H Piza-Katzer
Department of Plastic and Reconstructive Surgery,
Innsbruck Medical University, Innsbruck, Austria

Correspondence to: Dr P Werner, Department of
Neurology, Innsbruck Medical University, Anichstraße
35, A-6020 Innsbruck, Austria; Philipp.Werner@lkh.at

*P Werner and M Furtner contributed equally to the
manuscript.

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Retrobulbar optic neuritis: a
complication of Lyme disease?

Retrobulbar optic neuritis (RON) is an unusual
complication of Lyme disease. The diagnosis of
early Lyme disease is difficult, and the relationship
between RON and Lyme disease remains con-
troversial. None of the 14 cases of optic neuritis
described in the literature in association with
Lyme disease fulfilled the Halperin and Sibony
criteria for active Lyme disease. We report the first
case of acute Lyme disease complicated by RON
established using the Halperin and Sibony criteria.

Lyme disease is a multisystem infectious
disease caused by tick borne spirochetes of the
Borrelia burgdorferi group. Diagnosis of this
infection can be difficult and serological testing
such as western blot can be useful. Cranial
neuropathies are common but RON has been
reported in a few isolated cases.¹ A causal link
between optic neuritis and Lyme disease has
not been established and remains controver-
sial. We report a case of active neuro-Lyme
disease complicated by RON.

Case report

A 67-year-old man who lives in a wooded area of
southwest France developed an erythema
migrans 3 days after a tick bite on his right arm.
He was admitted to hospital 2 weeks later with
fatigue, myalgia, painful radiculopathy, facial
weakness, ptosis and diplopia. Physical examina-
tion showed fever (38°C), cervical radiculoneuro-
pathy with radicular pain and paresis in the right
arm, and peripheral right facial palsy with
involvement of the IIIth, Vth and VIth right
cranial nerves. Two days after hospital admission,
he developed retrobulbar pain that increased with
eye movements, rapid blurred vision and dimin-
ished colour perception in the right eye. Ophthal-
mological examination showed
decreased visual acuity (right eye: 5/10 and left
eye: 8/10) with central scotoma in the right eye.

Eye fundus revealed bilateral symmetric
intermediate uveitis without retinal vasculitis.
Visual evoked potentials (VEP) revealed a
delayed P100 latency to 136 ms in the right
eye whereas it was normal (99 ms) after left
eye stimulation. The amplitude of the right
P100 wave was slightly decreased (15 µV) in
comparison with the left side (20 µV) and was
associated with desynchronisation (P100 dura-
tion: 125 ms on the right side vs 38.9 ms on
the left side). Brain and optic nerve MRI was
normal without contrast enhanced lesions.
Syphilis serology was negative. Lyme ELISA
IgG antibodies were elevated in serum (99 U/

ml; positive serum >24 U/ml). Serum western
blot against *Borrelia garinii* showed three IgG
bands (41, 67 and 83 kDa) and one IgM band
(41 kDa). Serum Lyme western blot IgG anti-
body titre was 2 U and Lyme IgM titre was
20 U (positive values ≥10 U). Ten days later,
Lyme IgG titre was 12 U (positive values
≥10 U or titre increased at least twofold
between two successive measurements) and
Lyme IgM titre was 18 U. CSF analysis
revealed a white cell count of 21/mm³ (normal
<5/mm³) with 95% lymphocytes, a protein
level of 1.11 g/l (normal <0.40 g/l), normal
glucose level of 3.9 mmol/l (blood level was
5.2 mmol/l) and negative culture. CSF Lyme
western blot IgG titre was 13 U (positive values
≥4 U). CSF analysis also demonstrated oligo-
clonal synthesis of IgG and intrathecal Lyme
antibody production (CSF to serum Lyme
index IgG of 38.4, positive index >1.2).

The patient was treated with a 2 week course
of intravenous antibiotherapy (ceftriaxone)
followed by intramuscular injections for
1 week, without corticotherapy. Three months
after antibiotherapy initiation, the radiculo-
neuropathy and multiple cranial involvement
had regressed completely. Visual acuity had
improved to 10/10 in both eyes and ophthal-
mological examination was normal. VEP
obtained after right eye stimulation had
improved, with normalisation of P100 latency
(95 ms) and amplitude (20 µV). During the
same period, serum Lyme western blot IgG
(6 U) and IgM (3 U) antibodies had decreased.

