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Retinal Vasculitis in Lyme Borreliosis

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Three patients with retinal vasculitis are reported who were found to be seroreactive for Lyme borreliosis. Careful investigation revealed no other apparent etiology for the angiitis, and improvement of the retinal vasculitis on tetracycline therapy was documented by fluorescein angiography in one of them. Two cases of retinal vasculitis were presented at the International Conference on Lyme Borreliosis in Stockholm 18–21 June 1990, and two cases of cerebral vasculitis due to *Borrelia burgdorferi* have been published. To our knowledge, this is the first published report of retinal vasculitis occurring in patients seroreactive for Lyme borreliosis. Although further investigation will be necessary to prove a cause-and-effect relationship, ophthalmologists encountering patients with otherwise unexplained cases of retinal vasculitis, or Eales disease, are encouraged to study these patients carefully for the possibility of *Borrelia burgdorferi* infection.

Key Words: Retinal vasculitis—Lyme Borreliosis.

Lyme borreliosis, a systemic spirochetal infection, is now the most commonly reported vector-borne disease in the United States (1). Adding to the increasing list of neuro-ophthalmologic manifestations (2), we should like to document three patients with retinal vasculitis who were seroreactive for Lyme borreliosis. Careful investigation revealed no other apparent cause for retinal vasculitis in these patients, and improvement of the retinal vasculitis on tetracycline therapy was documented by fluorescein angiography in one of them.

CASE REPORTS

Case 1 (RC)

A 25 year old right-handed white male, whose early course was previously reported (3), was seen in July 1988 with a chief complaint of blurred vision for six weeks. He enjoyed good health until three years earlier, when, after a "severe viral infection," he developed a left facial palsy which within two days involved the right side of his face as well. He was started on oral prednisone and promptly improved. One year later, he had another episode of "Bell's palsy," again on the left side, which again responded to steroids. Late in 1987 a third, profound episode of left facial palsy occurred, but it responded again on prednisone. Six weeks prior to the first visit, he noted blurred vision in the right eye. Iritis was noted and treated with topical steroids and cycloplegics. A rheumatologic consultation gave negative results except for a serum Lyme enzyme-linked immunosorbent assay (ELISA) which was reported as 1.54 with a control of 0.9.

Past history revealed that he had unexplained arthritis in one knee for two months, occasional palpitations, was an avid outdoorsman who remembered a tick bite while hunting in the Ever-

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glades several years before, and who had camped at Cape Cod, Massachusetts at ages 11 and 14.

Examination at the Bascom Palmer Institute on July 26, 1988 revealed the corrected vision was 20/15 − 2 in the right eye and 20/30 + 2 in left eye. Mild aberrant regeneration of the left VII nerve was evident. Slit lamp examination revealed clear anterior chambers but 1.5-2+ cells in the vitreous of both eyes. Whitish deposits were seen in the preretinal space, and a retinal tear was seen in the left eye at 1:30 with whitish exudative material on an attached flap.

Laboratory studies included complete blood count, chemistry profile, urinalysis, sedimentation rate, rheumatoid factor, antinuclear antibody, anti-DNA antibody, angiotensin converting enzyme, HLA-B-27, rapid plasma reagin, FTA-ABS, *T. pallidum* immobilization, *T. pallidum* hemagglutination assay, toxoplasma titer, and HIV ELISA were normal. Chest radiograph and magnetic resonance imaging of the head were normal. Lumbar puncture revealed an opening pressure of 240 mm H_2O, 9/mm^3 white blood cells (90% lymphocytes, 10% neutrophils), 31 mg/dl protein, and 52 mg/dl glucose. Serum Lyme IFA IgG was <1:16 and IgM <1:16 (negative), but Lyme ELISA was 1.81. Microbiology Reference Laboratory reports Lyme ELISA <0.85 as negative, 0.85-1.25 as borderline, and >1.25 as positive. Serum Western blot test was also positive for antibodies to Lyme disease. The Lyme ELISA was repeated and confirmed as positive at a third laboratory.

