

*Case Report*

## SEVERE TRICHINELLOSIS WITH NEUROLOGICAL INVOLVEMENT – NEUROTRICHINELLOSIS: A CASE REPORT

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Received 11 March 2018; Accepted 03 June 2019

Published online: 07 October 2019

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**How to cite:** Mitrović Nikola, Milošević Branko, Urošević Aleksandar, Nikolić Nataša, Dakić Zorica, Nikolić Ivan, Korac Miloš. Severe trichinellosis with neurological involvement – neurotrichinellosis: a case report. *Veterinarski Glasnik*, 2019. 73 (2), 178-186. <https://doi.org/10.2298/VETGL180311015M>

### Abstract

Trichinellosis is the most common and most important parasitic zoonosis in Serbia. Complications of this disease are frequent, and a fatal outcome is possible. A particularly significant complication is the involvement of the central nervous system – neurotrichinellosis. This case report presents a previously healthy, 51-year-old female from Belgrade, Serbia, a teacher by profession. The disease started with symptoms of gastroenteritis in April, after which symptoms and signs characteristic of trichinellosis occurred (myalgia, fever, bilateral eyelid edema, conjunctivitis). About two weeks before the onset of the first symptoms, the patient consumed pork sausages that had been purchased at a green market. Seven days after the disease started, she was hospitalized at the Clinic for Infectious and Tropical Diseases in Belgrade and the diagnosis of trichinellosis was established. Two days after admission, neurological symptoms appeared – confusion, apathy, right side weakness of the mimic and limb muscles. The medical imaging techniques (CT scan, MRI) showed multiple hypodense changes in different parts of the brain, which corresponded to vasculitis due to parasitic infection. She was treated with approved antiparasitic and corticosteroid therapy. Despite adequate treatment, neurological sequelae were maintained in the follow-up period, and control imaging techniques revealed residual changes in the brain.

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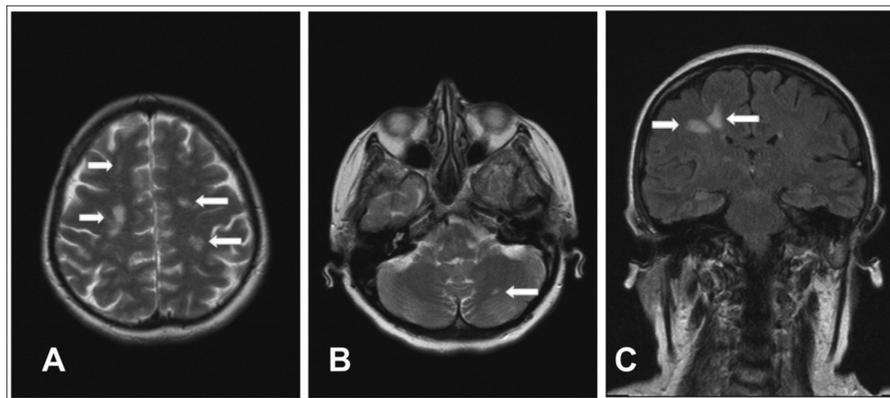
This case emphasizes the importance of the strict application of all foreseen preventive measures in the control of trichinellosis, and primarily, mandatory trichinoscopic examination of all meat intended for human consumption.

