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Opsoclonus-myoclonus Syndrome in a Child with Neuroborreliosis

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Opsoclonus-myoclonus is a rare neurological syndrome affecting children and adults. In children it occurs as a **para-infectious process** or a paraneoplastic syndrome in association with neuroblastoma. Here we report it presenting as an **unusual neurological manifestation of Lyme borreliosis**. To our knowledge, this is the first report which describes recovery from this syndrome in a child.

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Introduction

Lyme disease is the most common tick-borne infection in some temperate regions of the Northern Hemisphere. The most frequent clinical manifestation is erythema migrans, followed by neuroborreliosis and arthritis. Here we report a case with an unusual neurological manifestation of Lyme borreliosis.

Case Report

A 9-year-old-boy experienced acute febrile illness. He was resident in an area where borreliosis is endemic. One month previously he was bitten by a tick; erythema migrans skin lesions were not seen. At the end of the first week of his illness, he suddenly developed gait disturbance. In the next 2 days he was unable to walk or sit without support, and his parents reported that he exhibited peculiar eye movements and myoclonic jerks of the limbs.

On arrival in hospital he was afebrile and his vital signs were normal. There was no evidence of head trauma and the pupils

were normal and responsive to light. Nasopharynx, oropharynx, and tympanic membranes were normal. He was alert and oriented but he was irritable with signs of opsoclonic and myoclonic jerks of the face, neck, and limbs. Truncal instability was marked, with intermittent jerky movements of the neck and limbs. Less prominent jerky movements of the neck and limbs were also observed when he attempted to reach an object while sitting with support. There was no paresis or weakness present.

Laboratory data included: erythrocyte sedimentation rate was 45 mm/h; white blood cell count was 10000 mm³ (60% neutrophils, 35% lymphocytes, 5% monocytes), hemoglobin 14.0 g/dl; platelets 150000 mm³. Chest radiograph was normal as were chemistry and liver function tests.

Cerebrospinal fluid (CSF) analysis revealed 100 white cells/mm³ (80% lymphocytes, 20% neutrophils), normal total protein and glucose concentrations and normal blood brain barrier. The IgG index between serum and CSF was also normal.

The results of brain CT scanning (on the second day of hospitalization) and cranial MRI (on the 35th day of hospitalization) were normal with and without contrast. EEG showed diffuse slowing in the theta frequency range without paroxysmal activity or focal abnormalities. The auditory evoked brainstem responses were also normal.

Serum and CSF titres for Epstein-Barr virus (EBV), herpes simplex 1 and 2, echovirus, coxackie, varicella, human

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Table I IgM and IgG antibodies to *Borrelia burgdorferi* in serum and CSF specimens.

Days after hospital admission	Specimen	IgM IFA*	IgG IFA*	IgM ELISA**	IgG ELISA**
7	Serum	1:512	1:64	Pos (2.5)	Neg (0.07X)
7	CSF	1:4	0	Pos (1.402)	Neg (0.005)
35	Serum	1:256	1:32	Pos (2.5)	Neg (0.024)
35	CSF	0	0	Neg(0.181)	Neg (0.006)

*Indirect immunofluorescence assay (IFA) after absorption of cross-reactive antibodies. The positivity limit for both IgM and IgG was 1 : 64.

**The positivity limit of IGM was 0.541 in serum and 0.269 in CSF: the positivity limit for IgG was 0.262 in serum and CSF. (Dako Lyme Borreliosis Kit; Dakopatts A/S, Glastnup Denmark).

immunodeficiency virus, adenovirus, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, tick born encephalitis, mumps, and syphilis were insignificant. Tests for rheumatoid factor or anti-nuclear antibodies were negative. Serological examination confirmed the aetiological role of *B. burgdorferi*. Serum and CSF IgM and IgG antibodies were examined by in-house IFA after absorption, as previously described.^{1,2} Samples were also examined by commercial ELISA test from DAKO, Denmark.

We diagnosed the patient as having encephalitis. His condition did not change over the next 5 days. The lumbar puncture was repeated on the fifth day with unchanged findings. Once again, the attempt to isolate bacteria (including *B. burgdorferi*) and viruses from the spinal fluid was not successful.

Ceftriaxone was administered on the seventh day of hospitalization. The patient's condition started to improve at the end of the third week of hospitalization. The boy was able to sit without support and the signs of nystagmus were diminishing. At the end of the fourth week of ceftriaxone treatment the boy started to walk. The ceftriaxone treatment lasted 1 month.

Lumbar puncture was performed at the end of the third week of hospitalization (biochemical and cytological CSF parameters were normal). Serum and CSF antibody titres for Epstein-Barr virus, herpes simplex 1 and 2, echovirus, coxsackie, varicella, human immunodeficiency virus, adenovirus, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, tick-borne encephalitis, mumps, and syphilis were again insignificant at the end of the treatment. The results of the serological findings on *B. burgdorferi* are shown in Table I together with results after admission.

The boy was released after 6 weeks of hospitalization in good general condition (with only mild nystagmus). In the course of the next 10 months his condition continued to improve.

