BRIEF REPORT

Five Cases of Paralytic Strabismus as a Rare Feature of Lyme Disease

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Lyme borreliosis is the most common human tick-borne disease in the Northern Hemisphere. The prevalence of Lyme borreliosis is estimated to be 20–100 cases per 100,000 persons in the United States and 100–155 cases per 100,000 persons in Europe [1, 2]. It is caused by the spirochete *Borrelia burgdorferi* sensu lato [2, 3]. The course of clinical manifestations is thought to occur in 3 stages: early, disseminated, and chronic [2, 4]. Lyme borreliosis can cause a variety of ocular manifestations, and the frequency of these manifestations among cases of Lyme disease involving systemic manifestations is ~1% [5].

Neuro-ophthalmological features (papillary edemas or paralytic strabismus, notably, abducens palsy) are among the most frequent manifestations of ocular Lyme borreliosis. Most described cases of diplopia associated with Lyme borreliosis are secondary to abducens palsy complicating an intracranial hypertension [6]. Some cases of conjunctivitis (10% of cases of Lyme disease, according to some studies), keratitis, episcleritis, or scleritis can be caused by *Borrelia* infection. Among the pathologies of the anterior segment, granulomatous uveitis has been described. Some very rare cases of myositis, diagnosed on the basis of MRI findings, have been reported. Some occlusions of the central vein of the retina may also occur [5, 7, 8]. The diagnosis of Lyme borreliosis is often very difficult to demonstrate because of the very high frequency and the broad diversity of ophthalmological manifestations. This study focuses on 5 cases of isolated paralytic strabismus (not associated with intracranial hypertension) as a new symptom of ocular Lyme borreliosis.

Patients and methods. Because Strasbourg, France, is an area where Lyme borreliosis is endemic, we studied patients who presented with paralytic strabismus possibly caused by *Borrelia* infection at the Department of Ophthalmology of Strasbourg University Hospital from 2000 through 2007. The diagnosis was based on medical history (tick bite that occurred in an area of endemicity), ocular findings (visual loss, diplopia, or pain), and systemic clinical findings (erythema migrans, neurological manifestation, or arthritis). The biological diagnosis of *Borrelia* infection was made using antibody detection in patient serum samples (and also CSF samples for 2 patients) in 2 steps: (1) ELISA for screening and (1) Western blot for confirmation. *Borrelia burgdorferi* ELISA was performed on serum samples for IgG and IgM and on CSF samples for IgG with use of a commercial kit (Enzygnost borreliosis; Dade Behring) in accordance with the manufacturer's instructions. This kit is based on a whole-cell antigen of the *Borrelia afzelii* strain PKo and is valid for the diagnosis of infections due to the 3 main *Borrelia* species involved in human disease in Europe [9]. The antibody index was calculated as the ratio of the ELISA titer in CSF samples per the ELISA titer in serum samples to the total IgG titer in CSF samples per the total IgG titer in serum samples, as described elsewhere [10]. The antibody index is defined as positive when the result is ≥ 2, negative when the result is <1.5, and intermediate when the result is 1.5–1.9. Western blot was performed on both serum and CSF samples with use of the *Borrelia garinii* IBS6 strain isolated from CSF at passages <10 and was used as the antigen source. Interpretation criteria used for immunoblots of serum samples were selected from European rules validated in a multicenter study (2 bands among p41 and OspC for IgM or among p83/100, p39, p41, and p17 for IgG) [11]. Western blot IgM titers were associated with clinical symptoms of early Lyme disease. Exclusion of other infectious and inflammatory causes (e.g., diabetes, multiple sclerosis, sarcoidosis, and syphilis) was also part of the diagnosis criteria.

Results. All patients presented with acute binocular diplopia secondary to abducens palsy (10–30 dioptries) that was confirmed by Hess-Lancaster test (figure 1). The patients did not describe orbital pain or headache; however, they described a recent history of tick bites (during the past 3 months) in an area of endemicity, followed by erythema migrans. From a few days to a few weeks before or at the same time as paralytic strabismus occurrence, 4 patients also experienced arthralgia

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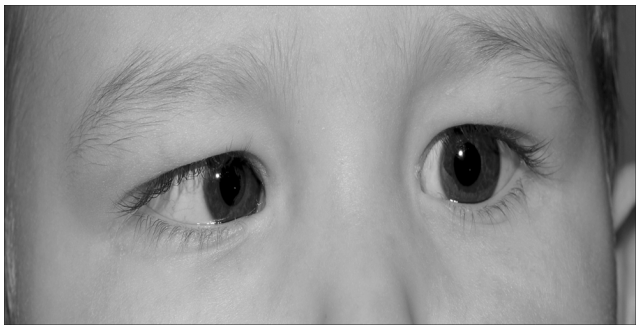

Figure 1. Abducens palsy secondary to Lyme disease. The patient is looking to the left.

and/or arthritis; 1 described unilateral peripheral facial palsy, and 1 described vestibular neuritis. The lack of contralateral adduction defects makes it easy to differentiate a nuclear lesion from a fascicular or nonnuclear lesion. Neither papilledema on fundus examination nor nystagmus were noted, which proved isolated paralytic strabismus.

Results of testing for antibodies to *Borrelia* species were positive for all patient serum samples. One patient also presented with anterior uveitis; *Borrelia* DNA was detected in an aqueous humor specimen from this patient. Laboratory studies included measurement of complete blood cell count, glucose levels, erythrocyte sedimentation rate, and C-reactive protein level and fluorescent treponemal antibody-absorption and antinuclear antibody tests. No abnormalities were found. Two patients had CSF samples analyzed. The opening pressure was normal, and the antibody index related to Lyme disease was negative. Findings of cranial and orbital imaging studies by CT, with and without contrast, or MRI (to eliminate elevated intracranial pressure and myositis) were normal for all patients.