Discussion

This is the first report of acute Lyme disease
complicated by RON and confirmed by VEP.
Independent of bilateral intermediate uveitis
which modifies the amplitude of response on the
right side, a delayed P100 latency was also
observed after right eye stimulation. This finding
suggests the fortuitous association of bilateral
uveitis and unilateral RON. Uveitis alone could

Table 1 Clinical, serological and imaging features of the reported cases of Lyme disease with retrobulbar optic neuritis: none had Halperin⁵ criteria for acute Lyme disease or Sibony¹ criteria for a causal link between retrobulbar optic neuritis and Lyme disease

Reference	Case No	Sex/age (y)	Tick bites	EM	Clinical features	MRI	Response to antibiotherapy	Lyme history
Sibony ¹	1	F, 35	No	No	RON alone	ONE	Yes (retreated)	9 y prior
Jacobson ¹	2	F, 52	Yes	Yes	RON alone	WMH	Yes (retreated)	13 y prior
	3	M, 18	Yes	No	RON alone	WMH	Yes	MD
	4	F, 22	Yes	No	RON alone	MD	Yes	10 y prior
	5	F, 19	Yes	No	RON alone	ONE (CT)	Yes (+prednisone)	MD
Scott ¹	6	F, 40	No	No	RON alone	MD	Yes	MD
	7	F, 10	No	No	RON, fatigue, ankle, wrist pain	ONE	No (+prednisone)	3 m prior
Karma ¹	8	F, 15	MD	No	ON (both eyes), hepatitis, peripheral neuropathy	MD	No (+prednisone)	2 y prior
	9	F, 33	MD	No	ON, recurring skin lesions	MD	No (+prednisone)	>4 y prior
	10	F, 70	MD	No	ON (both eyes), arthritis	MD	No antibiotherapy (prednisone only)	>3 y prior
	11	F, 32	MD	Yes	ON (both eyes), fatigue, headache, myalgia	MD	No (+prednisone)	4 y prior
Lesser ¹	12	M, 25	MD	Yes	RON, headache, dorsal pain	MD	Yes	3 m prior
	13	M, 59	MD	No	RON, fatigue, headache, VIth and VIIth nerves palsy	WMH	No	2 m prior died 6 y after onset
	14	F, 39	Yes	Yes	RON, spastic left hemiparesis,	WMH, lesion in right frontal cortex	No	4 m prior
Our case		M, 67	Yes	Yes	Right RON, radiculopathy, IIIth, Vth, VIth, VIIth cranial nerve involvement	Normal	Yes	2 wk prior

CT, cerebral tomography; EM, erythema migrans; MD, missing data; ON, optic neuritis without details; ONE, optic nerve enhancement; RON, retrobulbar optic neuritis; WMH, white matter hyperintensities on MRI.

Table 2 Additional clinical, serological and imaging features of the reported cases of Lyme disease with retrobulbar optic neuritis: none had Halperin⁵ criteria for acute Lyme disease or Sibony¹ criteria for a causal link between retrobulbar optic neuritis and Lyme disease

Reference	Case No	Serum ELISA	Serum WB	Serum VDRL/FTA	CSF protein (g/l)	CSF cell count/mm ³	CSF oligoclonal bands	Positive CSF to serum Lyme antibody index
Sibony ¹	1	+	—	—	0.38	28	Yes	No
Sibony ¹	2	+	—	—	0.56	2	No	No
Jacobson ¹	3	+	MD	—	MD	MD	MD	MD
	4	+	MD	—	0.25	27 (ly)	No	No
	5	+	—	—	0.33	47 (64% ly)	No	Yes
	6	+	—	—	0.22	2	No	Yes
Scott ¹	7	+	—	—	Normal	0	No	No
Karma ¹	8	+	—	—	MD	20	Yes	No
	9	+	—	—	MD	20	MD	No
	10	—	+ (IgG)	—	MD	MD	MD	MD
	11	—	—	—	MD	0	MD	MD
Lesser ¹	12	+	MD	MD	MD	MD	MD	MD
	13	+	MD	MD	MD	MD	MD	Yes
	14	+	MD	MD	MD	MD	MD	MD
Our case		+	+	—	1.11	21 (95% ly)	Yes	Yes

ly, lymphocytes; MD, missing data; VDRL/FTA, syphilis serology; WB, Western blot.

