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Tremor and Other Hyperkinetic Movements

Case Report

Myoclonic Jerks, Exposure to Many Cats, and Neurotoxoplasmosis in an Immunocompetent Male

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Abstract

Background: Myoclonic jerks are due to sudden, brief, involuntary muscle contractions, positive myoclonus, or brief cessation of ongoing muscular activity, negative myoclonus, and may be difficult to recognize.

Case Report: We describe an immunocompetent, adult, male patient with sleep-related, multifocal, myoclonic jerks and neurotoxoplasmosis with abnormal cerebrospinal fluid but normal brain imaging. There was complete resolution of the myoclonus with antitoxoplasmosis therapy after 1 week, and no relapse after 1 year.

Discussion: Neurotoxoplasmosis may be subtle in presentation, difficult to diagnose, and more common than realized, and it is being increasingly implicated in epileptogenesis in humans.

Keywords: Myoclonus, movement disorder, toxoplasmosis, epilepsy

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Introduction

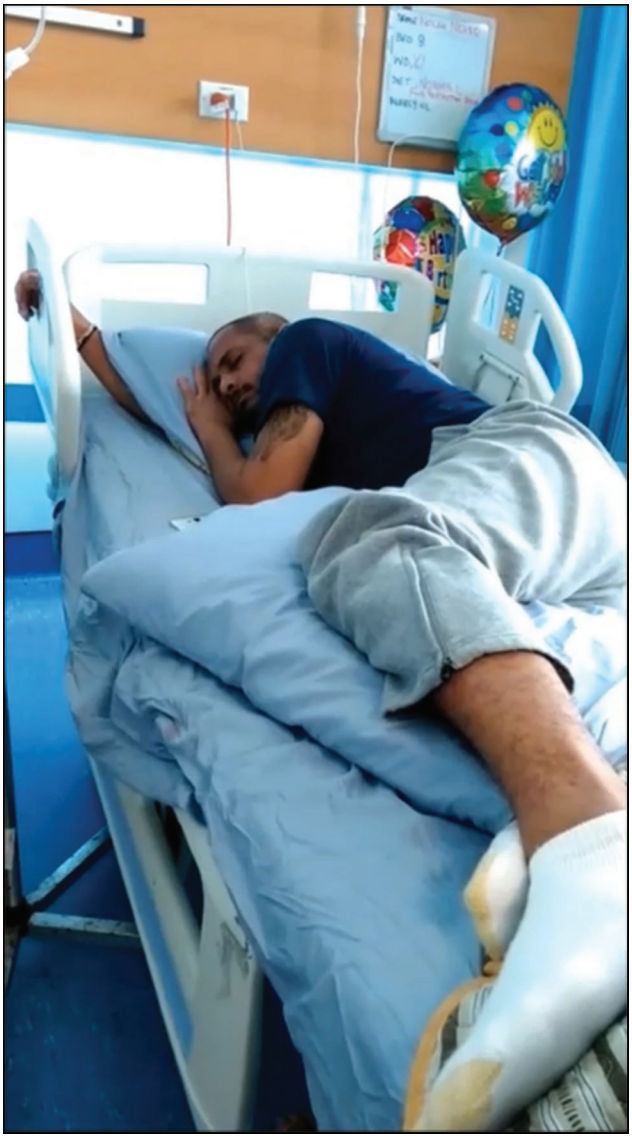
Neurotoxoplasmosis can induce a wide variety of movement disorders including myoclonic jerks especially in immunodeficient individuals.[1] We report a case illustrating sleep-related, multifocal, myoclonic jerks in neurotoxoplasmosis in an immunocompetent adult that responded adequately to treatment.

Toxoplasmosis is also a ubiquitous infectious illness, which has been considered a global threat. Neurotoxoplasmosis is additionally being increasingly recognized as a cause of cryptogenic epilepsy and this case provides further credence to this hypothesis.[1]

By this report, we highlight myoclonus as a manifestation of neurotoxoplasmosis even in the apparently immunocompetent patient, thereby promoting earlier and widespread recognition and consequently appropriate treatment.