Treatment was initiated (at the latest) a few days after the onset of the diplopia. All patients received antibiotic treatment (200 mg of doxycycline per day or 2 g of ceftriaxone per day); 3 patients received this treatment for 2 weeks, and 2 received it for 3 weeks. One patient who experienced facial palsy received oral therapy with prednisolone (1 mg/kg per day). The patient with concomitant uveitis was treated with topical corthicotherapy. Resolution of ocular symptoms and systemic symptoms, such as cranial nerve palsies and arthritis (with sequelae), was observed in all patients within 2 weeks to 3 months after the initiation of treatment, except in 1 patient, who required muscle injection of botulinum toxin in the medial rectus muscle of the paralyzed eye to weaken the force of contraction of this specific opposing muscle to straighten the eye. After a follow-up period of 6 months to 7 years, no relapse of Lyme borreliosis was noted in our study. Patient clinical characteristics are summarized in table 1.

Discussion. All of the treated patients presented with acute diplopia following a tick bite in an area of endemicity. Other frequent causes of acute abducens palsy were excluded (i.e., diabetes, multiple sclerosis, sarcoidosis, and syphilis). All patients also presented with systemic findings, such as arthritis or cranial nerve palsy, that were compatible with Lyme borreliosis. Similar to previous studies [6], abducens palsy was the most frequent type of paralytic strabismus in our series. Ocular symptoms resolved in all patients within a few months.

Acute paralytic strabismus remains a very rare manifestation of Lyme borreliosis. Paralytic strabismus often occurs in the context of intracranial hypertension or encephalitis; however, isolated paralytic strabismus, as described in our series, is quite possible in the context of Lyme borreliosis [3, 6]. A possible mechanism for acute isolated paralytic strabismus is an inflammatory mononeuritis or polyneuritis [3]. Isolated paralytic strabismus may also be misdiagnosed instead of neuroborreliosis [12]. CSF analysis was performed for 2 patients in our study, but neither of the 2 patients had a positive intrathecal anti-*Borrelia* antibody index.

With regard to the multiplicity of ocular signs and symptoms related to Lyme borreliosis, including paralytic strabismus, the rigorous application of diagnostic criteria is imperious to avoid excess diagnoses. One of the criteria is the obligatory microbiological confirmation [4]. Detection of *Borrelia* DNA is feasible only in aqueous humor or vitreous samples; therefore, serological examination is an argument for the diagnosis of Lyme borreliosis in the case of paralytic strabismus [8]. The specificity of a positive serological examination result, however, remains weak because of frequent false-positive results and cross-reactions with other bacteria. In addition, the prevalence of positive serological examination results among patients with potential tick bites (e.g., forest ranger or hiker) can reach 25%–30% in an area of endemicity [13] when only a very small proportion of these patients present with clinical manifestations associated with Lyme disease. Finally, there is no disease without signs or symptoms, and infection may not always induce clinical signs [2]. For these reasons, systematic serological examination is not recommended for patients with unexplained manifestations [14]. This is particularly the case for ocular symptoms; because ocular findings are multiple and may possibly be correlated with a broad etiology, the aforementioned criteria (notably, tick bites and erythema migrans) seem necessary to evoke a diagnosis of Lyme borreliosis [5].

After a diagnosis of Lyme borreliosis has been established, there is still no consensus regarding the treatment of paralytic strabismus associated with Lyme borreliosis, because of the unusualness of this symptom [15]. In our experience, treatment with antibiotics (doxycycline or ceftriaxone) was favorable for a few weeks to a few months. However, antibiotics did not necessarily influence the course of the abducens palsy, because many acute eye muscle palsies resolve spontaneously.

In conclusion, for any acute paralytic strabismus—and more

Table 1. Clinical characteristics of patients who presented with paralytic strabismus possibly caused by *Borrelia* infection at the Department of Ophthalmology of Strasbourg University Hospital (France), 2000–2007.

Patient	Age, years	Sex	Occupation and/or interests	Ocular findings	Systemic findings	Treatment	Outccome
1	4	M	Occasional walks in the forest	Acute diplopia and abducens palsy	EM and arthritis	Ctri for 3 weeks	Recovery; no recurrence
2	46	F	Regular walks in the forest	Acute diplopia and abducens palsy	EM, vestibular neuritis, and arthralgia	Dox for 2 weeks	Recovery; no recurrence
3	34	M	Woodcutter	Acute diplopia and abducens palsy	EM and arthritis	Dox for 2 weeks	Recovery; no recurrence
4	61	M	Woodcutter	Acute diplopia and abducens palsy	EM and facial palsy	Ctri for 3 weeks and oral corticotherapy (1 mg/kg/day for 7 days)	Muscle injection of botulinum toxin in the medial rectus muscle
5	39	F	Sheep farmer	Acute diplopia, pain, and redness; abducens palsy and anterior uveitis	EM and arthralgia	Ctri for 2 weeks and topical corticotherapy	Recovery; no recurrence

NOTE. All patients had a medical history of tick bites in an area of endemicity, a positive serological examination result, and exclusion of other causes of paralytic strabismus. Ctri, ceftriaxone (2 g/day); Dox, doxycycline (200 mg/day); EM, erythema migrans.

generally, for any acute ocular manifestation—Lyme borreliosis should be taken into account, especially in areas of endemicity. Early diagnosis allows the start of antibiotic treatment to prevent eventual chronic manifestations of Lyme disease.

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