Discussion

Opsoclonus-myoclonus is a rare neurological syndrome affecting children and adults. In children it occurs as a parainfectious process^{3,4} or a paraneoplastic syndrome in association with neuroblastoma.

Opsoclonus is a disorder of saccadic eye movement. Animal experiments show that an abnormality of the saccades is caused by lesions in the vermis, the cerebellar nuclei or both.^{5,6,7} Lesions in the cerebellar nuclei have also been found in humans with opsoclonus.⁸

A fatal case of late neuroborreliosis with opsoclonus myoclonus syndrome with death of female patient 4 years after the first symptoms has been described.⁹ Necropsy revealed multifocal inflammatory change in the cerebral cortex, thalamus,

superior colliculus, dentate nucleus, inferior olivary nucleus and spinal cord. The lesions showed spongiform change, neuronal cell loss, astrocytosis and proliferation of activated microglial cells. The use of Warthin-Starry stain demonstrated silver-impregnated organisms strongly suggesting *B. burgdorferi* in the affected tissues.

The present case may be an encephalitic form of neuroborreliosis in a paediatric patient with a clinical picture of opsoclonus myoclonus syndrome and with favourable response to ceftriaxone treatment. Serological examination by IFA and ELISA confirmed infection with Lyme disease in our patient. Cut-off titres of IFA with absorption (sera \geq 1:64 and CSF \geq 1:4) were regarded as significantly elevated or positive according to previous reports.^{1,2} Results of ELISA and IFA tests gave the same results so we did not perform an immunoblot test. Although immunoblot tests are considered to be confirmatory in many countries, they are not standardized and detection of IgM and IgG antibodies to *Borrelia* can differ using different strains as antigen. We expected ELISA IgG antibodies in our patient but they did not appear, possibly because early antibiotic treatment can abort or modify immune responses.

The disappearance of intrathecally produced IgM antibodies against *B. burgdorferi* correlates with clinical recovery and may reflect the elimination of antigen due to antibiotic treatment.¹⁰

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Candida albicans Meningitis: Clinical Case

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Candida spp. meningitis is still a rare clinical situation, although it is becoming more frequent. Literature references to it and therapeutic options are scarce. We present a case of a young male, HIV-positive drug addict, with Candida albicans meningitis which was treated with oral fluconazole, having a good outcome. © 2000 The British Infection Society

Introduction

Deep fungal infections are being increasingly described among HIV patients, particularly in drug addicts. Candida spp. are the most common agents involved in such infections. However, central nervous system (CNS) candidiasis is still rare and affects mostly premature neonates and immunocompromised patients. Therapeutic options are few, resulting in a guarded prognosis. Amphotericin B, sometimes associated with 5-flucytosine, is the classic therapeutic approach.¹⁻⁴

We report here a case of Candida albicans meningitis successfully treated with oral fluconazole. This is, to our knowledge, the second such case reported in the literature."

Material and Methods

A 23-year-old Caucasian male was admitted with fever, headaches and vomiting. He was an intravenous drug user for 8 years and was HIV-1 infected for 5 years, without any medical follow-up. In his recent history he referred a cranial trauma with loss of consciousness.

Three months before admission he started complaining of vespertine fever, night sweats, anorexia and asthenia. Some weeks later he had diffuse and intense headaches, nausea and vomiting.

At admission, he had fever, neck stiffness and Kernig +. Except for oropharyngeal candidiasis, the remaining physical examination was normal. Routine blood analysis only showed slightly elevated erythrocyte sedimentation rate (ESR) and transaminases. CSF was turbid, colourless, with 260 cells with a polymorphonuclear (PMN) predominance, Pandy +++, proteins 6 g/l, glucose 0.8 mmol/l. Cryptococcus spp. antigen, bacteriological and mycological examinations were negative (Table I).

Considering the high prevalence of tuberculosis in HIV-positive drug addicts and the cerebrospinal fluid (CSF) characteristics, therapy with isoniazid, rifampin, pyrazinamide and ethambutol was instituted. Simultaneously, fluconazole 100 mg/day was administered for oropharyngeal candidiasis (14 days).

Clinical improvement was observed, but CSF abnormalities persisted. Three weeks later the patient developed behavioural disturbances and occasional seizures. Cranial computed tomography (CT) scanning and electrocardiogram (ECG) were normal.

Table I. CSF characteristics

	Fluconazole 100 mg/day (x 14 days)			2Y /5			Fluconazole 800 mg/day	
	HRZE							
Pandy	1614	2114	28/4	1215	4/6	16/6	2217	2/9
Proteins (g/l)	+++	+++	+++	+++	+++	+++	++	+/-
Glucose (mmol/l)	6	4	4	4	4	3	1.28	0.98
ADA (U/l)	0.8	1.7	2.3	1.6	2.x	2.7	2.1	2.4
Cells (per mm ³)	15	13				7	4	
	260	82	224	16.5	11	16	9	0.4
Microbiol.	PMN	PMN	PMN	PMN	M N	M N	M N	M N
	Neg	Neg	Neg	Candida albicans	Neg	Neg	Neg	Neg

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