

CEREBRAL VASCULITIS CAUSED BY TOXOCARA CANIS - CASE REPORT

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Abstract: *Toxocara canis* is a ubiquitous parasite found worldwide. She can only complete lifecycle in dogs, and humans are accidental hosts. Among the neurological and neuropsychological disturbances produced by *Toxocara* infection, in humans, the most representative are meningitis, encephalitis, myelitis and cerebral vasculitis. We present a case of cerebral vasculitis and suspicious retinal vasculitis of a thirty-five-year old, HIV-negative woman. Predominant symptoms were trembling and tingling in the left side of the body, tremor of the hands and weakness of the extremities, more to the left, fever and visual disturbance. MR imaging of the brain showed obliterative endarteritis to the left. Visual acuity was impaired, the optic nerve was swollen and macula was thickened. Antibodies to *Toxocara canis* were detected by ELISA test. Antiparasitic therapy with corticosteroids has led to the reduction of symptoms and clinical findings.

Key words: *Toxocara canis*, vasculitis, central nervous system, visual impairment

1. INTRODUCTION

Toxocariasis is an infection transmitted from animals to humans. *Toxocara cati* and *Toxocara canis* are the etiological factors of human toxocariasis. *Toxocara canis* is parasitic roundworms can only complete its lifecycle in dogs, and humans are accidental hosts [1, 2]. People can become infected from eating undercooked meat containing *Toxocara* larvae, or by accidentally swallowing dirt that has been contaminated with dog feces that contain *Toxocara* eggs. At the time of intrusion in the host gastro-intestinal system, the progression continues through the portal vein to the liver, where it can be cantonated, but also, with the possibility of by-passing the liver and continuing to migrate through the circulation in systemic organs, causing the manifest form of the disease depending on the concerned organ [3]. Toxocariasis can be categorized into four main stages: asymptomatic-the most prevalent phase, visceral, ocular and neurotoxocariasis. The factors that contribute to the stage of the disease include: the quantity and quality of the infection, the patient's immune response and the concerned organs [4]. *Toxocara sp.* can cross the blood-brain barrier leading to neurotoxocariasis. The most representative diseases are meningitis, encephalitis, myelitis and cerebral vasculitis, but asymptomatic central nervous system infection is probably the most prevalent. *Toxocara canis* can caused ocular toxocariasis demonstrate a localized disciform macular detachment, multifocal granulomas with interconnecting tracks, peripheral retinal detachment, papillitis, peripheral retinal mass, pars plana mass, vitritis, endophthalmitis, or cataract. The most common causes for vision loss in the setting of ocular *Toxocara canis* are dense vitritis, cystoid macular edema and tractional retinal detachment [5].

The aim of this case report is to describe clinical and angiographic findings of cerebral vasculitis and suspicious retinal vasculitis caused by *Toxocara canis*.

2. CASE REPORT

A thirty-five-year old woman was treated on Department for Infectious and Tropical Diseases, General Hospital Uzice due to fever, headache, weakness, nausea, impaired mobility, tremor of the left arm and impaired vision.

The symptoms began six months ago. The initial symptoms were trembling and tingling in the left side of the body, tremor of the hands and weakness of the extremities, more to the left. Fever occurred about ten days before admission, up to 38.5°C. He did not report about diseases or substance abuse was described in his medical history. Patient was heterosexual, without history of chronic diseases. The patient lives in a rural household, has a dog and a cat.

At the time of admission she was conscious, orient in self, place and time, febrile 38.3°C, cardiac compensated. Facial skin is hyperemic, and banded erythematous changes occasionally appear on the skin of the trunk and extremities, which spontaneously recede. Auscultatory findings on the heart and lungs were normal. There was no palpable lymphadenopathy, or hepatosplenomegaly. Genital examination showed no rashes or ulcers.

The neurological findings include gait instability, hand tremor, mild convergent strabismus, diplopia, blurred vision, and slightly decreased left-sided sensibility. Pupillae were isocoric, direct and indirect light reflexes were bilaterally positive. Cranial nerves were intact. Romberg test was positive. Muscle tone on the upper and lower extremities is preserved, tendon reflexes are symmetrically evoked, there are no pathological reflexes, no phenomenon of lateralization. Meningeal signs were negative.

In his mental examination: attention, abstract thinking, reality testing and judgment were impaired. Associations in thinking process and its content were reduced.

MR imaging of blood vessels of the brain showed multiple small branch occlusions in the middle cerebral artery, with multiple consecutive cerebral infarcts to the left. The total blood flow was slow, more to the left.

