

A CLINICAL AND SEROLOGICAL FOLLOW-UP ON CATS WITH NEUROLOGICAL DISORDERS SUSPECTED FOR TOXOPLASMOSIS

EVOLUȚIA CLINICĂ ȘI SEROLOGICĂ LA PISICI CU MANIFESTĂRI NERVOASE, CU SUSPICIUNE DE TOXOPLASMOZĂ

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ABSTRACT | REZUMAT

Toxoplasma gondii is a widespread dioxen protozoan parasite, with a high zoonotic risk. Cats are the definitive host for *Toxoplasma gondii* and the only animals that pass oocyst in feces. The intermediate hosts represented by different species of birds and mammals, including cats, can develop infective tissue cyst (after ingestion of oocytes with *T. gondii*). In cats, toxoplasmosis is generally subclinical; however, it can generate frequent neural disorders, behavior changes, stupor, incoordination, atypical cry, seizures, but also ocular (uveitis, mydriasis, anisocoria, slow pupillary light reflex) and pulmonary (pneumonitis) pathology.

The present study describes a clinical follow-up of 15 owned cats originated from Bucharest area, suspected for toxoplasmosis. All cats included in the study presented different neurological disorders, mainly epileptic seizures (46.66%) and behavioral changes.

Blood samples were collected and tested for the presence of *T. gondii* IgG antibodies using serological immuno-chromatographic method. All 15 cats were serological positive for *T. gondii* at the beginning of the follow-up. A specific therapeutic protocol was applied for a period of 28 days and a new serological assay post treatment (p.t.) was performed.

The clinical signs stopped after treatment in all cats; however three cats were still positive for IgG p.t.

The study reveals the importance of serologic diagnosis and clinical management of cats suspected for toxoplasmosis and highlights the need for further epidemiological studies, considering the potential zoonotic risk factor.

Keywords: *Toxoplasma gondii*, cats, neurological disorders, IgG antibodies

Toxoplasma gondii este un parazit protozoar dioxen cu răspândire globală, cu un risc zoonotic major. Felinele reprezintă gazda definitivă a protozoarului și singurele animale care excretă oochiști prin fecale. Gazda intermediară este reprezentată virtual de toate speciile cu sânge cald, mamifere, inclusiv pisica, și păsări, la care se dezvoltă chisturile tisulare infectante. La pisică, toxoplasmoza este în general subclinică, dar poate determina frecvent semne nervoase (schimbări de comportament, stupoare, incoordonare, crize psiho-motorii, convulsii de tip epileptiform), semne oculare (uveită, midriază, anizocorie, reflex pupilar scăzut) și semne pulmonare (pneumonie).

Prezentul studiu descrie monitorizarea clinică a 15 pisici cu suspiciune de toxoplasmoză. Pisicile incluse în studiu au prezentat semne nervoase, predominant convulsii de tip epileptiform (46,66%) și schimbări comportamentale. Au fost recoltate probe de sânge pentru decelarea prezenței anticorpilor IgG anti-*T. gondii*, folosind o metodă serologică imuno-cromatografică. Toate cele 15 pisici au fost seropozitive. Consecutiv, a fost instituit un protocol terapeutic specific pentru o perioadă de 28 de zile, urmat de o nouă determinare serologică la 14 zile p.t.

La finalul tratamentului, tabloul clinic s-a ameliorat semnificativ, cu dispariția crizelor epileptiforme, dar serologic trei animale au fost pozitive.

Studiul reflectă importanța monitorizării serologice și supravegherea clinică a pisicilor cu suspiciune de toxoplasmoză, evidențiind necesitatea studiilor epidemiologice avansate datorită caracterului zoonotic al bolii.

Cuvinte cheie: *Toxoplasma gondii*, pisică, tulburări nervoase, anticorpi IgG

Toxoplasma gondii is a dioxen protozoan parasite responsible for a ubiquitous zoonosis which can infect all warm-blooded animals (4, 15). Cats are the definitive hosts and they complete the sexual phase in the

gastrointestinal tract, passing environmentally resistant oocysts in feces (5). The intermediate hosts are represented by different species of mammals, including cats and birds, which can develop infective tissues cyst (after ingestion of oocytes with *T. gondii*) (6).

Nearly one third of the human population was reported to be infected with the parasite and most of them are asymptomatic (8, 16, 18).

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However, *T. gondii* infection in pregnant women and immunocompromised patients can cause severe disease and even death (4).