**Key words:** *Trichinella*; parasite, foodborne, zoonoses, central nervous system, consciousness, vasculitis.

## CASE PRESENTATION

A 51-year-old female teacher from Belgrade, married with one child and previously healthy, was admitted to the Clinic for Infectious and Tropical Disease, Clinical Centre of Serbia, Belgrade, in April, due to high fever, edema of the eye lids, redness of the eyes and muscle pain in arms and legs. The onset of disease symptoms had started seven days previously, with several liquid stools over two days, followed by abdominal pain. She took a probiotic, adjusted her diet and seemed to recover. On the third day after onset of disease symptoms, fever of around 38.5°C appeared, accompanied by fatigue, edema of the eyelids and redness of the eyes. She was examined by a general physician in a primary health care center and was told that she had a viral infection. She was prescribed eye drops and paracetamol. Two days later, muscle pain affecting the arms and legs started, followed by pain on masticating, and she was sent to the Clinic for Infectious Diseases. On admission, the patient had no fever, was conscious, oriented, eupnoeic, had difficulties moving due to muscle pain, had no skin rash, and had a discrete edema of both eyelids accompanied by conjunctivitis. Physical examination showed normal heart rate (70 beats per minute) and blood pressure (120/60 mmHg). Lung function was normal, abdomen non-tender, with normal bowel sounds, and there was no tenderness of liver or spleen. Neurological examination was normal. Tenderness of the major muscle groups was registered. Biochemical analyses showed leukocytosis (13,100/mm<sup>3</sup>) with significantly increased eosinophils (5,430/mm<sup>3</sup>); elevated muscle enzymes creatine kinase (CK) 4,643 IU/L, lactate dehydrogenase (LDH) 1,234 (U/L), aspartate aminotransferase (AST) 203 IU/L; decreased proteins (59g/L), with hypoalbuminemia (29g/L), and increased factors of acute inflammation, erythrocyte sedimentation rate (ESR) 30 mm/h, c-reactive protein (CRP) 73.4 mg/L, and fibrinogen 6.4 g/L. Anamnesis showed that two weeks before the onset of symptoms (diarrhea), she had, over a couple of days, consumed pork sausages that had been purchased at a green market. Her husband had also consumed those sausages, but at that moment had no problems. The clinical diagnosis of trichinellosis was set and confirmed after four days by serological testing. The commercial enzyme-linked immunosorbent assay (ELISA) Novagnost® *Trichinella spiralis* IgG was used according to the recommendations of the manufacturer (NovaTec Immunodiagnostica GmbH, Dietzenbach, Germany), and the result was 69.6 antibody units (AU) (the test is positive over 11.5 AU). After admission to hospital, treatment with antiparasitic therapy was begun with albendazol at the dose of 2x400 mg per day, along with standard infusion therapy and regular administration of nonsteroidal anti-inflammatory drug (diclofenac). Two days after admission, the patient started to deteriorate with the

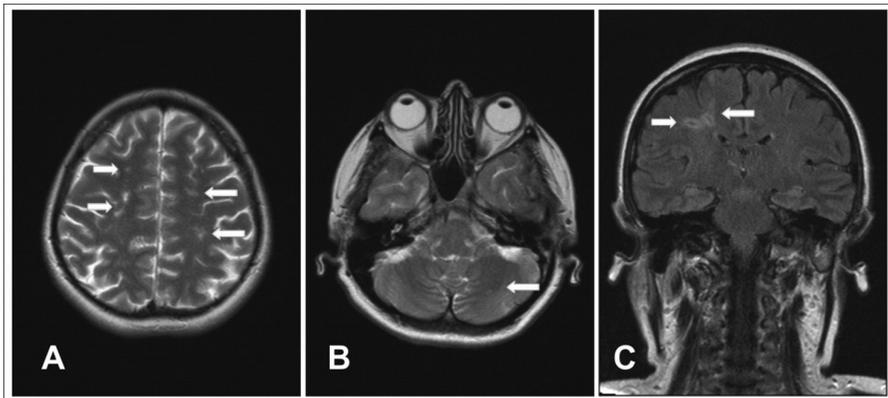
development of neurological symptoms – she became confused and uninterested in what was happening around her, although she preserved quantitative consciousness. Detailed neurological examination showed weakness of the mimic muscles with central paresis of facial nerves on the right side, weakness of the right arm with hyperreflexia of brachioradialis reflex and reflex of the triceps, and weakness of the right leg with increased patellar reflex. Abdominal skin reflexes were absent on the right side, and plantar response was decreased on the right side. Neurological findings in the left side of the body were normal and meningeal signs were negative. On the same day, a CT scan was performed and showed the existence of hypodense changes bilaterally in the parietal region, of which the biggest one was 10 mm in diameter, with no signs of compression. After three days, MRI of the endocranium was performed and showed focal lesions in the white mass bilaterally and supratentorially in the thalamus region on the right side (watershed zones ACA and ACM) and infratentorially on the left side, with the observation that those changes matched the complications of vasculitis during parasitic infection (Figure 1). Cytobiochemical analysis of cerebrospinal fluid (CSF) was normal, and there was no finding of *Trichinella* larvae. Electroencephalography (EEG) examination was normal. After neurological symptoms started, corticosteroid therapy was given in the form of prednisone 60 mg per day, with a gradually decreasing dosage during the next 14 days.