Case report

We describe a case of multifocal, myoclonic jerking during sleep (Video 1) in encephalitis as a result of neurotoxoplasmosis in a 39-year-old immunocompetent adult male who had daily contact with 20 resident cats for 2 years. The patient presented to hospital with a flu-like syndrome for 3 days and with multifocal, sleep-related, myoclonic jerks for 1 day. These movements consisted of abnormal, sudden, isolated, brief, small-amplitude, multifocal muscle jerks involving various body areas, in particular the patient's head, right upper limb, fingers, and legs. The phenomenon was observed only during sleep without causing incontinence or arousal and its occurrence was not noted during wakefulness. The myoclonus would start in the first hour of sleep and remained unchanged throughout sleep during the day or at night. We found a pattern of three to five sequences of muscle contractions



Video 1. Demonstration of Myoclonic Jerks in our Patient. This video shows multifocal, myoclonic jerks of the patient's head, right upper limb, fingers, and legs. These involuntary intermittent jerky movements took place during the day or night but only during sleep without causing incontinence or arousal. We found an observable pattern of three to five sequences of muscle contractions per minute, each lasting 2–3 minutes followed by a period of non- observable phenomena of 20–30 minutes' duration. These movements occurred four to six times daily for 7 days. Myoclonus was not observed after spontaneous arousal or while the patient was awake. The patient was always unaware of those events that subsided spontaneously without benzodiazepines.

per minute, each lasting 2–3 minutes followed by a period of a non-observable phenomena of 20–30 minutes' duration. These movements occurred four to six times daily for 7 days. The patient was always unaware of those events that subsided spontaneously without benzodiazepines (Video 1). There was no clinical evidence of other sleep disturbances such as obstructive sleep apnea, sleep-related hypoxemia (saturation of oxygen was 100% on room air), hypoventilation syndromes, narcolepsy, or insomnia.

There was no history of previous illness, surgery, exposure to chemicals, use of recreational drugs, consumption of alcohol, or recent travel abroad. He was febrile (38.8°C), tachycardic (110 beats/minute) with blood pressure of 145/82 mmHg and a respiratory rate of 20 breaths per minute, and he had 100% oxygen saturation on room air. Two, non-tender, soft lymph nodes, 1.2 cm in diameter, were palpable in the cervical region.

There was leukocytosis (13.8×10^9/L) with eosinophilia (14.1%) and elevated C-reactive protein at 31.1 mg/dL. Immunoglobulin (Ig) G antibodies to *Toxoplasma gondii* were detected in the serum and cerebrospinal fluid (CSF) with an elevated titer of 198 and 20 IU/mL respectively by using an electro-chemiluminescence immunoassay. Serum and CSF IgM antibodies to *T. gondii* were also positive. The CSF contained 47 cells/mm^3 and 0.8 g/L protein, both being elevated values. An enzyme-linked immunosorbent assay for human immunodeficiency virus infection (HIV) was non-reactive in serum and polymerase chain reaction testing was unavailable. Magnetic resonance imaging of the brain and spinal cord and scalp electroencephalography (EEG) were normal. The patient had an excellent outcome after specific treatment for toxoplasmosis (trimethoprim–sulfamethoxazole) and the myoclonic jerking disappeared completely in 7 days. The investigations and treatment of the patient are illustrated in Tables 1 and 2. He remained healthy at the 1-year follow-up.

Discussion

Central nervous system (CNS) toxoplasmosis can cause multiple movement disorders and seizures including multifocal myoclonic jerks, even with normal EEG and magnetic resonance imaging/magnetic resonance angiography scans of the brain.[1–3]

Myoclonic jerks because of neurotoxoplasmosis in immunocompetent individuals are rare and we found no other similar reports in the literature. Recent studies have also implicated chronic or latent toxoplasmosis as a possible cause of cryptogenic seizures and/or epilepsy in the immunocompetent individual, which gives added relevance to this case.[1] We suggest that mild clinical expression of disease and normal imaging studies in this case were due to immunocompetence in the patient.

