Ocular Lyme disease: case report and review of the literature

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Abstract

Lyme disease is an emerging new spirochaetal disease in which ocular complications may arise. We have seen a 45-year-old woman who developed unilateral endophthalmitis leading to blindness during the course of this disease. Ocular tissue showed the characteristic spirochete. A literature review shows that the commonest ocular manifestation of Lyme disease is a mild conjunctivitis, but other symptoms may include periocular oedema, ocular motor palsies, uveitis, papilloedema, papillitis, interstitial keratitis, and others. Ophthalmologists treating patients from Lyme disease endemic areas need to be aware of the protein clinical manifestation of this disease.

Lyme disease, a tick-borne spirochaetal infection, often begins with a characteristic rash, erythema chronicum migrans. Ocular manifestations have been infrequently reported, but, as the disease is increasing in frequency and occurring in new geographical areas, more cases with ocular involvement can be expected. We report in detail the eye findings in a patient previously reported on who developed severe, unilateral endophthalmitis five weeks after erythema chronicum migrans. Spirochaetes were found in the vitreous in specimens obtained at surgery. In addition we review the literature of the ocular and neuro-ophthalmic manifestations of Lyme disease.

Case report

On 15 July 1982 a 45-year-old woman from Westchester County, New York, developed severe headache, light headness, chills, and fever. Three days later she also had nausea and vomiting. On 21 July she noted red lesions on her right foot and upper arms that looked like insect bites. In addition a large annular erythema with an indurated centre was noted on the right thigh. This lesion expanded and developed a bright red outer border with central clearing. She remembered having been bitten by many flying insects during the 4 July weekend but recalled no tick bites. She was treated with diphenhydramine hydrochloride 50 mg four times a day and a cortisone skin ointment for what was thought to be a local skin allergy to insect bites. On 30 July, because of daily fevers, malaise, and skin lesions, she was admitted to a community hospital.

A physician removed fragments of a presumed insect stringer from her right foot accompanied by a white mucoid discharge. Her white blood cell count was 22 x 10⁹/l with 73% polymorphonuclear leucocytes and 18% band forms, and the erythrocyte sedimentation rate was 48 mm/h. She was treated empirically with intravenous cefazolin, 6 g a day for seven days, but continued to have daily fevers up to 40-1°C (104-2°F). She was then changed to oral tetracycline, 500 mg four times a day for seven more days. She responded well to this regimen.

Two weeks later, on 25 August 1982, a sting on the left thigh by a bee caused local erythema. Two days afterwards she awoke with a painful red left eye. She had no eye complaints previously. The patient treated herself with sulphasulfazone (sulfoisoxazole) drops, but sought an ophthalmologist when the vision decreased in the left eye and periocular oedema developed. She was noted to have iritis and posterior synechiae and was treated with topical atropine 1% and Predforte 1% (dexamethasone) drops, with resultant breaking of the synechiae. However, the iritis persisted, and despite subconjunctival injection of triamcinolone 40 mg hypopyon developed along with vitritis. Oral prednisone 60 mg per day was begun. The visual acuity nevertheless worsened, and the prednisone dose was increased to 100 mg daily. She was then transferred to Westchester County Medical Center.

Her visual acuity was 20/20 right eye and hand motions left eye. The results of ocular examination including tension were normal in the right eye. The left eye showed mild conjunctival ecchymosis and ciliary vessel injection. There was mild periocular oedema. The ocular rotations were full, though splitting of the left eye was noted in extreme fields of gaze. There was no measurable proptosis. The cornea showed microscopic epithelial oedema with stippled fluorescein staining. There was a severe inflammatory reaction in the anterior chamber, with 3+ flare and cells, and a 20% hypopyon was present. After dilatation of the pupil pigment residua were noted on the anterior lens surface from the previously treated posterior synechiae. The lens was otherwise clear. The ocular tension was 18 mmHg. The left fundus could not be seen, and no red reflex was obtained through the cellular debris in the media. Ophthalmic A and B scan ultrasound revealed diffuse debris in the vitreous cavity, with marked thickening of the choroid consistent with a
severe panophthalmitis. The retina was attached.

The initial impression was severe uveitis of unknown etiology. Prednisone was continued at 100 mg daily and tapered to 60 mg over the next seven days. Roentgenograms of the chest, skull, sinuses, orbits, and sacroiliac joints were normal.

