

OCULAR MANIFESTATIONS OF LYME BORRELIOSIS

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SUMMARY

Ocular manifestations can occur in all stages of Lyme borreliosis. Eye involvement can be one of the first and even the only obvious manifestation of the disease. The eye may be involved as a consequence of an extraocular manifestation of borrelial infection or primarily by inflammation of ocular tissues. Conjunctivitis, episcleritis, keratitis, iridocyclitis, retinal vasculitis, choroiditis, optic neuropathy, panuveitis and panophthalmitis have been described. Eye manifestations seem to be rare and are often difficult to diagnose. The extent, character and frequency of the eye findings in Lyme borreliosis have yet to be clearly defined.

Long-standing intraocular inflammation may result in loss of vision; the data on therapeutic efficacy are limited but it seems that prompt systemic antibiotic treatment is effective and leads to recovery of visual acuity. Patients with ocular involvement possibly related to Lyme borreliosis need to be carefully and fully evaluated in order to rule out all other possible etiologies, however, even suspected ocular Lyme borreliosis should be treated with antibiotics.

KEY WORDS:

Lyme borreliosis, manifestations, eye symptoms, review

INTRODUCTION

Lyme borreliosis is a multi-system illness caused by *Borrelia burgdorferi* and transmitted by ticks (in Europe by *Ixodes ricinus* ticks) (1,2,3). There is a strong experimental and clinical evidence for ocular involvement in Lyme borreliosis (4). However, eye

manifestations seem to be rare and are often difficult to diagnose.

The eye may be involved as a consequence of an extraocular manifestation of borrelial infection or primarily by inflammation of ocular tissues. Similar to syphilis, Lyme borreliosis seem to be a great imitator of ocular inflammation (5).

CLINICAL FEATURES

OCULAR MANIFESTATIONS

Conjunctivitis

Conjunctivitis develops early in the course of Lyme borreliosis. Usually it is closely associated with erythema migrans and probably represents a manifestation of the early disseminated stage of Lyme borreliosis.

Conjunctivitis was the first reported ocular Lyme borreliosis manifestation (6). It was found in 35 out of 314 patients (11%) with erythema migrans (6) and is therefore the most common eye manifestation of early Lyme disease in the USA. In Europe conjunctivitis is discovered less often. It was reported in only one of 104 patients with erythema migrans in Munich, Germany (7), and in 5.4% (23 out of 425) of patients with typical erythema migrans in Ljubljana, Slovenia (5). The prevalence in the last group was significantly higher in patients with more than one skin lesion than in patients with solitary erythema migrans (5) which points to the conclusion that conjunctivitis is a manifestation of the early disseminated (second stage) Lyme borreliosis (2,5). It is usually mild, short-lived and does not require special treatment. In our patients with erythema migrans the duration of conjunctivitis ranged from 2 days to 6 weeks (median 8 days) before treatment and 1 to 28 days (median 4 days) after inducing antibiotic therapy (5).

There is also a report of bilateral chronic follicular conjunctivitis which the authors attribute to the late borrelial infection (8).

Episcleritis

There are two reports of patients with episcleritis associated with late Lyme borreliosis (8,9).

Keratitis

Keratitis is a manifestation of late borrelial infection. It is similar to syphilitic keratitis and can become manifest months to years after the onset of Lyme borreliosis with painless, progressive blurring of vision. Photophobia can be the first symptom. Multiple infiltrates at all levels of the corneal stroma can be seen with episodic recurrences and changing localization. Response to topical steroids is usually good. However, there is a possible progression into neovascularization and scarring. There are several reports on borrelial keratitis, predominantly in

American literature (5,9-13).

Iridocyclitis

Iridocyclitis may be present in early disseminate as well as in late Lyme borreliosis.

Granulomatous inflammation of iris and ciliary body with posterior synechia and cellular infiltration of the vitreous body was described in some patients from the USA (14-17) and also from Europe (5).

One patient developed panophthalmitis leading to blindness in spite of treatment with multiple i.v. and oral antibiotics and topical, subconjunctival and systemic corticosteroids (18,19). However, this seems to be an exception; in the majority of patients response to antibiotic treatment (usually i.v.) was good. The efficacy is difficult to assess because there is not enough information on natural course of borrelial eye manifestations and because many patients were treated simultaneously with topical or systemic prednisone.