Topical steroids and cycloplegics, oral doxycycline, and erythromycin were given, but with little improvement. The patient developed bilateral iridocyclitis, tender swelling of the tongue and submandibular nodes, and his eyes became red and painful. The vitritis had worsened in both eyes. He was treated with intravenous ceftriaxone 2 g/day, and later 12 million units/day of intravenous aqueous penicillin G was also given. At follow-up examination two weeks later, visual acuity was 20/15 in both eyes and the inflammation was markedly reduced. After completing a one-month course of intravenous antibiotics, 1 g/day of oral tetracycline was started. In May 1989 after his eyes had been quiet for nine months, the tetracycline dose was tapered. Within one month, however, a recurrence of the iritis and vitritis occurred with posterior synechiae. Cefuroxine (Ceftin) therapy, 500 mg/day, resulted again in improvement; the patient was maintained on this orally. On 12 September 1989 the patient returned with a recurrence of blurred vision. Vision was 20/30 right eye and 20/60 left. The anterior chambers were quiet and there was minimal, if any, active vitritis. Snow banking inferiorly and small tufts of retinal neovascularization were seen just off the disc in both eyes. Definite cystoid macular edema was seen in left eye. Fluorescein angiography showed retinal vasculitis manifested by prominent diffuse fluorescein leakage predominantly from the veins, but with some arteriolar leakage as well (Figs. 1 and 2). He was started on oral tetracycline 250 mg four times a day, because he felt it was more effective than Ceftin. Twenty mg subtenons Kenalog was given to the left eye; no oral steroids were given. Three weeks later the patient was notably improved; vision was 20/25 − 2 right and 20/40 + 2 left. There was a definite decrease in vitreous veils, total regression of the neovascularization, and less cystoid macular edema as well. Repeat fluorescein angiography documented marked lessening of retinal vasculitis with absence of fluorescein leakage in the previously noted sites of inflammation (Figs. 3 and 4)

The patient was maintained on oral tetracycline 1 gm/day thereafter. Follow-up on 26 July 1990 revealed corrected vision of 20/20− in the right eye and 20/25 + 3 in the left eye. The anterior segments were white and quiet but bilateral vitreous detachments with 1+ old vitreous cells were seen in both eyes. The discs were normal and subtle parafoveal change was seen in left eye as residual of the former cystoid edema. Some peripheral vitreous changes were present as well as a few upper temporal areas of lattice degeneration. The old retinal tear in left eye at 1:30 had been circumscribed with laser therapy; the retina was flat; and the pa-

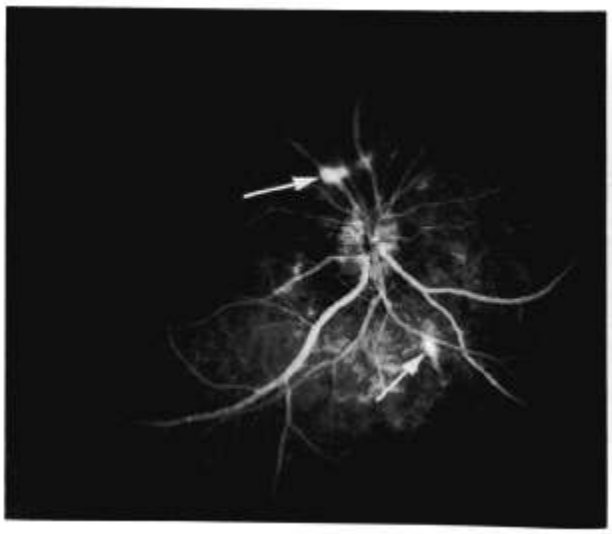

FIG. 1. Case #1, right eye, on 9/12/89. Note prominent retinal vasculitis as evidenced by prominent fluorescein leakage from both veins and arteries (arrows).

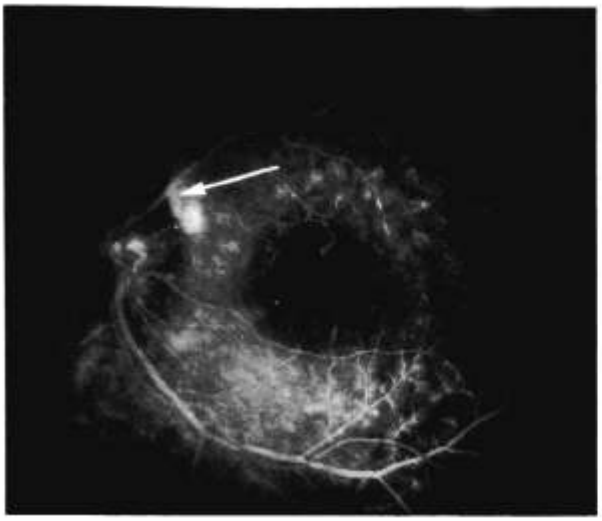

FIG. 2. Case #1, left eye, on 9/12/89. Note perivascular fluorescein leakage (arrow).

tient was comfortable. Applanation tensions were 17 in both eyes.

Comment

This 27-year-old man has had chronic bilateral vitritis with recurrent episodes of iridocyclitis in both eyes associated with Lyme borreliosis. During a recurrence of this he developed bilateral retinal vasculitis, neovascularization, and cystoid macular edema in both eyes (Figs. 5 and 6) after an attempt to taper him off oral antibiotics. He was given a subtenons injection of aqueous triamcinolone to the left eye and was placed back on oral tetracycline therapy. No oral steroids were given. Marked improvement in the retinal vasculitis in both eyes occurred within three weeks and was documented by fluorescein angiography. He has since been maintained on oral tetracycline 1 gram/day for nine months without further recurrence.