Serological tests for syphilis (FTA-abs, VDRL), anti-nuclear antibodies, antigensin converting enzyme, cryoglobulins, rheumatoid factor, toxocara, toxoplasmosis, histoplasmosis, and cytomegaloviruses were negative. A 5 TU tuberculin skin test was negative. Serum creatinine and liver enzymes were normal. Serum obtained on 17 September showed an IgG antibody titre with the Lyme spirochaete of 1:64 and an IgG titre of 1:512 (normal for both <1:64) determined by indirect immunofluorescence.

Eight days after admission to hospital and while on prednisone 60 mg daily the patient developed a rapid rise in intraocular pressure in the left eye to 40 mmHg along with 5 mm proptosis, a conjunctival purulent discharge, and the rapid onset of a dense cataract. Computerised tomography showed no evidence of a lesion to explain the proptosis. Orbital cellulitis was suspected, and nafcillin 12 g/day plus gentamicin 80 mg every 8 hours was given intravenously in 35 (11%).

Ocular manifestations included topical neomycin-polyoxin D (Neosporin) and dexamethasone. The ocular tension was controlled with acetazolamide 1 g orally daily and timolol 0.5% topically. Conjunctival cultures were negative for bacteria, fungi, and mycobacteria.

One week later, 19 days after admission, a lenticotomy and vitrectomy were performed and purulent vitreous material was removed. Intravitreal gentamicin 0.2 mg in 0.1 ml and chloramphenicol 0.2 μg in 0.1 ml were injected and systemic antibiotics were maintained, while systemic steroids were tapered. Cultures and smears for bacteria, fungi, and acid fast organisms were negative. A cytological examination of a fresh vitreous specimen revealed only white cells. One week later a second vitrectomy to remove increasing amounts of vitreous debris was performed. Examination of the material by dark field microscopy was negative for spirochaetes.

Pathological examination of the lens and vitreous contents showed lens fragments and necrotic cells with a heavy infiltration of mononuclear cells. Later the eye tissue was stained by the Dieterle method."Despite the advanced cell necrosis, occasional intact spirochaetes, morphologically compatible with the Lyme spirochaete, were demonstrated in vitreous material.

After surgery the patient continued to have mucous secretions from the eye and experienced occasional myalgias and arthralgias. A good red reflex was obtained, vision returned to hand motions, and on 13 October she was discharged from hospital. However, over the ensuing three months she developed a dense cyclophoveolar membrane in her eye and lost all functional visual activity, with the eye becoming phthisical. On 28 October IgM antibody to the spirochaete was no longer detectable, and the titre of specific IgG had decreased to 1:64. By May 1983 neither specific IgM nor IgG antibody was found. After one year the patient was given a cosmetic contact lens shell covering the phthisical left eye. She developed no manifestation of Lyme disease in her right eye, which continuously maintained 20/20 vision throughout the course of her disease.

**Discussion**

Our patient presented with a unilocular uveitis due to Lyme disease which progressed to a panendophthalmitis and ultimate destruction of useful uniconal vision. Other examples of Lyme related uveal tract involvement include case reports of patients with iritis, uveitis, and choroiditis with exudative retinal detachment. The visual outcome of the other reported cases was favourable, with uveitis spontaneously resolving and visual acuity in the others improved after the use of specific systemic antibiotics with or without concomitant ocular steroids.

Additional ocular manifestations of Lyme disease include conjunctivitis, photophobia, periorbital oedema, cranial nerve palsies, keratitis, pupillary abnormalities, papilloedema, optic neuritis, and optic atrophy (Table 1).

The commonest ocular finding in Lyme disease appears to be conjunctivitis. Steere et al in a study of 314 patients with erythema chronicum migrans noted conjunctivitis in 35% of patients with Lyme spirochaete, with 19% (6%), and periorbital oedema in 10% (3%). Unfortunately the authors did not elaborate further. By inference and from our anecdotal experience conjunctivitis is not very prominent in this disease and is short-lived.