**Figure 1.** MRI images (**A** and **B**, T2W axial plane, **C**, FLAIR coronal plane) three days after development of neurological symptoms in an ill patient, and signs showing several nodular lesions of the brain supra- and infratentorial regions, with slight signal increases in the white mass and subcortical regions (arrows).

During the following days, the patient's condition gradually started to improve, with normalization of consciousness and regression of the right-sided weakness of mimic and limb muscles. Levels of the muscle enzymes normalized after two weeks. The antiparasitic therapy was continued over the course of 14 days. She was discharged after 26 days of hospitalization, with advice for physical rehabilitation and regular ambulatory control. Physical examination on discharge showed paresis of mimic muscles (central

type, moderate grade), slight pronation of the right arm, with increased reflexes in both arms, but neurological examination of the legs showed normal reflexes. During the 3-month follow-up from the onset of the disease, MRI of the endocranium was performed and showed focal lesions in the white mass in the frontoparietal region, subcortical and bilateral. The lesions were in regression compared to their status in the previous examination, but they were now chronic phase lesions, related to the sequelae of the infectious process (Figure 2). The last ambulatory control was conducted in November, seven months from the onset of disease, and biochemical analyses were normal. The patient complained about difficulties in concentration, and she still presented with paresis of facial nerve (central type), while the remaining neurological examinations were normal.



**Figure 2.** MRI images (A and B, T2W axial plane, C, FLAIR coronal plane) three months after onset of disease and after treatment, showing nodular lesions have regressed but are in a chronic and permanent phase (arrows)

The data that the husband had trichinellosis was later provided; his disease was without complications and lasted for 12 days. There was no epidemiological data for other persons who bought meat at the same place as our patient, and nor was it proven whether the meat was checked for the presence of *Trichinella*.

## DISCUSSION

Trichinellosis is a widespread zoonosis caused by parasites from the *Trichinella* genus. This zoonosis is present worldwide and with the exception of Antarctica, it can be found in all other continents. In Serbia, trichinellosis is the most common and most important parasitic zoonosis. In the previous 10-year period (2008-2017), there were, on average, 100 new patients per year (from 46 in 2012, to 190 in 2016), with an average annual incidence of 1.4 per 100,000 persons (from 0.64-2.68) (Institute of Public Health of Serbia Dr Milovan Jovanovic Batut, 2009-2018). People can become infected by larvae of *Trichinella* spp. that are encapsulated in the muscle tissue of fresh

and uncooked or insufficiently cooked meat of domestic or wild animals. In Serbia, the most important animals as sources of infection are pigs, horses, and game animals, especially wild boars. The severity of clinical presentation depends on the number of ingested larvae, but also on the immunological response of the host. It is considered the infective dose is 100 to 300 larvae, and ingestion of over 1000 parasites causes severe clinical presentation (Dupouy-Camet & Bruschi, 2007). Complications of trichinellosis are consistent with the severe form of the disease, and their frequency varies between 0.5% to 25% of trichinellosis cases. The most important complications affect the cardiovascular system, nervous system, kidneys and liver (Kazuea, 2015).

At the onset of symptoms, our patient had a fever and signs of conjunctivitis, and therefore, the general practitioner suspected a viral infection. Brief diarrhea in the patient could not help in early diagnosis. Considering the non-specific start of the disease in patients suffering from trichinellosis, regardless of whether they are first cases in epidemics or sporadic cases, the disease is rarely recognized at the outset, and so initiation of appropriate treatment is delayed (Kazuea, 2015). Early diagnosis of the disease, during the intestinal phases, can be made by finding *Trichinella spiralis* larvae in stool or by detecting excretory-secretory (ES) antigens of intestinal infective larvae (Wang et al., 2017).

