

# Neurotoxocariasis associated with lower motor neuron disease. Report of one case

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## ABSTRACT

*We report a 51-year-old male with a history of palpitations, hepatopathy and hypercholesterolemia, who habitually ate raw goat meat, and developed general fasciculations, muscle cramps in the lower limbs, distal muscle weakness and wasting, without upper motor neuron signs or sensory abnormalities. Diagnostic work-up revealed positive antibodies against *Toxocara canis* in the serum and cerebrospinal fluid. Nerve conduction studies revealed a proximal and distal axonal lesion of motor nerves and needle electromyography was indicative of acute and chronic denervation with giant motor unit action potentials. Despite a therapy with albendazole and riluzole, muscle weakness and wasting further progressed and affected also the respiratory muscles. Follow-up nerve conduction studies and electromyography confirmed progression of the axonal degeneration. Whether lower motor neuron disease was causally related to neurotoxocariasis or due to a general metabolic defect, remains speculative. (Rev Med Chile 2010; 138: 483-486).*

**Key words:** Electromyography; Motor neuron disease; Neuromuscular diseases; Toxocariasis.

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Recibido el 26 de Agosto de 2009, aceptado el 19 de Marzo de 2010.

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## Neurotoxocariasis asociada a enfermedad de motoneurona inferior. Presentación de un caso

*Presentamos un hombre de 51 años con una historia de palpitaciones, hepatopatía e hipercolesterolemia que comía habitualmente carne de cabra cruda, que desarrolló un cuadro caracterizado por fasciculaciones generalizadas, calambres musculares en las extremidades inferiores, pérdida de fuerza y atrofia muscular distal, sin signos de lesión de motoneurona superior o alteraciones sensitivas. El laboratorio mostró anticuerpos anti *Toxocara canis* en suero y líquido cefalorraquídeo. La electromiografía mostró una lesión axonal proximal y distal de nervios motores y denervación con potenciales de acción gigantes en las unidades motoras. A pesar de tratarse con albendazol y riluzona, la debilidad muscular y atrofia continuaron progresando. Una nueva electromiografía confirmó la progresión de la degeneración axonal. La asociación entre esta enfermedad de motoneurona inferior y la neurotoxocariasis, es especulativa.*

Infection with *Toxocara canis* (*T. canis*) occasionally manifests in the central-nervous-system (CNS) and peripheral-nervous-system (PNS)<sup>1</sup>. One of these CNS or PNS-manifestations is myelitis and radiculitis<sup>1-14</sup>. Here we report a patient with previous neurotoxocariasis who clinically and electromyographically developed lower motor-neuron-disease (LMND).

### Case report

The patient is a 51 yo-male with a history of hepatitis-A in childhood with increase in liver enzymes presumably since then, depression and anxiety for which he received carbamazepine for 15 y until age 49 y, hyperlipidemia since several years, pollakisuria, benzodiazepine misuse, palpitations since age 50 y, and a positive family history for hepatopathy (father, two sisters) and arterial hypertension (mother). He had developed general fasciculations since twelve months, muscle cramps in the lower limbs (LL) since six months, weakness of the distal upper limb (UL) muscles since five months, and weakness in the LL when climbing stairs since age 50 y. He occasionally reported transient double vision and palpitations.

Neurologic investigations revealed sore neck-muscles, weakness for right elbow-extension (M5-), finger straddling bilaterally (M5-), and foot-extension bilaterally (M4-), reduced respectively absent tendon-reflexes, fasciculations in the intrinsic hand muscles, UL distal wasting, and hypotonia. All sensory modalities were intact. Creatine-kinase was repeatedly elevated with a maximal value of 529U/l (n, < 170 U/l) but resting lactate was normal. Repeatedly elevated were also the transaminases and the gamma-glutamyl transpeptidase. Nerve-conduction-studies showed reduced CMAP-amplitude upon stimulation of the right and left median, the right and left ulnar, and the left tibial nerve(s) and reduced nerve-conduction-velocity on the right median, left ulnar, right and left peroneal, and left tibial nerve(s). F-waves were absent upon retrograde stimulation of the right ulnar nerve. Nerve conduction studies of sensory nerves showed normal conduction velocities of the right median, left median, left ulnar and left sural nerves. Needle electromyography of two muscles revealed extensive fibrillations and fasciculations, prolonged mean MUAP-duration,

increased polyphasicity, and reduced interference-pattern with increased amplitude. Cerebrospinal fluid (CSF)-investigations revealed a protein of 53 mg/dl (n, 18-43 mg/dl) and elevated lactate. *T. canis* antibodies were positive in the serum and CSF (40 AKE). Westernblot for IgG-antibodies against *T. canis* was positive in the CSF. Creatine-kinase, glutamate-oxalate-transaminase, glutamate-pyruvate-transaminase, and gamma-glutamyl-transpeptidase were moderately elevated. Resting serum lactate and lead were normal. Investigations for worm eggs in the stool were negative. Cardiac examination revealed paroxysmal atrial fibrillation and a small pericardial effusion.