Ophthalmic examinations: Visual acuity was 3/9 in the right eye and 3/150 in the left eye. The optic nerve was swollen. Macula was thickened with underlying subretinal fluid.

The heart and lung x-rays were normal. X-ray of the cervical spine indicated discrete sinistroconvex scoliosis of the thoracic spine. Ultrasound of the abdomen showed a 2.7 cm liver cyst.

Laboratory findings and cerebrospinal fluid (CSF) were within normal limits. The blood and CSF bacterial, fungal and acid fast bacteria cultures revealed no growth. Anti HIV antibodies and HIV antigen were negative. No bacteria, amoebae, parasites or fungi were detected in the stool.

They were not diagnosed echinococcosis (by Enzyme-linked Immunosorbent Assay), cysticercosis (by ELISA and Western blot), brucellosis (by Brucella Microagglutination test), toxoplasmosis (by Chemiluminescent Immunoassays).

Diagnosis of *Toxocara canis* (anti IgG antibody titer) was established by ELISA test (1:400).

Patient was treated with albendazole and methylprednisolone in pulse therapy initially, later oral prednisone. Five days after starting the therapy, she becomes afebrile. Three months later, the patient had improved cognitive function, the visual acuity remained at 3/30, and fundus examination showed improving macular star, optic nerve edema, and retinal exudates. Visual acuity improved to 3/4 in the right eye and 3/9 in the left eye fifteen months later.

3. DISCUSSION

Cerebral vasculitis is inflammation of blood vessel walls in the brain. It is often accompanied by autoimmune diseases, infection and systemic vasculitic disorders. It can also occur without any associated systemic disorder. A wide range of infections (virus, bacteria, parasite and fungi) may cause cerebral vasculitis. Headache, seizures, encephalopathy and stroke are common forms of presentation. Infection and inflammation of intracranial vessels may cause pathological vascular remodelling, vascular occlusion and ischemia [6].

Worldwide seroepidemiological surveys as assessed by IgG antibody reveal that human toxocarosis is among the most frequently occurring helminthiasis, highest in rural areas, ranging from 35% to 42%. Dogs may increase the risk of infection to humans in 15% to 20% [7]. Our patient stated the presence of a dog in the household, which was indicated by examinations in the direction of parasitosis.

Patients with toxocarosis have a wide variety of inflammation-related conditions, such as asthma, pneumonia, lymphadenopathy, endomyocarditis, granulomatous hepatitis, generalized endophthalmitis, meningoencephalitis, and cutaneous manifestations [8, 9]. Vasculitis is a well-documented finding in many organs in patients affected by *Toxocara canis* infection [10]. Neurotoxocarosis is a severe disease that has been associated with a decrease in mental activity, social changes and neurodegenerative diseases. Regarding immunopathogenesis, TES antigens have been found to play a role in triggering granulomatous inflammation. The immune response is Th 2 mediated which implies IgE antibodies titer, eosinophilia, and enhanced cytokine expression (IL-13, IL-4) [11]. Evidence suggests that infection with *Toxocara* sp. is associated with a polarized CD4 Th2 response with elevated IgE levels and eosinophilia, mediated by human leukocyte antigen (HLA) class II molecules. HLA class II molecules have been linked to disease severity and host genes affecting exposure-related behaviors [12].

The diagnosis in our patient was made more difficult by the absence of eosinophilia in the blood picture and the orderly finding of the cerebrospinal fluid. The IgE class was not elevated.

Cerebral vasculitis was seen by MR angiography, similar to the cases described earlier [13]. Xinou and coauthors detected cerebral infarction near cerebral granulomas. Cerebral vasculitis can develop during anthelmintic treatment, and whether infarctions are caused by a type IV hypersensitivity to anthelmintic therapy or an acute inflammatory response to the antigen remains to be elucidated [14]. In our case, vasculitis was diagnosed before the application of antiparasitic therapy.

In addition to the pronounced neurological symptoms, our patient had impaired mental functions like attention and abstract thinking. Visual disturbance was her most pronounced symptom even were not seen endophthalmitis or granulomas in the peripheral retina. Granulomas have been described in the literature in 50% to 64% of cases,

posterior pole granuloma seen in 25% to 36% of cases and endophthalmitis seen in 25% of cases [15]. Besirli and Elner described retinal vasculitis demonstrated leakage of fluorescein from the optic nerve and the retinal veins [16]. Although clinical symptoms indicated possible retinal vasculitis, it was not confirmed in our patient because fluorescent angiography was not performed.