After characteristic symptoms and signs of the disease developed (muscle pains), with biochemical analysis (leukocytosis with eosinophilia, elevated muscle enzymes), firstly the clinical and then the serological diagnosis of the disease was set. High eosinophilia and highly elevated levels of muscle enzymes pointed to massive infestation, with considerable risk of disease complication (Capó & Despommier, 1996). Immediately after admission to hospital, the patient was given antihelmintic therapy. Around day 10 of the disease, disease complication involving the central nervous system occurred. Neurological involvement of trichinellosis, sometimes referred as neurotrichinellosis, is one of the most important complications in severe forms of this disease and can be fatal, along with myocarditis and thromboembolic disease (Kociecka, 2000). The frequency of major neurological disturbance is from 1-2% of trichinellosis cases (Ancelle et al., 1998), while the frequency of minor neurological disturbance is much higher (18-52%), noted in a 10-year German prospective study (Harms et al., 1993). Either gray or white matter of the brain, including cerebrum, diencephalon, brainstem, cerebellum, or spinal cord can be involved. Damage can occur by the direct influence of the parasites which migrate into the CNS, or indirectly as a result of the host's inflammatory response to trapped and consequently destroyed larvae. These complications usually appear in the second or third week of the disease but can occur sooner. The signs and symptoms are usually headaches, insomnia, tinnitus, psychological lability, forgetfulness, difficulty in remembering new things, apathy, deafness, and hallucinations. Clinical presentation of severe encephalitis with altered consciousness or even coma can develop, as can paresis and paralysis of extremities. Depression or dementia are not rare (Neghina et al., 2011; Bruschi et al., 2013).

Our patient predominantly had signs of left frontal lobe damage with right sided hemiparesis, changed behavior, and apathy. The medical imaging techniques of the brain (CT, MRI) showed focal changes, diffuse in the brain, that matched vasculitis. This type of damage occurring on the blood vessels, as a consequence of vasculitis and granulomatous inflammatory reaction surrounding the larvae, is considered the pathohistological and pathophysiological basis of neurological damage (Bruschi et al, 2013). In our case, cytological and biochemical findings of the CSF were normal. During neurotrichinellosis, larvae can be present in CSF or meninges (8-28% of cases), while in CSF, increased protein level, moderate cellularity with lymphocytes and eosinophils predominating, and normal glucose level can be registered. However, most reports of neurotrichinellosis describe normal CSF findings, as in our case (Madariaga et al., 2007; Knezević et al., 2001). EEG findings were also normal in our patient, while pathological EEG findings can indicate deceleration of the cortical electric activity without critical aspect (Bruschi et al., 2013). The number of eosinophils in our patient at admission was  $5,400/\text{mm}^3$ , which corresponds to hypereosinophilia. According to Fourestie et al.(1993), patients with eosinophilia higher than  $4,000/\text{mm}^3$  during trichinellosis are more likely to develop neurologic dysfunction than to not exhibit neurologic signs, and the level of eosinophilia correlates with the intensity of infection (Fourestie et al. 1993).

Immediately after the diagnosis was set, antiparasitic therapy was started – the patient was given albendazole – while just after neurological complications occurred, corticosteroids were administered. The antihelminth drugs, albendazole (at a dosage of 15 mg/kg/day divided in two doses for adults and 10 mg/kg/day for children older than 2 years) and mebendazole (5 mg/kg/day divided in two doses) for 10-15 days are the drugs of first choice in trichinellosis treatment. It is important the treatment starts as early as possible because its efficacy greatly depends on this. It is of great importance that antiparasitic therapy is given before corticosteroid therapy to prevent delayed expulsion of adult worms from the gastrointestinal system (Kazuea, 2015; Pozio et al., 2001).