Neurological complications in Lyme disease occur in approximately 10% of cases, and over half of patients with them have cranial nerve palsies, most commonly involving the seventh nerve. Oculomotor weakness is infrequent, but may be due to cranial nerve palsy of the III, IV, or VI cranial nerves. Such palsies may occur individually, or in combination with one another and/or with the neurological manifestations. Papilloedema is the typical ocular complaint in these instances. Like other neuropathies, oculomotor weakness usually resolves within two weeks to five months after onset. Whether antibiotics improve the rate of recovery has not been established.

One patient with an Argyll-Robertson pupil and another with a reversible Horner's syndrome have been reported on, and optic atrophy has been noted in several patients (see below).

Papilloedema of diverse causes has been seen occasionally. It has been observed in a minority of Lyme disease patients with meningitis. It is then typically bilateral and may be asymptomatic, leading to complaints of blurred vision. It is of interest that the intracranial pressure is often not raised, so that the pathogenesis of this condition is obscure. Too few data are available to assess the natural history of papilloedema in Lyme disease meningitis, but antibiotic therapy appears to hasten the resolution of certain other clinical signs.

In one report resolution of papilloedema was accompanied by the development of pigment epithelial mottling at the fovea, and in two other cases optic atrophy ensued.

Papilloedema has also been reported in several Lyme disease patients who had increased intracranial pressure but no evidence of meningitis.

Sixth nerve palsy was sometimes present in these
patients. Cranial tomography failed to reveal mass lesions or enlarged ventricles resulting in a diagnosis of Lyme disease-associated pseudotumor cerebri for some of these patients. Anti-biotics plus additional medications for reducing intracranial pressure have been useful therapeutically.

Anecdotal cases of optic neuritis and optic atrophy have been reported. Bertuch et al. described a patient who developed progressive temporal pallor of the right optic disc six months after onset of an illness presumed to be Lyme disease. In addition Schechter described a patient who developed papillitis of the right eye with an inferior altitudinal visual defect three months after the onset of Lyme disease. Despite a course of high dose systemic corticosteroids, the left eye of this patient also became involved. The process eventually stabilised after a course of antibiotics plus corticosteroids. The author's diagnosis in this latter case was ischaemic optic neuritis due to Lyme disease.

Other late ophthalmic manifestations of Lyme disease have been described. Corneal abnormalities presumed to be due to Lyme disease have been described in four patients who developed a form of interstitial keratitis six months to as long as five years after the diagnosis of Lyme disease. None of these patients had other symptoms attributable to Lyme disease when the ocular disease was demonstrated, and all four had previously received antibiotic therapy for Lyme disease. The keratitis was characterised by scattered corneal opacities that occurred randomly within the corneal stroma from Bowman's membrane to Descemet's membrane, either unilaterally or bilaterally. Bilateral involvement of the cornea was noted in one case in which the corneal stroma was involved asymetrically. In one patient minimal neovascularisation was seen. Two patients were asymptomatic, one of whom was found to have diminished visual acuity on routine school screening; the other two patients complained of decreased vision. The keratitis responded to topical corticosteroids but apparently not to systemic or topical antibiotics, which supports the conjecture that this process has an immunological rather than an infectious origin.

Eye involvement in Lyme disease shares certain similarities with that seen in syphilis. Syphilitic uveitis or iritis occurs in about 4% of patients with secondary syphilis, but may also follow inadequately treated primary syphilis or may be a part of tertiary syphilis. Keratoiritis is the commonest manifestation, but choroiditis, lenticular opacities, retinitis, and panophthalmitis may occur. The vitreous often shows multiple yellow-grey exudates, which tend to spread along retinal vessels. An important differentiating feature of syphilitic keratitis from that so far reported in Lyme disease is the early and massive neovascularisation of the cornea in syphilis.

Most authors suggest treatment of ocular syphilis with high-dose intravenous penicillin, sometimes accompanied by systemic corticosteroids. However, steroids alone may be permissive to the spirochaete and are likely to worsen the condition. Similarly, steroids may have contributed to the marked severity of the ocular infection in our patient.

Lyme disease is an emerging infectious disease which may cause eye lesions requiring treatment. Ophthalmologists caring for patients from endemic areas need to be aware of its protean clinical manifestations.

The authors thank Mrs Shirley M Gamble and Ms Susan Friedlander for their valuable assistance in preparing this manuscript and Dr Jorge Benach for performing the Lyme serological tests.

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Br J Ophthalmol 1990 74: 325-327
doi: 10.1136/bjo.74.6.325

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