Atypical toxoplasmosis encephalitis with limited clinical expression and with normal conventional imaging may also demonstrate multifocal myoclonic jerking in an immunocompetent host and be due to atypical genotypes of *T. gondii*. Reinfection with toxoplasmosis has been reported among immunocompetent human hosts. Reinfection with toxoplasmosis can occur among people chronically and with heavy exposure to *T. gondii* such as in our patient. Owing to the severity of encephalitis caused by these atypical genotypes that can cause latent or subclinical infections worldwide, suspicion, early diagnosis, and appropriate treatment are essential even in settings with limited resources.[1–3]

Multifocal myoclonic jerks are characterized by sudden, isolated, arrhythmic, asynchronous and asymmetric involuntary brief twitches, and jerks of muscles or muscle fibers involving various body areas,

Table 1. **Medical Investigations**

Tests Performed on Admission	Result	Reference Range
Blood test		
WBCs	13.8 × 10^9/L	4.5–11.0 × 10^9/L
Eosinophils	14.1%	0.0–0.6%
Hemoglobin	15.2 g/dL	14.0–17.5 g/dL
Mean corpuscular volume	83.2 fL/red cell	80–96 fL/red cell
Platelet count	350 × 10^3/μL	156–373 × 10^3/μL
Serum potassium	4.1 mmol/L	3.5–5.1 mmol/L
Serum sodium	138 mmol/L	135–145 mmol/L
Serum creatinine	0.8 mg/dL	0.5–1.2 mg/dL
BUN	11 mg/dL	3–20 mg/dL
Uric acid	4.5 mg/dL	2.5–8 mg/dL
Alanine aminotransferase	60 IU/L	20–60 IU/L
Aspartase aminotransferase	40 IU/L	5–40 IU/L
Gamma glutamyl transpeptidase	60 U/L	8–61 IU/L
Lactate dehydrogenase	330 IU/L	105–333 IU/L
Alkaline phosphatase	129 U/L	40–129 IU/L
Albumin	4.9 g/dL	3.5–5.5 g/dL
Albumin-corrected calcium	9.6 mg/dL	9.6–11.2 mg/dL
CRP	31.1 mg/dL	0.0–1.0 mg/dL
Fasting blood sugar	80 mg/dL	60–120 mg/dL
VDRL test	Non-reactive	Non-reactive or reactive
FTA-ABS	Negative	Positive or negative
Elisa for HIV	Non-reactive	Non-reactive or reactive
Antistreptolysin O titer	90 IU/mL	0–200 IU/mL
Toxoplasma gondii IgG antibodies	198 IU/mL	Positive: greater than 1.09 IU/mL
Toxoplasma gondii IgM antibodies	Positive	Positive or negative
Toxoplasma gondii specific IgG avidity	High avidity (AI > 50%)	Low avidity (AI ≤ 50%) High avidity (AI > 50%)
Herpes virus 1 IgG antibodies	Less than 0.9	Index negative: Less than 0.9
Herpes virus 1 IgM antibodies	Less than 0.9	Index negative: less than 0.9
Herpes virus 2 IgG antibodies	Less than 0.9	Index negative: Less than 0.9

Table 1. Continued

Tests Performed on Admission	Result	Reference Range
Herpes virus 2 IgM antibodies	Less than 0.9	Index negative: less than 0.9
CMV IgG antibodies	0.800 UA/mL	Negative: less than 1.5 UA/mL
CMV IgM antibodies	0.778 UA/mL	Negative: less than 1.1 UA/mL
EBV IgG antibodies	3.3	Positive: Greater than 22
EBV IgM antibodies	0.1	Negative: less than 0.8
Hepatitis BsAG	Negative	Positive or negative
Hepatitis C IgG antibodies	Negative	Positive or negative
Hepatitis C IgM antibodies	Negative	Positive or negative
Echinococcus granulosus IgG antibody	Negative	Positive or negative
Anti-double stranded DNA	Negative	Positive or negative
Antinuclear antibody	Negative	Positive or negative
Perinuclear antineutrophil cytoplasmic antibodies	5.42 U/mL	Negative: less than 10.0 U/mL
Cytoplasmic antineutrophil cytoplasmic antibodies	3.73 U/mL	Negative: Less than 10.0 U/mL
PCR for viral infections or toxoplasmosis	Tests not obtained	Negative or positive
Other investigations		
Mantoux test	Negative	Positive or negative
Electrocardiogram	Sinus tachycardia	Normal or abnormal
Chest X-ray	Normal	Normal or abnormal
Echocardiogram	Normal ejection fraction 75%	Normal or abnormal
CT scan of the brain with contrast	Normal	Normal or abnormal
MRI/MRA scans of the brain	Normal	Normal or abnormal
CSF analysis	CSF opening pressure was 14 cm of H_2O. CSF contained 47 cells/mm^3, 0.8 g/L of proteins, and the glucose concentration was 60 mg/dL. CSF culture showed no bacterial growth and cytology was negative for neoplastic cells. VDRL was non-reactive and India ink test for *Cryptococcus neoformans* was negative	
Toxoplasma gondii IgG antibodies in CSF	20 IU/mL	Positive: greater than 1.09 IU/mL
Toxoplasma gondii IgM antibodies in CSF	Positive	Positive or negative