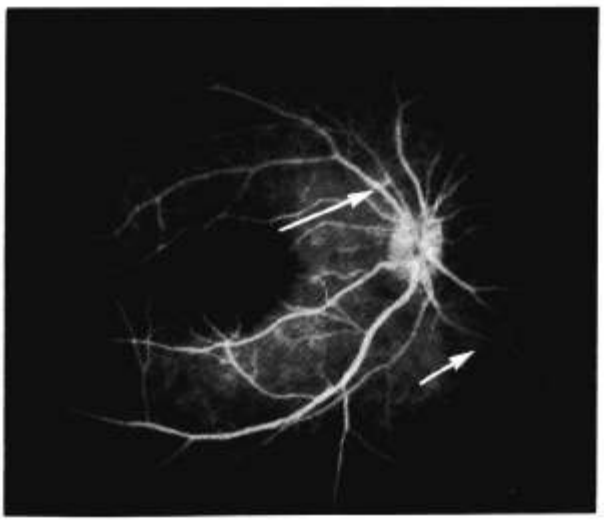

FIG. 3. Case #1, right eye, on 10/10/89. After oral tetracycline therapy, note dramatic improvement in retinal vasculitis. Compare areas with arrows with Fig. 1 showing absence of fluorescein leakage after therapy.

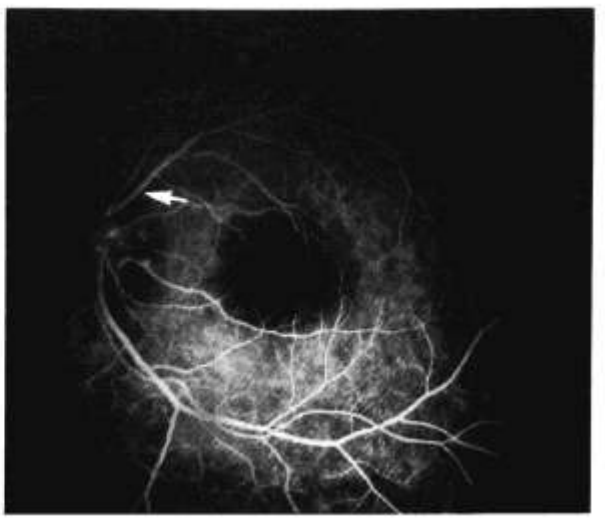

FIG. 4. Case #1, left eye, on 10/10/89. After oral tetracycline therapy, note improvement in retinal vasculitis. Compare area with arrow with Fig. 2 to document absence of fluorescein leakage after therapy.

Case 2 (BM)

This 58-year-old right-handed black man from Curaçao, Netherlands, Antilles was referred to the Bascom Palmer Eye Institute on 29 November 1989

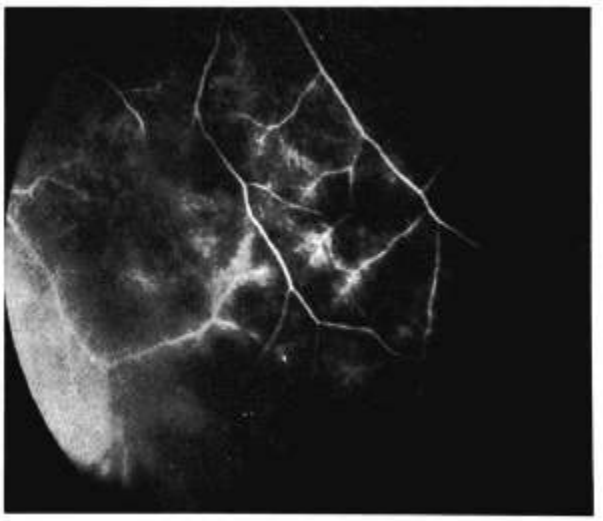

FIG. 5. Case #1, right eye, 10/10/89. Note perivascular fluorescein leakage from small vessels.

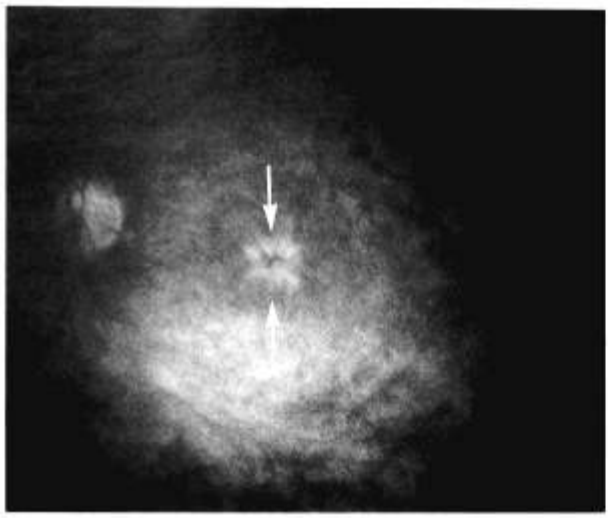

FIG. 6. Case #1, left eye, 10/10/89. Note cystoid macular edema (arrow) in this late fluorescein angiogram.