Application of antiparasitic and corticosteroid therapy have a significantly improved the prognosis of neurotrichinellosis, with the mortality of the disease reduced from 46% to 17% (Kociecka et al, 2003). It is considered that early application of therapy, with appearance of neurological manifestations in a timeframe shorter than one month from the onset of the disease, most commonly brings about complete recovery with withdrawal of neurological deficit (Kociecka et al., 2003). Also, lesions found on CT scan and/or MRI usually disappear 1-2 months after infection (Dupouy-Camet et al., 2002). Our patient developed neurological symptoms in the early stage of the disease (on day 10), and she received antihelminthic and corticosteroid therapies in adequate dosages and for adequate durations, but still remained with neurological sequelae. Seven months from the disease onset, weakness of the right side mimic muscles, weaker concentration than she had before, and focal lesions observable on MRI were still persistent. It is probable the severity of disease was the most determining factor

for the sequelae, while adequacy of treatment and host immune competence were of lesser importance (Neghina et al., 2011).

## CONCLUSION

We present the case of a patient with a severe form of trichinellosis with central nervous system involvement, and with the permanent neurological sequelae despite early diagnosis and treatment. This highlights the enormous importance of strict implementation of all measures in order to prevent transmission of parasites from the genus *Trichinella* spp. to humans. Effective preventive measures are mandatory trichoscopic examination of meat by veterinary inspection services, preventing pigs or wild animals, including rats, from eating uncooked meat, scraps, or carcasses of any animals, and adequate heat treatment of meat before human consumption. All these measures can prevent the infection of *Trichinella*, both in humans and in animals, and must be implemented, since Serbia is still an endemic country for trichinellosis, and this disease has high public health and economic significance for both individuals and society as a whole.

### Authors contributions

All authors, MN, UA, MB, NN, DZ, NI and KM, have made substantial contributions to the preparation of the manuscript, regarding the conception and design of the study, analysis and interpretation of data, drafting the article and revising it critically for final approval of the version to be submitted. All authors are in agreement with the content of the manuscript.

### Competing interests

The authors declare that they have no competing interests.

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## **TEŽAK OBLIK TRIHINELOZE SA NEUROLOŠKIM KOMPLIKACIJAMA – NEUROTRIHINELOZA: PRIKAZ SLUČAJA**

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### **Kratak sadržaj:**

Trihinelozu je najučestalija i najznačajnija zoonoza u Srbiji. Komplikacije ove bolesti su česte, a moguće je i smrtni ishod. Naročito značajna komplikacija predstavlja zahvaćenost centralnog nervnog sistema – neurotrihinelozu.

Predstavljen je slučaj prethodno zdrave pacijentkinje stare 51 godinu, iz Beograda, učiteljice po zanimanju. Razbolela se u aprilu mesecu simptomima infekcije gastrointestinalnog trakta, nakon čega su se pojavili simptomi i znaci karakteristični za trihinelozu (mijalgije, povišena telesna temperatura, otok kapaka, konjunktivitis). Oko dve nedelje pre pojave prvih simptoma pacijentkinja je jela svinjske kobasice kupljene na pijaci. Sedam dana od početka bolesti hospitalizovana je u Kliniku za infektivne i tropske bolesti u Beogradu i postavljena je dijagnoza trihineloze. Dva dana nakon prijema pojavila se neurološka simptomatologija - konfuznost, apatija, desnostrana slabost mišićne muskulature i desne plovine tela. Vizualizacionim metodama snimanja mozga (CT, NMR) registrovane su multiple hipodenzne promene endokranijalno, koje su po karakteristikama odgovarale vaskulitisu usled parazitarne infekcije. Lečena je antiparazitarom i kortikosteroidnom terapijom. Nakon završetka lečenja, u periodu praćenja, zastale su neurološke sekvele, a kontrolnim snimanjem registrovane su rezidualne promene u mozgu.

Na ovaj način istaknut je značaj stroge primene svih predviđenih preventivnih mera u kontroli trihineloze, a naročito obaveznog sprovođenje veterinarskog trihinoskopskog pregleda svog mesa predviđenog za humanu upotrebu.

**Ključne reči:** trihinela, parazit, zoonoza prenosiva hranom, centralni nervni sistem, vaskulitis