A case of Neospora caninum infection in a dog

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ABSTRACT
Infection with Neospora caninum in a dog is described. The predominant clinical findings were proprioception deficit, involuntary and continuous contracture of the pelvic extremity muscles. N. caninum is structurally similar to Toxoplasma gondii, but it is immunologically distinct. Therefore, infections had been misdiagnosed as toxoplasmosis. The diagnosis was confirmed by an immunofluorescence antibody test. The parasite is sensitive to clindamycin and trimethoprim/sulphonamide, however the prognosis is poor especially if the muscle contractures have occurred.

Keywords: Neospora caninum, IFAT

INTRODUCTION
Neospora caninum is an obligate intracellular, tissue-cyst forming, apicomplexan parasite that infects domestic and wild canids, ruminants, and horses (Dubey et al., 1996a, 2006b). The first identification has been observed in 1984 in dogs in Norway (Bjerkås et al., 1984). It is structurally similar to Toxoplasma gondii, but it is immunologically distinct. Therefore, infections had been misdiagnosed as toxoplasmosis (Knowler and Wheeler, 1995). Dogs are both confirmed to be definitive and intermediate hosts for N. caninum (McAllister et al., 1998). Also, several species of mammals are intermediate hosts such as ruminants and horses (Dubey et al., 2007). The life cycle of N. caninum consists of 3 infectious stages: Tachyzoites, tissue cysts, and oocysts. Tachyzoites and tissue cysts are found intracellularly in the intermediate host (Dubey et al., 2002). Domestic dogs are the only known definitive host for unsporulated oocysts. The oocysts sporulate outside of the host (Lindsay et al., 1999). The main clinical sign in dogs is neuromuscular disorders (Basso et al., 2005).

This case was carried out to emphasize that the findings found in vivo can be attributed to N. caninum because it is frequently misdiagnosed as T. gondii infection and to remind veterinarians about the importance of N. caninum infection.

CASE
A 2-year-old, male, mixed breed dog presented with movement disorders (Figure 1). The owner had realized involuntary movements in his right hind leg 6 months ago. Then the same involuntary movements had begun on the left hind leg. According to the information obtained from the patient’s owner, the dog had stayed in a dog shelter for 2 months before the symptoms started and then used clindamycin for 3 weeks in another veterinary clinic due to suspected toxoplasmosis. But the dog’s condition worsened day by day.

On presentation, the dog was clinically depressed with an increased respiratory rate (64 breaths per minute) and effort. Rectal temperature was 38.3 °C with a pulse rate of 132 beats per minute. There were injuries in the hind legs due to the friction caused by the involuntary movements. The pelvic limbs had a complete loss of conscious proprioception with absent tendon reflexes. He was able to stand up and walk only with support. There was diffuse muscular pain and also
The radiography of lungs showed an interstitial pneumonia. Routine serum biochemical parameters were in normal ranges. Haematological parameters were normal with the exception of a slight eosinophilia at 1.8 K/µL (normal, 0.5 to 1.5 K/µL) (IDEXX VetAutoread Haematology Analyser, USA). Clindamycin and phenobarbital were started after the patient’s serology test has a weak positive for toxoplasmosis in another veterinary clinic and the patient had stopped clindamycin at the third week but continued to phenobarbital. In this process, the owner mentioned about the dog getting worse day by day.

Then, blood specimen to anticoagulant-free tube from the vena cephalica antebrachi of the patient and a punch biopsy from left gluteal muscle of the patient were sent to the laboratory. In the process of waiting for laboratory results, phenobarbital (Luminal®, Bayer Türk, Türkiye) was continued as an antiepileptic agent and gabapentin (Neurontin®, Pfizer, USA) was started to be used for neuropathic pain caused by continuous involuntary muscle movement, but no improvement had been observed.

According to the results from the laboratory; canine distemper virus, canine adenovirus and canine parvovirus specific tests were negative. In immunopathology tests performed with immunofluorescence antibody technique (IFAT), T. gondii (weak immunoreactivity), N. caninum positive and Leishmania sp. found negative. According to the laboratory results of gluteal muscle biopsy; hyaline degeneration and Zenker necrosis were seen in striated muscle and macrophage and leukocyte infiltration were seen in the interstitial area. In immunoperoxidase assays performed using T. gondii and N. caninum specific primer antibodies: intense granular N. caninum immunopositivity was detected in muscle fibres, necrotic vein walls and macrophage cytoplasm. A weak cross reaction was observed with T. gondii.

With these findings, acute clinical Neospora caninum infection was diagnosed and 11 mg / kg PO clindamycin (Clindan®, Bilim Ilac, İstanbul) twice a day for 3 weeks; 15 mg/kg PO trimethoprim-sulfamethoxazole (Bactrim Forte, Deva Holding A.S., Istanbul) twice daily for 3 weeks and 9 mg/kg PO toltrazuril (Baycox®, Bayer Türk, Türkiye) once daily for 3 days were started. In addition, gabapentin (Neurontin, Pfizer, USA) 20 mg / kg twice daily was continued and the dog was supplemented with vitamin B12. At the end of three weeks, involuntary leg movements were reduced. After the clinical improvement, the dog did not come to the control because the owner had considered the dog was clinically recovered.