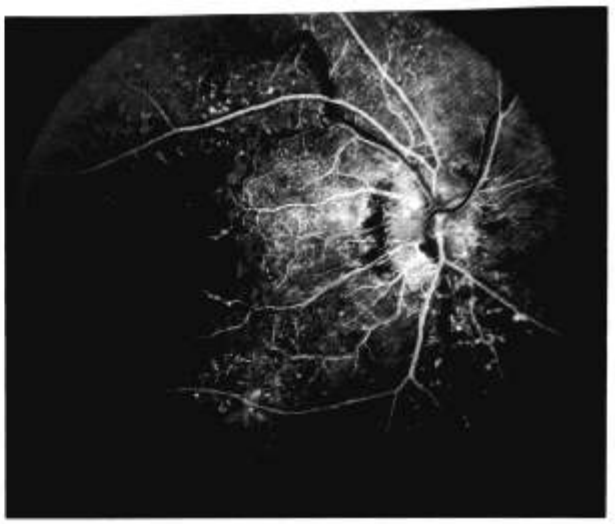

FIG. 7. Case #2, right eye, 11/30/89. Note new-formed vessels on disc and retinal vasculitis.

because of decreasing vision in both eyes. He had no eye problem until one year previous when painless, decreasing vision began in both eyes. This fluctuated a bit, but slowly progressed. He denied any history of pain or ocular redness. The past history and family history were negative.

Examination on 4 December 1989 revealed a best-corrected acuity of 10/70 in the right eye and 10/700 in the left eye. External examination revealed the eyes were white, pupils had been dilated with cycloplegics, and extraocular movements were full. The peripheral visual fields were full, but dense central scotomas were present in both eyes. Slit lamp examination revealed no anterior chamber reaction and no iris rubeosis. The lenses were clear but 2+ vitreous cells were present in the left eye. Ophthalmoscopy revealed extreme retinal vasculitis in the right eye with new-formed vessels on the disc. Peripheral vessels were extremely sheathed and resembled advanced Eale's disease. One or two areas of focal retinal lesions were seen, but arteries were very narrow and significant new-formed vessels were also seen at the macula. The left eye showed similar changes, but a much more extensive, large, subretinal disciform hemorrhage was seen under the macula in this eye, also with extreme peripheral retinal vasculitis. Fluorescein angiography performed 30 November 1989 documented these changes (Figs. 7–9).

Medical consultation revealed a blood pressure of 180/104 and repeat was 170/90 in both arms. The patient had a positive sickle cell preparation with 58% A-1 hemoglobin, 40% S-hemoglobin, no C-hemoglobin, and fetal hemoglobin less than 2%. Serum HIV ELISA was negative. Chest radiograph was normal. Spinal fluid revealed a clear acellular fluid with protein 48 and glucose 45, and nonreactive CSF VDRL. Rheumatoid factor was negative, ANA was less than 40 (normal), and sedimentation rate was 15, BUN was 10. Serum RPR was nonreactive. The impressive was bilateral severe diffuse retinal vasculitis, with hypertension and sickle cell trait. A Lyme/treponemal panel sent to Microbiology Reference Laboratory on 4 December 1989 revealed nonreactive RPR, nonreactive FTA-ABS, Lyme ELISA 1.29 (positive), and Lyme IFA IgG 1:128 (positive) and IgM <1:16.

Because the FTA-ABS had been reported posi-

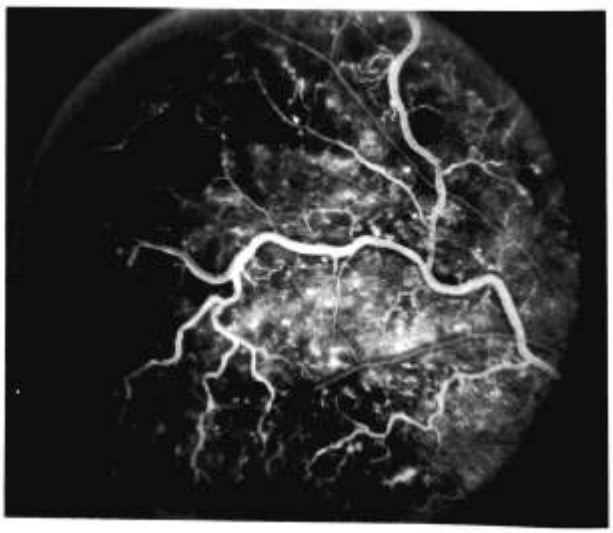

FIG. 8. Case #2, right eye, 11/30/89. Note venous participation in the retinal angiitis in this venous-phase angiogram.