Toxoplasmosis is recognized as one of the most common diseases in cats with neurological signs and has been associated with infections like FIV (Feline immunodeficiency virus) and FeLV (Feline Leukemia Virus) (11). In cats, common clinical signs include fever, ocular inflammation, ataxia, seizures, muscle pain and respiratory distress (3). Although neurological disorders aren't the most common clinical signs in toxoplasmosis, they are the most severe due to localization (central nervous system) (4).

Chronic toxoplasmosis in cats should be on the differential diagnosis list for cats with seizures, ataxia, uveitis, chorioretinitis, cutaneous lesions, fever, muscle hyperesthesia, myocarditis with arrhythmias, weight loss, anorexia, icterus, diarrhea, respiratory distress, or pancreatitis (3).

Diagnosis of clinical feline toxoplasmosis is difficult. Radiographic, hematologic and biochemical changes sometimes occur but are not pathognomonic (14).

Detection of oocysts in cats has a poor negative predictive value for clinical toxoplasmosis, because most clinical toxoplasmosis results from disseminated infections that occur after oocyst shedding has been completed. Detection of *T. gondii* antibodies in serum is used most frequently for the diagnosis of clinical toxoplasmosis. Different techniques have been assessed, including ELISA, immunofluorescent antibody (IFA), Western blot immunoassay and a variety of agglutination tests (12).

IgA antibodies are considered to be a marker of acute infection, which are produced earlier than IgM, and may persist for several months. The shorter period of IgE may give a greater indication of current infection. The presence of IgG antibodies suggests the occurrence of infection, but does not provide any information about the timing of infection (18).

In cats with suspected clinical toxoplasmosis a supportive therapeutic protocol should be administered. For the treatment of clinical toxoplasmosis, clindamycin hydrochloride (10 to 12 mg/kg, orally [PO], every 12 hours) or a trimethoprim-sulfonamide combination (15 mg/kg, PO, every 12 hours) should be administered for 4 weeks (13). Atovaquone has also been used with some success, although its efficacy has so far appeared to be less than what is seen with the pyrimethamine combinations (1).

A presumptive ante-mortem diagnosis can be done using the following combination: demonstration of

antibodies in serum, demonstration of an IgM titer >1:64 or a greater increase in IgG titer, which suggests recent or active infection, clinical signs of disease, exclusion of other common causes of clinical syndrome and a positive response to appropriate treatment (13).

For the reasons discussed above, antibody test results alone cannot be used to make a diagnosis of toxoplasmosis; for this, a more complex approach is required, according to the clinical signs associated with long-term monitoring. Therefore, the aim of the present study was to perform a clinical and serological follow-up in cats suspected with chronic toxoplasmosis.

MATERIAL AND METHODS

A number of 15 cats (owned cats), originated from Bucharest area, aged between 1 and 12 years, with neurological signs, suspected for toxoplasmosis were included in the present study. The cats were subjected to a complete medical history, clinical and neurological examination. Serological tests for IgG anti-*Toxoplasma gondii* antibodies were carried out. For this, serum samples were examined by an immuno-chromatographic assay using a commercially available test (Biogal ImmunoComb kit). The intensity of the color result was read using the CombScale (Score 0-negative, Score 1 and Score 2-inconclusive, Score 3 and Score 4-positive, Score 5 and Score 6-high positive). The test has a specificity of 100% and a sensitivity of 92.3%, thus false negative results can be possible.

Biochemical profile (liver enzymes and renal parameters) and complete blood count were performed in all cats. After serological and clinical tests, the seropositive cats for *Toxoplasma gondii* and with clinical signs associated with toxoplasmosis were submitted to the same therapeutic protocol, for 28 days with: antibiotic therapy: clindamycin 10 mg/kg twice a day orally for 28 days; liver support according to body weight; antiepileptic drugs: levetiracetam 250 mg 1/8 twice a day and phenobarbital 4mg/kg administered orally, when seizures occurred.

The clinical follow-up was performed at the end of the treatment (28 days). In cats with remitted clinical signs, 14 days after the finish of the treatment (42 days from the beginning of the first examination), serological assay was performed.

