymphocyte; LM=large mononuclear cell

pathic categories have SRTS. These similar results were also shown in other studies (2,10). In this case, mononuclear pleocytosis was observed. However, it should be considered that many dogs with SRTS have the results of CSF analyses within reference ranges (8,9). These results of the dogs with SRTS were discriminated against the polymorphonuclear pleocytosis associated with mycotic and bacterial infections and the mixed-cell pleocytosis typical of GME and protozoal diseases (7).

Until recently, the underlying cause of SRTS has not been known. Histological examinations of the CNS of the dogs with SRTS showed various results. A mild non-suppurative meningoencephalitis with mild perivascular cuffing, especially in the cerebellum, was evident, but normal CNS tissue can also be found (7). A few theories have been proposed. Autoimmune-mediated disruption of neurotransmitter metabolism resulting in decreased conversion of tyrosine to dopamine was presented (1,3,9). Other possible causes include altered function in cells of similar embryologic origin that produce melanin and neurotransmitters and a genetic predisposition (2,3,9).

It was reported that the tremor of SRTS may have not been controlled by corticosteroid only and the term "SRTS" may not be suitable for most canine cases with the generalized tremors (9,10). Many cases were also treated with the combination therapy of corticosteroid and benzodiazepine (9,10). Bagley (2) reported that corticosteroids and benzodiazepines alone are not rapidly and consistently effective. Thus, the use of both types of drug simultaneously can be more effective and reliable (6). However, clinical signs were completely improved for 5 days using only corticosteroid in this case. Thus, single application of corticosteroid may be useful if tremors and clinical signs are not severe.

In conclusion, we diagnosed the dog as SRTS based on the exclusion of other causes of the tremor, clinical signs, and response to treatment. This is a first case report of SRTS in our country.

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말티즈 견에서 발생한 스테로이드 반응성 진전 증후군

강병택 · 정동인 · 박 철 · 김주원 · 김하정 · 임채영 · 고기진 · 조수경 · 이소영 · 박희명[1]

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요 약 : 4년령의 중성화된 암컷 말티즈 견이 급성으로 발병하고 4일 동안 지속된 전신 진전, 우측으로의 사경, 수평성 안구진탕, 그리고 약간의 보행실조에 대한 평가를 위해 내원하였다. 환견은 의식이 뚜렷하고 외부자극에 잘 반응하였다. 신경계 검사 상에서 양안의 수평성-, 위치성 안구진탕, 그리고 약간의 보행실조가 나타났다. 또한 양안의 위협반사가 소실된 상태였다. 중등도의 전신 긴장성 진전이 사지와 두부에서 특이적으로 관찰되었다. 혈액검사, 방사선, 그리고 자기공명영상에서 이상소견이 관찰되지 않았다. 뇌척수액의 세포학적 검사를 통해 약간의 비화농성 염증 소견을 확인하였다. 이와 같이 염증성 그리고 특발성의 특징을 가지고 있었기 때문에 스테로이드 반응성 진전 증후군이 강하게 의심되었다. 환견은 면역억제 용량으로 투여된 코르티코스테로이드에 매우 잘 반응하였다. 따라서 진전을 유발하는 다른 원인들을 배제하고, 임상증상 및 치료에 대한 반응에 근거하여 스테로이드 반응성 진전 증후군으로 최종 진단하였다. 이것은 국내에서 스테로이드 반응성 진전 증후군의 최초 보고이며, 이 질환의 임상적 그리고 신경학적 특징들을 기술하고 있다.

주요어 : 스테로이드 반응성 진전 증후군, 전신 진전, 말티즈 견, 뇌척수액, 자기공명영상.