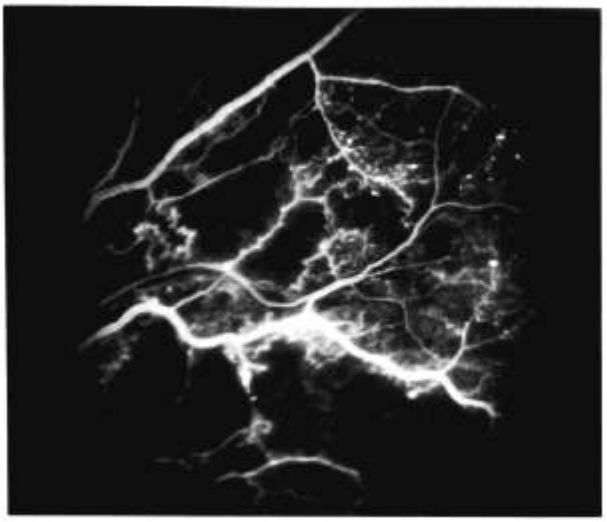

FIG. 9. Case #2, right eye, 11/30/89. Note areas of retinal capillary nonperfusion, multiple small retinal capillary aneurysms, and somewhat comparable appearance to focal beaded appearance as seen in cerebral angiograms showing angiitis.

tive in one laboratory and negative on repeat at another, blood from this patient was sent to Institut Alfred Fournier in Paris. They reported nonreactive VDRL, TPI, FTA-ABS, TPHA, and syphilis IgM tests, as well as a negative Lyme IFA (total and IgM). The patient was treated with 20 million units of daily intravenous aqueous penicillin in hospital, but no follow-up has been available since discharge.

Comment

A 58-year-old man from Netherlands Antilles presented with progressive visual loss for one year due to severe bilateral retinal vasculitis. Examination revealed dense bilateral central scotomas with marked sheathing of retinal vessels, active retinal vasculitis in both eyes, with venous stasis in left eye. Complete medical investigation otherwise revealed only sickle cell trait and hypertensive vascular disease but the fundus changes were not thought to be typical of sickle cell disease or hypertension. The patient was found to have positive serologic tests for Lyme borreliosis. Follow-up on this patient was not available.

Case 3 (RS)

A 23-year-old man from Honduras noted the sudden onset of blurred vision in his left eye and was referred to the Bascom Palmer Eye Institute on 12 October 1989 with an initial diagnosis of ocular phlebitis. Visual acuity at that time was 20/15 in the right eye and 20/20 in the left. The anterior segments were quiet. Fundoscopic examination revealed subhyaloid and vitreous hemorrhages in the left eye. Retinal vein and artery occlusions involved the mid- and far periphery of both eyes with sheathing of many vessels. Focal neovascularization was seen clinically and confirmed by fluorescein angiography in both eyes. Figs. 10–12 (made 14 November 1989) documented the extensive fundus changes in this patient.

The patient was otherwise in good general health and denied any systemic symptoms. Laboratory studies revealed that serum RPR, FTA-ABS, and HIV tests were negative. Hemoglobin electrophoresis, lupus anticoagulant and anticardiolipin antibodies were normal. The patient had a positive PPD skin test, and a negative chest radiograph, and was therefore started on oral INH. Bilateral subtenon Depomedrol injections were given. Subsequent panretinal photocoagulation was performed to both eyes over the next month due to increasing vitreous hemorrhage and neovascularization. Increasing traction and blood-obscuring adequate laser treatment to the left eye necessitated posterior vitrectomy with membrane peeling on 12 January 1990. Grain stains of the vitreous specimen showed no organisms and bacterial cultures showed no growth.

Increasing vitreous hemorrhage as well as organized vitreous inflammatory balls inferiorly in the right eye were noted shortly thereafter. A Lyme panel revealed an IFA IgG 1:64 and IgM 1:16 and Lyme ELISA was 1.39. Patient was then given intravenous Rocephin 2 grams/day i.v. for two weeks as an outpatient. The vitreous inflammatory

FIG. 10. Case #3, left eye, 11/14/89. Note diffuse retinal and preretinal hemorrhages.

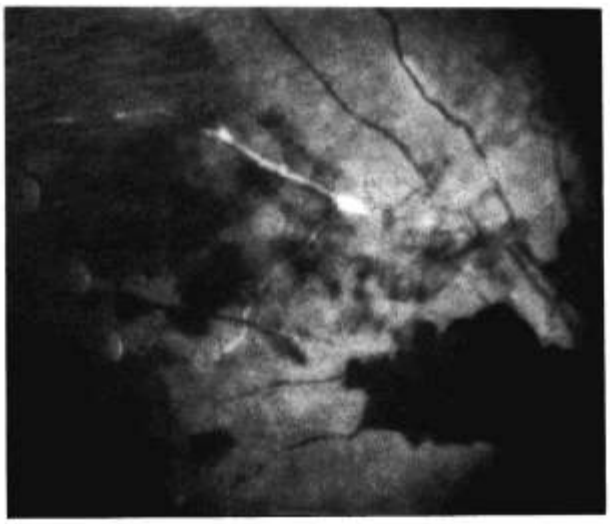

FIG. 11. Case #3, right eye, 11/13/89. Note white stripes on vessels showing marked perivascular sheathing.

balls persisted but did not progress after this treatment.