Western blot is considered positive if it meets CDC⁵ or European requirements (EUCALB).⁴

not explain why P100 latency was delayed, as previously reported in four cases of RON associated with human T lymphotropic virus type 1 uveitis.² Our case fulfilled the criteria for acute Lyme disease³ with positive western blot according to European criteria (European Union Concerted Action on Lyme Borreliosis: EUCALB)⁴ and with strong evidence of a causal link between optic neuritis and Lyme disease, as described by Sibony and colleagues¹ and Halperin and colleagues.⁵ According to Sibony's recommendations,¹ strong evidence of optic neuritis associated with active Lyme disease requires the following elements: optic neuritis, endemic exposure, negative VDRL, exclusion of multiple sclerosis and a positive serum titre (ELISA or indirect fluorescent antibody), in association with at least one of the following: (1) encephalitis or meningitis with CSF pleocytosis, intrathecal antibody production or CSF PCR positive for *Borrelia burgdorferi* DNA and a positive serum or CSF western blot; (2) recent signs of Lyme disease, such as facial nerve palsy, arthritis or radiculoneuritis, with positive serum ELISA confirmed by western blot; and (3) recent physician diagnosed erythema migrans.

RON has been reported in very few cases (14 cases) of Lyme disease and the relationship between these two disorders remains elusive (tables 1, 2).

Among these cases of Lyme disease with optic neuritis, none fulfilled the Halperin⁵ or Sibony¹ criteria because of negative Lyme ELISA or western blot in both serum and CSF. Two of these patients (patient Nos 3, 4) were diagnosed as having multiple sclerosis 12 years later. In our case, multiple sclerosis cannot be definitely excluded but Lyme disease is a criterion of exclusion for multiple sclerosis. However, CSF showed intrathecal antibody Lyme production with an elevated protein level, brain MRI was normal and the patient was in good health 2 years later. Moreover, we ruled out a diagnosis of vasculitis because there was no papillitis or retina vasculitis in the eye fundus, autoimmune laboratory tests were negative and RON had completely regressed without corticotherapy.

Conclusion

We report the first case of strong evidence of a causal link between RON and acute Lyme disease.

Neuro-ophthalmologic manifestations of Lyme disease remain underdiagnosed. VEP may be helpful in confirming early RON for which a relationship with Lyme disease may be established using the Halperin⁵ and Sibony¹ criteria.

E Krim

Service de Neurologie, Hôpital du Haut Lévêque, Pessac, France

D Guehl, P Burbaud

Service d'explorations fonctionnelles du système nerveux, Hôpital du Haut Lévêque, Pessac, France

A Lagueny

Service de Neurologie, Hôpital du Haut Lévêque, Pessac, France

Correspondence to: Dr Elsa Krim, Service de Neurologie, Hôpital du Haut Lévêque, Avenue de Magellan, 33600 Pessac, France; elsakrim@hotmail.com

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Tacrolimus induced leukoencephalopathy presenting with status epilepticus and prolonged coma

Neurological side effects from calcineurin inhibitors (ciclosporin, tacrolimus) are most

commonly mild, such as headaches, dysarthria, visual changes or postural tremor.¹ More severe side effects can include psychosis, opisthotonus with severe rigidity, cortical blindness and seizures.¹ Neurotoxicity is more common early after initiation of tacrolimus, but may occur months or even years later.²

We report a patient who presented with refractory generalised status epilepticus and prolonged coma associated with extensive leukoencephalopathy caused by tacrolimus neurotoxicity.

Case report

A 55-year-old woman with a history of insulin dependent diabetes mellitus and pancreatic transplant 3 months prior to presentation consulted for a 3 week history of daily headaches, dizziness and ataxia. The patient denied cognitive changes, episodic confusion, diplopia, dysarthria or fever. Examination revealed subjective diplopia on right lateral gaze without oculoparesis or papilloedema, truncal ataxia and sensory loss in stocking and glove distribution. As the patient was receiving tacrolimus as part of her immunosuppressive regimen, neurotoxicity from this agent was suspected. Brain MRI was normal. Tacrolimus trough level was 10.3 ng/ml (therapeutic range 5.0–15.0). Spinal fluid studies were unremarkable. The patient improved over the subsequent 2 weeks and failed to return for a 3 month follow-up.

Eight months later, the patient developed worsening headache and nausea for 2 days followed by altered mental status progressing to unresponsiveness. She required intubation for airway protection. On examination, the patient was comatose and exhibited rhythmic head turning and clonic eye movements to the right. Emergent EEG showed multifocal epileptiform discharges intermixed with generalised seizures. Diffuse slowing and loss of the normal posterior background activity were also noted. After administration of lorazepam and loading with fosphenytoin, the recording showed less frequent partial seizures, but propofol infusion was needed to control the electrographic seizures. Head CT revealed diffuse white matter changes, predominantly in the posterior head regions, consistent with