Therapies with albendazole (400 mg/d) during three weeks and with diethyl-carbazine were ineffective and *T. canis* antibodies remained elevated in the serum and CSF. Weakness slowly but continuously progressed and resulted in gait-disturbance, repeated falls, and wheel-chair boundness. Six months after the first visit nerve-conduction-velocity of the left sural nerve was reduced. Needle-electromyography of the right tibial and right common extensor digitorum muscles showed signs of acute and chronic denervation. Lung-function parameters and bulbar functions were normal. During the following months weakness also involved the respiratory muscles resulting in respiratory insufficiency, emergency intubation, and long-term mechanical ventilation upon the patient's explicit request.

### Discussion

The patient reported is interesting for the association of neurotoxocariasis and the subsequent development of LMND. Whether there was a causal relation between neurotoxocariasis and LMND remains speculative. Either the patient developed LMND as a consequence of the infection with *T. canis* or neurotoxocariasis and LMND were causally unrelated and occurred coincidentally in a time-related manner. Arguments for a causal relation are that myelitis and polyradiculitis have been reported as manifestations of an infection with *T. canis*<sup>2-14</sup>, that there are human and animal studies indicating that larvae of *T. canis* also migrate to the spinal cord<sup>9,15</sup>, that antibodies against *T. canis* persisted in the CSF during clinical deterioration, and that neurotoxocariasis and

**Table 1. Nerve conduction studies in the patient reported**

Investigated nerve	DI	NCV (m/s)	NAP (mV)
Right median (motor)	4.9	37.6	4.2
Left median (motor)	7.5	52.4	0.4
Right ulnar (motor)	4.2	51.3	5.2
Left ulnar (motor)	6.0	33.3	1.3
Right peroneal (motor)	6.2	3.81	4.3
Left peroneal nerve (motor)	5.1	40.0	2.9
Left tibial (motor)	4.3	40.6	5.2
Right median (sensory)	2.6	56.9	9.2
Left median (sensory)	3.1	50.0	4.8
Left ulnar (sensory)	2.6	49.3	11.0
Left sural	2.2	41.3	12.0

DI: distal latency, NCV: nerve conduction velocity, NAP: nerve action potential.

LMND were time-related. Arguments against a causal relation are that serial MRIs did not show swelling, enhancing structures, or granuloma in the spinal cord or surrounding meninges, that the patient did not develop upper motor neuron signs, as has been previously reported<sup>10</sup>; that there was no eosinophilia, neither in the serum nor CSF, although acute myelitis could have passed already and LMND and antibodies against *T. canis* in the CSF may have been the only remains of the disease, and that albendazole did not resolve the clinical manifestations.

Clinical manifestations of myelitis from an infection with *T. canis* may include motor and sensory abnormalities (paresthesia, hypesthesia, positive Lhermitte-sign)<sup>10</sup>. Blood investigations may show leukocytosis, eosinophilia, or antibodies against *T. canis*<sup>9-11</sup>. CSF-investigations may reveal pleocytosis with a high percentage of eosinophils, elevated protein, increased IgG-synthesis, and *T. canis* antibodies<sup>9-11</sup>. On MRI myelitis usually manifests as swelling of the spinal cord with or without enhancement but without compression<sup>10,12,13</sup>. Additionally, there may be T2-hyperintensities, preferentially in the posterior and lateral columns<sup>5,10,13</sup>. Myelitis and radiculitis may go along with or without cerebral manifestations, such as enhancing cortical or subcortical lesions<sup>11</sup>, and may respond to albendazole, mebendazole, thio-bendazole, diethyl-carbazine, or corticosteroids but may nonetheless recur<sup>5,9,13</sup>.

To explain a possible causal relation between neurotoxocarosis and LMND in the patient reported, three pathogenetic scenarios can be put forward: First, larvae of *T. canis* on their migration from the intestines to target tissues carry with them bacteria, viruses, or other infectious agents<sup>16-18</sup>. Via this pathway some patients may have been infected with the polio-virus or other agents. In a study on 191 patients with poliomyelitis 13,6% were positive for antibodies against *T. canis*<sup>18</sup>. Second, it is well known that larvae in humans do not usually mature after their migration but die and become a focus of granulomatous tissue-reaction around their disintegrating bodies<sup>18</sup>. Such a mechanism is assumed to cause epilepsy. Accordingly, patients with epilepsy are four times more frequently positive for antibodies against *T. canis* than controls<sup>18</sup>. Similarly, larvae may cause a focal granulomatous reaction when they reach the spinal cord, compromising anterior horn cells. Third, LMND may be due to allergenic or immune mechanisms of undetermined significance since myelitis frequently recurs despite adequate treatment<sup>11</sup>.

The clinical manifestations of our patient could be also explained by the presence of a mitochondrial disorder assumed upon transient double vision, tinnitus, paroxysmal atrial fibrillation, progressive weakness and wasting, mimicking LMND<sup>19,20</sup>, elevated CK and transaminases, increased CSF-lactate, hepatopathy and the positive family history for it, affection of the sensory

nerves, and hyper-cholesterolemia. Possibly, the infection caused oxidative stress, such that a pre-existing mtDNA mutation with low heteroplasmy rate became pathogenic by exceeding a critical threshold level.

Neurotoxocariasis may be associated with LMND although it remains speculative if the relation was causal or coincidental. Patients with LMND should be screened for antibodies against *T. canis* and vice versa LMND should be excluded in patients with neurotoxocariasis.

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