We saw a 33 year-old female patient (5) who had erythema migrans at the site of a tick bite. In the following weeks arthralgias, paresthesias and mild headache appeared. Three months after the beginning of erythema migrans unilateral iridocyclitis was found. Results of cerebrospinal fluid examination were in normal range. *B. burgdorferi* serological tests (IFA) showed elevated antibody titers (IgM 1:512, IgG 1:1024). The patient was treated with ceftriaxone 2 g i.v. for 14 days. Iridocyclitis improved substantially and extraocular symptoms disappeared with the exception of mild intermittent pain in large joints.

Retinal vasculitis

The onset of retinal vasculitis is most likely at the time of early disseminate infection. It may show a chronic course (5). Inflammation of the retinal vessels leads to a breakdown of the inner blood-retina barrier and is followed by an outflow of blood proteins and cells and infiltration of the vitreous body. The consequence is vitreous clouding (5,20,21).

Occlusive retinal vasculitis may cause larger local ischemic retinal areas which can lead to preretinal neovascularization (5,22).

Choroiditis

Choroiditis belongs to early disseminate borrelial infection. It seems that it is the most common intraocular borrelial manifestation. In the recent series of 19 patients with intraocular involvement seen at University Eye Hospital, Erlangen and De-

partment of Infectious Diseases, Ljubljana 63% (12 out of 19 patients) had choroiditis (5).

The inflammation of the choroid may be unilateral or bilateral, focal (5,23) disseminated (5,21,24) or diffuse with inflammatory exudative retinal detachment (5,25-27). In the majority of patients there is a prompt response to antibiotic treatment (5).

Optic neuropathy

There are relatively numerous reports on the optic nerve involvement in the course of early disseminate and late Lyme borreliosis. Depending on severity and duration of the different optic neuropathies, atrophy of the optic nerve can develop and result in poor visual acuity or in almost complete blindness (5).

The most common borrelial manifestation involving the optic nerve is papilledema i.e. optic disc edema caused by increased intracranial pressure. In the acute phase of the disease visual acuity in these patients is typically good. Papilledema is most commonly observed in children with early disseminated infection who usually had cerebrospinal fluid pleocytosis (4,28-34). In patients with normal cerebrospinal fluid edema of optic disc is designated as pseudotumor cerebri. However, in some patients a spinal tap performed early in the presentation of the disease, might fail to detect cerebrospinal fluid pleocytosis or elevated protein but subsequent taps show abnormal cerebrospinal fluid results (29). Papilledema uniformly do well with complete resolution after treatment with i.v. ceftriaxone (4).

In ischemic optic neuropathy due to occlusion of the posterior ciliary arteries, the disc edema can be segmental with corresponding segmental visual field loss (5,35,36).

Papillitis is a nondemyelinating inflammation of the optic nerve head leading to sudden loss of vision. It is the manifestation of the early borrelial disseminate infection (5,17,37).

In neuroretinitis, papillitis is associated with vasculitis of the peripapillary retinal vessels (5,34,38-40).

Retrobulbar neuritis was reported in patients with late borrelial encephalomyelitis (32). It should be stressed that in demyelinating neuritis the optic nerve head is not involved because the myelin sheath begins behind the globe.

Panuveitis

In panuveitis all parts of the uvea (iris, ciliary body and choroid) are inflamed. Some patients with panuveitis of borrelial etiology were reported. (26,41).

Panophthalmitis

In panophthalmitis all tissues of the eye are involved. There is a report of a patient with Lyme borreliosis who developed panophthalmitis in spite of the treatment with antibiotics and corticosteroids (18,19).

OCULAR INVOLVEMENT DUE TO EXTRAOCULAR MANIFESTATIONS

Cranial nerve palsy

In peripheral facial palsy, which is a common sign of Lyme borreliosis (42), lack of surface protection can lead to exposure keratoconjunctivitis or corneal ulceration (4,5). Because the duration of facial palsy is usually short, exposure problems can be treated with ocular lubricants (4).