Table 1. Continued

Tests Performed on Admission	Result	Reference Range
Tests performed in the follow-up blood test		
Toxoplasma gondii IgG antibodies	20 IU/mL	Positive: greater than 1.09 IU/mL
Toxoplasma gondii IgM antibodies	Positive	Positive or negative
PCR for viral infections or toxoplasmosis	Tests not obtained	Negative or positive
Other investigations		
Scalp EEG	Normal	Normal or abnormal
EMG and nerve conduction studies	Normal	Normal or abnormal
PCR for viral infections or toxoplasmosis in CSF	Tests not obtained	Negative or positive
Video-EEG, polysomnography and jerk locked backed averaging studies	Tests not obtained	Normal or abnormal

Abbreviations: BUN, Blood Urea Nitrogen; BsAG, B surface antigen; CMV, Cytomegalovirus; CRP, C-reactive Protein; CSF, Cerebrospinal Fluid; CT, Computed Tomography; DNA, Deoxyribonucleic Acid; EBV, Epstein–Barr Virus; EEG, Electroencephalogram; ELISA, Enzyme-linked Immunosorbent Assay; EMG, Electromyography; FTA-ABS, Fluorescent *Treponema Pallidum* Antibody Absorption; HIV, Human Immunodeficiency Virus; Ig, Immunoglobulin; MRI/MRA, Magnetic Resonance Imaging/Magnetic Resonance Angiography; PCR, Polymerase Chain Reaction; VDRL, Venereal Disease Research Laboratory; WBC, White Blood Cell.

Table 2. **Medical Treatment**

	Dosage	Period of Treatment
Intravenous therapy initiated on admission day		
Trimethoprim–sulfamethoxazole	160 mg/800 mg 3 times daily	2 weeks
Normal saline isotonic solution	1 L daily	1 week
Pantoprazole	40 mg twice daily	3 days
Oral drugs initiated on admission day		
Carbamazepine	200 mg 2 times daily	6 days
Paracetamol	1 g three times daily	7 days
Other oral drugs		
Trimethoprim–sulfamethoxazole	80 mg/400 mg per tablet 2 tablets 2 times daily	4 weeks initiated on day 15
Pantoprazole	40 mg once daily	14 days initiated on day 4

in particular the corners of the mouth, fingers, toes, limbs, several limbs, or a combination of limbs plus face, palate, head, jaw, neck, tongue, eyes, or trunk. Myoclonic jerks may have their origins at different levels of the nervous system and have many causes, and specialized tests such as video EEG, electromyography, and polysomnography are often necessary to ascertain its precise origin and accurate classification.[3]

Myoclonus may be cortical, subcortical, spinal, or peripheral in origin. Myoclonic jerking that is fleeting at the onset of sleep, or hypnic myoclonus, is considered physiological. It can be multifocal but seldom

Table 3. **Differential Diagnosis of the Causes of Myoclonus**

Causes	Disease states
Endocrine	Hyperosmolar hyperglycemic state
Ischemic states	Brain hypoxia, strokes
Vasculitis	CNS vasculitis
Autoimmune	Systemic lupus erythematosus
Drugs	Tramadol, morphine, hydromorphine, pethidine, quinolones, benzodiazepine, gabapentin, sertraline, lamotrigine, and any drug or chemical poisoning
Infection–sepsis	Neurosyphilis, HIV encephalopathy, CNS toxoplasmosis in HIV-AIDS, Lyme disease
Neurodegenerative	Parkinson's disease, multiple sclerosis, Alzheimer's disease
Trauma	Head or spinal cord injury
Neoplasia	Brain tumors
Genetic	Mitochondrial encephalomyopathy, lipid storage disease
Organ failure	Kidney or liver failure
Other causes	Negative myoclonus, tremor, opsoclonus myoclonus syndrome, Creutzfeldt–Jacob disease, Tourette syndrome