Posterior vitrectomy was performed on the right eye 16 February 1990 due to increasing vitreous hemorrhage. Cultures from the vitreous specimen showed no growth. Two months postoperatively the patient had stabilized visual acuity of 20/15 in both eyes, and showed no progression of his vascular occlusions or recurrence of the vitreous inflammation. Figure 13 shows the patient's right eye on 13 March 1990 after therapy (compare with Figs. 11 and 12 before the medical and surgical therapy).

Comment

A 23-year-old Honduran presented with abrupt visual loss due to a severe bilateral retinal vasculitis. This resembled advanced Eale's disease and progressing vitreous hemorrhage required panretinal photocoagulation and bilateral vitrectomy procedures. He was found to be seropositive for Lyme borreliosis, and after intravenous Rocephin therapy the process stabilized. However, it was not obvious how much of the improvement was surgical and how much was medical in this individual.

DISCUSSION

To our knowledge, there has been no previously published report on retinal vasculitis in Lyme borreliosis. However, through the courtesy of Mme. A. Paris-Hamelin, an abstract presented at the IV International Conference on Lyme Borreliosis in Stockholm, Sweden 18–21 June 1990 was brought to our attention. Dr. U. Schonherr and associates (4) from the University Eye Hospital in Erlangen-Nurnberg, West Germany presented a paper entitled "Intraocular manifestations of Lyme borreliosis." They reported 10 patients—5 with focal or diffuse choroiditis, 3 with neuroretinitis, and 2 with retinal vasculitis. All had increased IgG and 5 had positive IgM titers. Six out of 10 had extraocular signs such as arthritis, meningitis, cerebral demyelination, or Bell's palsy. Six patients were diagnosed early and did well with treatment; but 3 out of the 4 who were not diagnosed early showed later symptoms and poor visual acuity. The au-

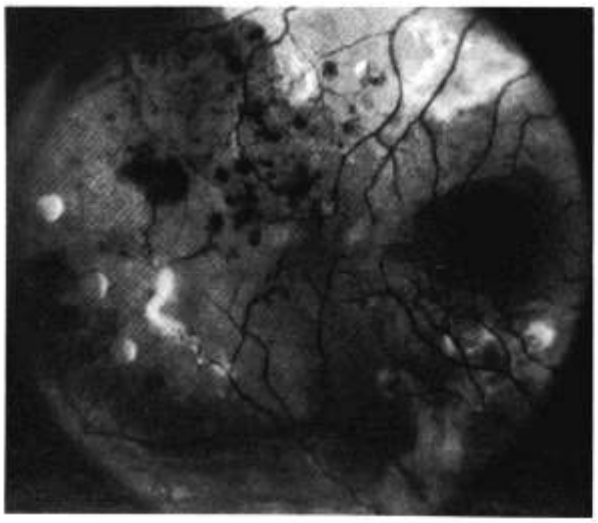

FIG. 12. Case #3, right eye, 11/13/89. Note punctate retinal hemorrhages and capillary aneurysms temporal to macula in this eye.

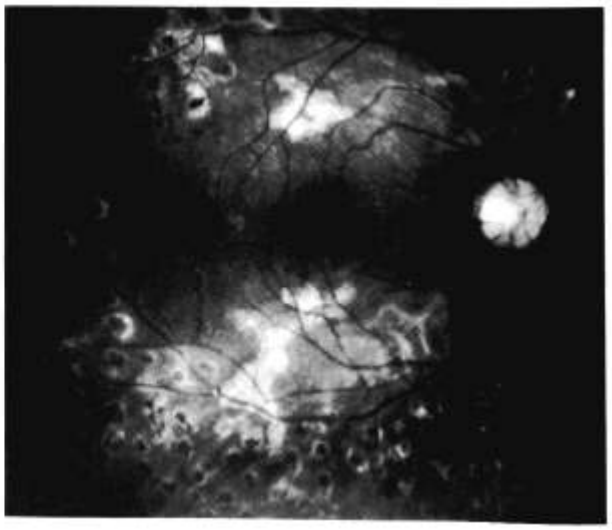

FIG. 13. Case #3, right eye, 3/13/90. after medical and surgical therapy. Note improvement in this eye compared to pretreatment state seen in Figs. 11 and 12.

thors concluded that optic neuritis should not be treated with steroids until Lyme borreliosis had been excluded.