**DISCUSSION**

* N. caninum, which causes infertility and abortion in cows and great economic loss all over the world, was first seen in a dog with central nervous system (CNS) symptoms in 1984 but not identified (Bjerkås et al., 1984). In 1988, it was isolated and named as *N. caninum* (Dubey et al., 1988). Although it is often reported in young dogs, neosporosis is also seen in older dogs. Cattle are most important intermediate hosts and the dogs are both definitive and intermediate hosts. Although vertical transmission is possible in dogs and intermediate hosts, the most common mode of transmission is seen when the infected tissues are eaten by dogs (McAllister et al. 1998). In transplacental infections, the bitch may be asymptomatic and clinical neosporosis may not occur in all of the offsprings. No breed or sexual predisposition is known, although there is a common occurrence among breeds such as; Labrador Retriever, Golden Retriever, and Boxer (Dubey and Lindsay, 1996).

In this case the owner informed us that she has not ever given the patient raw meat but during the time that the dog stayed in a shelter he might have been fed with raw meat. There were two more dogs that the owner took care of in the same house, and no signs in these dogs were observed.

Dogs infected with *N. caninum* vary in age from five weeks to 15 years, but the majority of patients are younger than one-year-old. The infection is more severe in young animals.
The characteristic clinical findings of neosporosis in young animals are proprioception deficits that progress to paraplegia within a week. The dogs can be paraplegic with a rigid extension of the pelvic limbs due to muscle contracture. In these dogs fecal and urinary incontinence are present. Affected dogs may have pneumonia or hepatic disorders. Paralysis causes rapid quadriplegia, cervical weakness and dysphagia (Cummings et al., 1988; Dubey et al. 1988a). The cause of death is usually myocarditis, respiratory disease or hepatic dysfunction (Dubey et al., 1988a; Dubey 1992b). In this case, proprioception deficit, involuntary and continuous contracture of the pelvic extremity muscles, interstitial pneumonia and urinary incontinence was present in similar to literatures (Cummings et al., 1988; Dubey et al. 1988a; Dubey 1992).

Since the *N. caninum* was structurally similar to *T. gondii*, infections were considered and misdiagnosed as toxoplasmosis until the *N. caninum* was identified. In this case, Toxoplasmosis was misdiagnosed due to a weak positive result with serology test and the treatment was started.

Tests such as; IFAT and ELISA in *N. caninum* detection also have high sensitivity and specificity (Björkman and Uggla, 1999). In order to diagnose an acute infection > 1: 800 titrations are determinant. Anti-*N.caninum* antibody titers higher than 1: 800 can be indicative of the clinical form of the disease (Barber and Trees, 1996). It has been reported that with antibody titers of 1/50 and above are accepted as seropositive with IFAT (Ghalmi et al., 2009). In this case, weak immunoreactivity for *T. gondii* and high immunoreactivity for *N. caninum* were determined with IFAT.

It seems more likely that neosporosis treatment will be successful before the pelvic extremity hypertension develops. Clindamycin has been used in toxoplasmosis-induced polymyositis successfully (Greene et al., 1985). However, clindamycin has failed in a dog with CNS defects with paralysis and muscle cotracture due to neosporosis. (Hay et al., 1990). It is recommended that clindamycin should be given twice a day, with 10 to 40 mg / kg PO dosage in dogs. Although therapeutic concentrations are obtained in most tissues (Panzer et al., 1972), the penetration to CNS of this agent is weak. Side effect reported with this drug is gastroenteritis, which usually disappears when the drug is stopped (Greene et al., 1985). In this case, the vomiting complaint has been reported after the treatment started.

Trimethoprim-sulphamamide has been successfully used in the treatment of toxoplasmosis for many years. With 15 mg/kg dosage, two or three times a day is recommended. Possible side effects include keratoconjunctivitis sicca, hepatitis, gastrointestinal problems, polyarthritis and hemolytic anemia.

Toltrazuril is frequently used for the treatment of coccidiosis in poultry and pigs. At the same time, it is used for *Isospora canis* in dogs. In some studies it has been reported that toltrazuril can be used in dogs combined with trimethoprim sulfonamid against *N. caninum* infection (Cuteri et al., 2005). The recommended dosage of toltrazuril in dogs is 9 mg / kg PO once daily.

In this case, the combination of clindamycin, trimethoprim-sulphonamide and toltrazuril was used. At the end of 3 weeks, the owner informed us that involuntary movements in the pelvic limbs have regressed and the dog has been able to walk. Afterwards, the patient did not come to the control because the owner was considering that the dog had recovered. She stopped giving the medication to the patient. That is why we cannot follow up the patient.

Since *N. caninum* was structurally similar to *T. gondii*, infections were considered and misdiagnosed as toxoplasmosis until *N. caninum* was identified. In this case, Toxoplasmosis was misdiagnosed due to a weak positive test result for serology test and the treatment was started. Due to a weak positive test result for toxoplasmosis, further tests were not applied in order to justify the diagnosis. Hence the diagnosis was taken as toxoplasmosis where the treatment was not successful.

This case is written to attract attention of veterinarians to *N. caninum* infection which is frequently misdiagnosed as toxoplasmosis and economically important due to abortion in cattle and sheep in our country.

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