Involvement of ocular motor nerves, which is much less often than peripheral facial palsy, results in diplopia (4,5). The sixth nerve is most commonly involved, followed by the third and fourth cranial nerve. (4,42-44).

Miscellaneous

There have been isolated reports of pupillary abnormalities associated with Lyme borreliosis such as a patient with Argyll Robertson-like pupil (30) and a patient with reversible preganglionic Horner's syndrome (33).

Orbital myositis has been described in a child with erythema migrans, peripheral facial palsy associated with CSF pleocytosis and knee arthritis (45).

Occipital cortex lesions due to focal encephalitis or cerebral vasculitis may cause homonymous visual field defects (46,47).

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Despite multiple descriptions of the eye involvement, the extent and character of the eye findings in Lyme borreliosis have yet to be clearly defined (4). It is very difficult to prove that an ocular sign is of borrelial etiology.

In Lyme borreliosis there is no pathognomonic eye manifestation which would allow a definite clinical diagnosis and intraocular material which would serve for isolation of the etiological agent is usually not available from humans. Even the diagnosis of definite Lyme borreliosis does not entirely confirm

that all clinical signs and/or symptoms are causally related to the *B. burgdorferi* infection i.e. the associated ocular findings may be coincidental and unrelated to the presence of Lyme borreliosis. In praxis, serology is often the main aid in diagnosis. However, serologic testing has many limitations: differences in specificity and sensitivity of various serological assays, interlaboratory variability, the absence of antibody formation particularly in the early stage of the disease, false positive results in some other infections like syphilis and high background rate of seropositivity in some endemic regions without the ability to differentiate between past exposure and active ongoing infection (3-5,48-50).

Despite these limitations there is a firm evidence for ocular involvement in Lyme borreliosis (4,5). However, in an individual patient other possible causes have to be actively searched for and ruled out. The spectrum of ocular manifestations seen in Lyme borreliosis is well known in ocular syphilis but there are also many other illnesses that may mimic borrelial ocular involvement (4,5,51). Granulomatous iridocyclitis or choroiditis can be due to bacterial illnesses (tuberculosis, syphilis, leprosy), fungal infections, or immunologic processes of unclear etiology such as sarcoidosis, Vogt-Koyanagi-Harada syndrome, or Still's disease. Optic neuropathies and retinal vasculitis are seen in encephalitis disseminata or may be induced by viruses (varicella-zoster virus). Some other illnesses may have ocular presentation similar to Lyme borreliosis including certain viral infections and postviral syndromes, vasculitis, lymphoma, Behcet disease and others.

TREATMENT

There are no comparative therapeutic studies in Lyme borreliosis patients with ophthalmic manifestations.

Knowledge is based on the results of treatment in relatively small number of patients with ocular involvement associated with Lyme borreliosis; in some of them the diagnosis of Lyme borreliosis is doubtful. In addition, the assessment of the treatment efficacy is difficult because in the majority of borrelial ocular manifestations natural course is not known.

General recommendation for antibiotic treatment of intraocular inflammation would be to use the agents effective in treatment of Lyme borreliosis, with pharmacokinetics and in dosage which enable high enough concentrations of the agent intraocularly (in some antibiotics diffusion of the drug from the blood into the aqueous humour of the eye is substantially limited).

In ocular involvement corticosteroids are often used (4,5). As a rule they should be combined with an appropriate antibiotic treatment (5). Accompanying systemic corticosteroid therapy is thought to reduce the extent of damage caused by the inflammatory reaction in severe uveitis and orbital myositis. Keratitis responds well to topical steroids (4,5,52).

In uveitis it is necessary to keep the pupil dilated (4,5,52).

CONCLUSION

Ocular manifestations can occur in all stages of Lyme borreliosis. Eye involvement can be one of the first and even the only obvious manifestation of the disease. Long-standing intraocular inflammation may result in loss of vision; the data on therapeutic efficacy are limited but it seems that prompt systemic antibiotic treatment is effective and leads to recovery of visual acuity. Patients with ocular involvement possibly related to Lyme borreliosis need to be carefully and fully evaluated to rule out all other possible etiologies. However, even suspected ocular Lyme borreliosis should be treated with antibiotics.

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