One other pertinent reference was by Brogan et al. (5) concerning Lyme cerebral vasculitis. These authors reported a 37-year-old woman who presented to the emergency department complaining of a severe headache of 24-hours' duration. She was 10 days postpartum after a cesarean section. She was not hypertensive, the fundi were described as within normal limits, and there was no meningismus. After a computed tomography (CT) scan, the headache intensified and she developed left ptosis and flattening of the left nasolabial fold. Lumbar puncture was performed and while the CSF data was pending, the patient had a grand mal seizure. Repeat CT without and with contrast showed an acute nonhemorrhagic infarct in the right thalamic region near the posterior limb of the internal capsule. The CSF revealed 40 RBC, 1WBC, protein 178, and negative VDRL, cryptococcal antigen, tuberculosis, and fungal tests. The patient was admitted to ICU and a cerebral angiogram showed irregular small-to-moderate-sized vessels with narrowing and beading in the frontal and parietal regions. The venous phase ruled out the possibility of venous sinus thrombosis and the interpretation was cerebral vasculitis. She was treated initially with prednisone with slight improvement. However, two days later serum Lyme titer was 0.200 by optical density with a control of 0.091, and the CSF Lyme titer was 0.167 by optical density with a control of 0.091. The steroid therapy was discontinued and the patient was treated with 2 g Rocephin i.v. daily. The symptoms resolved and a follow-up angiogram two months later showed notable improvement from the irregularity, beading, and narrowing noted on initial examination. The authors stated that Lyme cerebral vasculitis had not been described in the United States, and found only one similar case in the world literature, by Uldry et al. (6).

In Uldry's case (6), a 40-year-old woman noted a tick bite under the left breast in 1983, followed by red lesions on the chest and limbs. One year later, she experienced headaches, with paresthesias around the mouth and in the left hand. In November 1985 she developed a left ataxic hemiparesis, and CT showed a hypodense infarction in the right lenticular nucleus. Blood pressure was 170/120 and she was treated with amiloride and hydrochlorothiazide. Four months later she developed blurred vision, with numbness in the hands. In August 1986 she developed diplopia, confusion, and a stumbling gait. Examination revealed a skew deviation with LE down, superimposed microsaccadic movements on pursuit attempts to the left, and an abduction palsy in left eye. There was a limitation of vertical gaze, particularly upward. The optokinetic nystagmus quick phase was decreased to the right. There was a slight left hemiparesis and mild ataxia in left arm. She was disoriented and had periods of irritability alternating with drowsiness. No meningeal signs were present. The spinal fluid had 27 cells (82% lymphocytes and 9% plasmocytes), protein 267. Titers of specific antibodies against *B. burgdorferi* were in CSF: IgM = 1:4 IgG = 1:128 and in blood: IgM = 1:32 and IgG = 1:256 (positive test: >1:32). Reagin tests to *T. pallidum* were negative in CSF and blood. The patient was treated with 24 million units/day penicillin G and prednisone 60 mg/day tapering over 8 weeks. Neurological state improved within 3 weeks. CSF then showed 8 cells (92% lymphocytes and 1.5% plasmocytes) protein 123. Clinical right carotid arteriogram showed segmental narrowing and obstruction of branches of the middle and anterior cerebral arteries. More distal branches received collateral flow in a retrograde fashion via leptomeningeal anastomoses. The thalamic arteries were extremely narrowed bilaterally. The impression was cerebral arteritis. These authors noted the close similarity between *B. burgdorferi* and *T. pallidum*. They noted that strokes secondary to meningovascular syphilis are often associated with prodromal disorders similar to this patient's during the 3 years before the diagnosis was made. The authors stated that the cerebral angiopathy demonstrated on angiography had not been previously reported in *Borrelia burgdorferi* infections and thought this was probably because angiography is not currently performed in this condition, even when relapsing CNS dysfunction is present. The angiographic findings in this case were similar to those observed in meningovascular syphilis.

It would not be unexpected for retinal and cerebral vasculitis to occur in Lyme borreliosis because of the known frequency of such involvement in disseminated disease due to another spirochete, *Treponema pallidum*. Some pertinent references in this regard may be of interest to the reader. Stokes (7) in his classic 1944 text on syphilology stated, "One of the most obvious localizations of the organism has probably escaped more emphasis because of its universality—namely, that to the vascular system. While of course undoubtedly influenced by the mode of distribution of the organism through the blood stream, the tremendous importance of syphilis of the blood vessels in every phase of the disease as a whole points as strongly

as any single piece of clinical evidence toward a distinct vasculotropism." In 1938 Olsen (8) stated, "The complications centering about vasculitis and perivasculitis from aorta to capillaries are legion, and have even been invoked by critical students of the pathology of the disease, such as Brown, as quite sufficient explanation without reference to allergic phenomena for most of the late manifestations of the disease."