Abbreviations: AIDS, Acquired Immune Deficiency Syndrome; CNS, Central Nervous System; HIV, Human Immunodeficiency Virus.

constant and lasting for minutes, when it may be pathological and indicative of an underlying neurological disorder as in our patient. Benign myoclonus can occur in healthy individuals and is most commonly caused by muscle contractions or during the induction of general anesthesia with intravenous etomidate and propofol or in benign fasciculation syndrome.[3]

Epilepsy syndromes and a variety of acquired factors, such as focal brain lesions, may cause cortical myoclonus. Subcortical myoclonus occurs mainly in toxic-metabolic encephalopathy, electrolyte disturbances, liver and respiratory failure, or as a reaction to several drugs. In cortical myoclonus, the electroencephalogram may be normal as seen in our patient, and this point was recently emphasized in a description of myoclonus in Wilson's disease.[2] Also, typical classification of physiological, hypnic, or hypnagogic jerks describes generalized jerks noted on falling asleep. The jerks observed in our patient presented within the first hour after sleep and they were multifocal.[3]

The differential diagnosis of myoclonus includes negative myoclonus, tremor, Parkinson's disease, CNS toxoplasmosis in HIV and acquired immune deficiency syndrome, and mitochondrial encephalopathy. Myoclonus may develop in response to neuroinfection, hyperosmolar hyperglycemic state, head or spinal cord injury, stroke, brain tumors or hypoxia, kidney or liver failure, lipid storage disease, chemical or drug poisoning, as a side effect of certain drugs such as tramadol, morphine, hydromorphine, pethidine, quinolones, benzodiazepine, gabapentin, sertraline, and lamotrigine. Myoclonus may also be present in multiple sclerosis, Parkinson's disease, Alzheimer's disease, opsoclonus myoclonus syndrome, Creutzfeldt–Jacob disease, Lyme disease, systemic lupus erythematosus, Tourette syndrome, and mitochondrial encephalomyopathy.[1–3] Clinical, video-imaging, laboratory and serological examination, radiological studies, and electrophysiological analysis should be performed to identify the underlying cause; however, electrophysiology was not performed in our patient. Analysis of the differential diagnoses showed no other disease that could explain our patient's reversible encephalopathy (Table 3).

We implemented Bayesian inference, response to treatment, and long-term follow-up for accuracy in diagnosis and here raise awareness of this rare movement disorder associated with serological evidence of a ubiquitous pathogen, whose role in epileptogenesis is being interrogated.

The treatment of myoclonus includes correction of the underlying cause such as electrolyte disturbances or, as in our case, specific anti-toxoplasmosis therapy. However, if necessary, benzodiazepines such as clonazepam or antiepileptic drugs can be administered to suppress the symptoms in some patients.[3]

The hypothesized mechanism of the neurotoxicity in the pathogenesis of myoclonus is inhibition of gamma-aminobutyric acid receptors and activation of excitatory N-methyl-D-aspartate receptors, leading to a toxic encephalopathy.[1–3]

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References

1. Flegr J, Prandota J, Sovičková M, Israili ZH. Toxoplasmosis–a global threat. Correlation of latent toxoplasmosis with specific disease burden in a set of 88 countries. *PLoS ONE* 2014;9:e90203. doi: 10.1371/journal.pone.0090203

2. Verma R, Holla VV, Pandey S, Rizvi I. Multifocal myoclonus as a heralding manifestation of Wilson disease. *Pediatr Neurosci* 2016;11:358–360. doi: 10.4103/1817-1745.199468

3. Kojovic M, Cordivari C, Bhatia K. Myoclonic disorders: a practical approach for diagnosis and treatment. *Ther Adv Neurol Disord* 2011;4:47–62. doi: 10.1177/1756285610395653