RESULTS AND DISCUSSIONS

The neurological changes observed in cats included in the present study were as follows: status was

Table 1

Clinical signs displayed by cats suspected for toxoplasmosis

No. of affected cats	Changes in appetite	Defecation after seizure	Urination after seizure	Loss of conscience	Salivation during seizure	Gait abnormalities	"menace" and "cotton ball" reflexes	Vestibular symptoms	Ocular symptoms	Changed status	Behavioral changes
3	+	-	-	-	-	+	+	+	-	-	-
2	-	+	+	+	+	+	+	-	-	-	-
1	-	-	-	+	-	+	+	-	-	-	-
1	-	-	-	-	-	+	+	-	-	-	-
3	-	-	-	-	-	-	-	+	-	-	-
5	-	-	-	-	-	-	-	-	+	-	-
15	-	-	-	-	-	-	-	-	-	+	+

depressed on all patients, behavioral changes on all cats, four out of fifteen cats (26.66%) presented epilepsy-like seizures only and three cats (20%) had epilepsy-like seizures and vestibular symptoms, five cats out of fifteen (33.33%) had ocular symptoms and three cats (20%) had only vestibular disorders. There were no changes in proprioception, spinal reflexes, panniculus and perianal reflex (Table 1).

The epilepsy-like seizure in cats, ranging from 30 seconds to 2-3 minutes, did not present a classic clinical pattern and they were determined at a variable period of time (from one per day till 7-8/day). During the seizures two cats (28%) manifested defecation and urination and after the seizures, three cats out of seven (42%) manifested changes in appetite.

Unlike the classic epilepsy seizure only three cats (42%) have lost their conscience and in two cats (28%) salivation was observed.

All seven cats with epilepsy like-seizure presented gait abnormalities with the tendency to lean the head against objects and to fall on the affected cerebral area. Also, the "menace" and "cotton ball" reflexes were delayed on all cats with epilepsy-like seizures.

Six cats out of fifteen (40%) presented vestibular symptoms manifested with head tilt, tight circling on the side of the affected lesion and head tremors.

Five cats out of fifteen (33.33%) had ocular symptoms manifested with delayed palpebral/pupillary reflex, spontaneous nystagmus in four cats (26%) and one cat with blindness (10%).

Chronic toxoplasmosis imposes differential diagnoses for cats with anterior or posterior uveitis, cutaneous lesions, fever, muscle hyperesthesia, myocarditis with arrhythmias, weight loss, anorexia, seizures or pancreatitis (13).

In the study performed by Lappin et al. (14), 60% (9/15) of cats presented ophthalmic signs. In contrast, in the present study only 33.33% (5/15) of cats presented ocular lesions and only one cat was compa-

tible with ocular toxoplasmosis (blindness).

The serological test for IgG anti - *T. gondii* was positive for all cats included in the present study and a clinical follow-up was performed.

The high prevalence of *Toxoplasma* infection in animals, including cats, in different area of Romania was reported. Thus, a study in western Romania has reported high prevalence rates of *Toxoplasma* infection in cats (77.42%) and sheep (61.33%) with a commercial ELISA test (9). In the study performed by Iovu et al. (10), in the center and north-west part of Transylvania, the seroprevalence registered in cats with toxoplasmosis was 57.7% and also, the study revealed that seropositivity in cats increased with age.

Overall, a high seroprevalence of *T. gondii* in cats may indicate potential risks to public health, pointing out the common sources of infections for both humans and cats (15).

Biochemical markers and hematologic results were within normal range, with the exception of a mild increase in leukocytes in all 15 cats suggesting the presence of inflammation.

After clinical examination and serological assay, the same therapeutic protocol was applied to all seropositive cats for *T. gondii* which manifested clinical disorders associated with toxoplasmosis. At the end of the treatment (28 days), clinical signs were significant improved in a high percentage 93% (14/15), with no epilepsy-like seizure.

Fourteen days post-treatment (at 42 days) serological tests for IgG anti-*T. gondii* were performed.

The results were negative (Score 0) were obtained in a high percentage 80% (12/15); however, for three cats, the test was positive (Score 3) but with no clinical signs, and these cats were advised for long-term monitoring.

This evolution of cases in the present study could be explained and according with other studies. Thus, some cats with low *T. gondii* antibody titers can be-

come seronegative, even though *T. gondii* is still within tissues. Some cats with low positive IgG titers (1:64) can be positive for IgG antibodies on one analysis and negative on subsequent analysis or vice versa based on a approximate 10% interassay variation (13).

CONCLUSIONS

In the present study clinical toxoplasmosis in cats was suspected based on serological evidence of infection and neurological disorders, correlated with response to specific therapy, and subsequently a serological and clinical follow-up was performed. At the end of the treatment clinical signs were significant improved and serological tests for IgG anti-*T. gondii* performed 14 days p.t. revealed that 80% of cats were negative. The study reveals the importance of serologic monitoring and clinical management of cats suspected for toxoplasmosis and highlights the need for further epidemiological studies, considering the potential zoonotic risk factor.

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