Duke-Elder (9) stated "In the retina, vascular lesions are common—angiospasm, arterial obstruction, venous thrombosis, and aneurysms, occasionally miliary; retinal hemorrhages may occur, sometimes recurrent, sometimes massive, sometimes intraretinal, sometimes preretinal, and occasionally followed by the outgrowth of new vessels into the vitreous, sometimes to form a rete mirabile, or a retinitis proliferans. A perivasculitis is probably a rarity (common in the author's experience, however) as also is a retinal edema with exudative appearances (stellate retinitis) or a neuroretinitis with exudative characteristics (neuritis papulosa)."

Elwyn's *Diseases of the Retina* (10) differentiates the following clinical pictures of retinal syphilis. A modification (11) of Elwyn's (10) classification of syphilis of the retina is

SYPHILIS OF THE RETINA

Acquired syphilis
1. diffuse syphilitic chorioretinitis
2. neuritis papulosa of Fuchs
3. gummatous lesions of retina
4. gummatous lesions originating in optic nerve
5. syphilis of retinal blood vessels

Congenital syphilis
6. salt and pepper fundus
7. disseminated congenital syphilitic choroiditis
8. syphilitic retinitis pigmentosa
9. syphilitic retinal perivasculitis

Walsh (12) stated

> Acquired syphilis may produce involvement limited to the retina, and such a process was first described by Haab as syphilitic arteritis. . . . In general, syphilitic retinitis is characterized by retinal edema likely to be most pronounced in the region of the disc and macula, and at the macula there may be a star-shaped figure. Often there is sheathing of the vessels, particularly the arteries, and there may be hemorrhages in the nerve fiber layer or hemorrhages which have broken through into the vitreous. Haab remarked that the flow of blood is rarely completely obstructed; he noted that vision may remain normal or nearly normal even when the entire retinal circulation seems to be greatly impeded. Roth observed an almost constant minimal narrowing of vessels in individuals suffering from general paresis. Von Hippel found thickening of the retinal vessels, endarteritis and lymphocytic infiltration of the adventitia in cases of early syphilis." Walsh also described new-formed vessels in the vitreous making a striking ophthalmoscopic picture and in some instances such vessels are accounted for by syphilis.

In summary, three patients with a clinical picture of retinal vasculitis (mild in the first case, and severe in the two others) have been observed. The first patient had a history consistent with Lyme borreliosis, including a history of visiting an endemic area, history of tick exposure, recurrent facial palsies, palpitations, arthralgias of the knees, with positive serum Lyme ELISA titers from three different laboratories, as well as a positive serum Western blot for this disease. During an active recurrence of his chronic vitritis and iridocyclitis, active retinal vasculitis with definite fluorescein leakage occurred. He was given a subtenon's steroid injection to the left orbit only with no other oral or systemic steroids. He was placed on oral tetracycline. The patient showed a prompt and dramatic improvement in both eyes, with marked lessening of the retinal vasculitis on follow-up three weeks later. One could raise the question of the improvement being due to the subtenon's steroid injection; however, the fact that he has been well-controlled on tetracycline and that both eyes responded equally might make one consider the improvement primarily to be due to the tetracycline therapy.

In Cases 2 and 3 the retinal vasculitis was severe. Both of these patients had careful medical investigations to determine other causes for a retinal vasculitis and complete work-ups were negative in both. However, both of these patients were seroreactive for Lyme borreliosis. One improved after intravenous Rocephin, but also had photocoagulation and vitrectomy surgery, so that one cannot differentiate how much of the improvement was due to the medical versus the surgical therapy. Follow-up was not available on the other patient.

Since cerebral vasculitis due to *B. burgdorferi* has been reported, and two other cases of retinal vasculitis were observed in Germany, it is urged that ophthalmologists investigating patients for retinal vasculitis should include careful testing for Lyme borreliosis in the work up of those patients. In our institution, this includes the following: 1) Lyme/treponemal panel (RPR with titer, FTA-ABS, Lyme IFA IgG and IgM, Lyme ELISA); 2) Lyme Western blot; 3) Lyme lymphocyte stimulation test; 4) Lyme PCR; and in some cases 5) Lyme urine antigen studies. There is no question that seronegative Lyme borreliosis exists. Karlsson et al. (13) recently

cultured *Borrelia burgdorferi* out of the cerebrospinal fluid of four patients in a series of 38 patients who fulfilled the criteria of having neuroborreliosis. All four patients had pleocytosis in their spinal fluid and a history of neurological symptoms of only 4–10 days in duration. However, two of the four had no detectable antibodies against any of the isolated spirochetes in their cerebrospinal fluid, both when tested with an enzyme-linked immunosorbent assay and when tested by immunoblotting. The diagnosis of intermediate and late Lyme borreliosis continues to be primarily a clinical one and continues to show more and more similarities to syphilis. It is felt that further reports of careful clinical observations with long range follow ups should be made before establishing absolutely rigid diagnostic criteria. Although a low-yield procedure, culturing *Borrelia burgdorferi* from aqueous or vitreous humor and/or from cerebrospinal fluid will be necessary to finalize controversies about this disease.

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