Based upon the high levels of exposure to *Toxocara* worldwide but the relatively small numbers of human cerebral toxocariasis cases reported in the literature, Fan and associates concluded that most cases of human toxocaral brain involvement are likely to involve small numbers of larvae that do not present with significant clinical neurological signs [17]. However, research on mouse models has linked this parasitosis to the onset of Alzheimer's disease [18]. At the last check-up, our patient had an improvement in mental functions. Unfortunately, she did not come for the next check-ups and we have no information about further recovery.

4. CONCLUSION

Toxocariasis needs to be considered in the differential diagnosis of cerebral vasculitis and retinal vasculitis. Suspicion of *Toxocara canis* infection is especially important in people who report contact with dogs. Antibody titer on *Toxocara canis* is necessary for diagnosis, as well as MR angiography. Early diagnosis and treatment with antiparasitic therapy and corticosteroids leads to recovery of neurological and ocular symptoms and fundoscopic findings.

4. REFERENCES

1. STEWART J.M, CUBILLAN L.D, CUNNINGHAM E.T. Prevalence, clinical features, and causes of vision loss among patients with ocular toxocariasis. *Retina* 2005; 25:1005–13.
2. TAYLOR M.R. The epidemiology of ocular toxocariasis. *J Helminthol* 2001; 75:109–118.
3. SAKAKIBARA A, BABA K, NIWA S, YAGI T, WAKAYAMA H, YOSHIDA K, ET ALL Visceral larva migrans due to *Ascaris suum* which presented with eosinophilic pneumonia and multiple intra-hepatic lesions with severe eosinophil infiltration-outbreak in a Japanese area other than Kyushu. *Intern Med.* 2002; 41: 574-9.
4. JANECEK E, BEINEKE A, SCHNIEDER T, STRUBE C. Neurotoxocarosis: Marked preference of *Toxocara canis* for the cerebrum and *T. cati* for the cerebellum in the paratenic model host mouse. *Parasit Vectors* 2014; 7: 194.
5. BESIRLI C.G, ELNER S.G. Retinal vasculitis in *Toxocara canis* neuroretinitis. *Journal of Ophthalmic Inflammation and Infection* 2013, 3:5.
6. ARTAL FJC. Clinical management of infectious cerebral vasculitides. *Expert Rev Neurother* 2016; 16:205-21.
7. WOLFE A, WRIGHT IP. Human toxocariasis and direct contact with dogs. *Vet Rec.* 2003; 152:419–22.
8. CALDERA F, BURLONE ME, GENCHI C, PIRISI M, BARTOLI E. *Toxocara* encephalitis presenting with autonomous nervous system involvement. *Infection* 2013; 41:691–94.
9. RANASURIYA G, MIAN A, BOUJAOUDE Z, TSIGRELIS C. Pulmonary toxocariasis: a case report and literature review. *Infection* 2014; 42:575–78.
10. RUBINSKY-ELEFANT G, HIRATA CE, YAMAMOTO JH, FERREIRA MU. Human toxocariasis: diagnosis, worldwide seroprevalences and clinical expression of the systemic and ocular forms. *Ann Trop Med Parasitol* 2010; 104:3–23.
11. KAYES SG. Human toxocariasis and the visceral larva migrans syndrome: correlative immunopathology. *Chem Immunol* 1997; 66:99–124.
12. QUINNELL RJ. 2003. Genetics of susceptibility to human helminth infection. *Int J Parasitol* 2003; 33:1219–31.
13. LOMPO LD, KAMDEM FK, REVENCO E, ALLIBERT R, MEDEIROS E, VUILLIER F, ET ALL. *Toxocara canis* cerebral vasculitis revealed by iterative strokes. *Rev Neurol* 2012; 168:533–7.
14. XINOU E, LEFKOPOULOS A, GELAGOTI M, DREVELEGAS A, DIAKOU A, MILONAS I, ET ALL. CT and MR imaging findings in cerebral toxocaral disease. *Am J Neuroradiol* 2003; 24:714–8.
15. STEWART JM, CUBILLAN LD, CUNNINGHAM ET. Prevalence, clinical features, and causes of vision loss among patients with ocular toxocariasis. *Retina* 2005; 25:1005–13.
16. BESIRLI CG, ELNER SG. Retinal vasculitis in *Toxocara canis* neuroretinitis. *Journal of Ophthalmic Inflammation and Infection* 2013; 3:5.

17. FAN CK, HOLLAND CV, LOXTON K, BARGHOUTH U. Cerebral Toxocariasis: Silent Progression to Neurodegenerative Disorders? *Clinical Microbiology Reviews* 2015; 3: 663-86.
18. GOSSELET F, SAINT-POL J, CANDELA P, FENART. Amyloid- peptides, Alzheimer's disease and the blood-brain barrier. *Curr Alzheimer Res* 2013; 10:1015–33.