Branch Retinal Arterial Occlusions in Multifocal Retinitis With Optic Nerve Edema

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Objective: To determine the natural history and visual prognosis of patients with branch retinal arterial occlusions secondary to multifocal retinitis.

Methods: Cases were reviewed for seven patients who exhibited multifocal retinitis and branch retinal arterial occlusion. The average age of the patients was 27 years (age range, 14 to 19 years).

Results: Six patients had systemic illnesses associated with their ocular findings. Four patients were scratched by a cat or exposed to a cat with fleas within 1 month of symptoms. Three of these patients were tested and had positive cat-scratch disease titers. At presentation, five patients complained of a scotoma, and two noted blurred vision. On examination, visual acuity was 20/25 or better in all but one eye. Five patients had vitritis, which was bilateral in three. Four patients exhibited optic nerve edema, which was bilateral in two. White intraretinal infiltrates were present in all patients, and were bilateral in five. The six patients who were examined within 1 week of symptoms had a white retinal infiltrate at the site of vascular occlusion. The retinal findings resolved in 2 to 6 weeks and did not recur. The final visual acuity was 20/20 OU in all patients.

Conclusions: Branch retinal arterial occlusions represent a complication of multifocal retinitis and idiopathic optic nerve edema. The arterial occlusions are probably caused by a focus of retinitis. This self-limited disorder has an excellent visual prognosis and may be related to cat-scratch disease.

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DURING THE convalescent phase of a nonspecific systemic flulike illness, multifocal retinal infiltrates, optic nerve edema, or both, develop in some patients.[1-3] In addition, retinal infiltrates and optic nerve edema can develop in patients with cat-scratch disease.[4] Branch retinal arterial occlusion has been described in one patient with multifocal inner retinal infiltrates.[2] In addition, branch retinal arterial occlusion has been described in one patient with Lyme disease[5] and one patient with Mediterranean spotted fever.[6]

This report describes seven patients with idiopathic multifocal retinitis and optic nerve edema complicated by branch retinal arterial occlusion. Six of these patients had an associated systemic illness. Visual symptoms in these patients were usually related to the arterial occlusion and not to the retinitis. The visual prognosis for this disorder is excellent. All patients had a visual acuity of 20/20 OU at the last examination.

RESULTS

Seven patients with an average age of 27 years noted a sudden change in vision, and they were found to have branch retinal arterial occlusion with associated white retinal lesions at examination. **Table 1** summarizes the presenting symptoms, systemic complaints, and infectious exposures. Four of the patients had a history of a recent cat scratch. Ocular characteristics are tabulated in **Table 2**. All but one of the 13 involved eyes had good initial visual acuity. Bilateral vascular occlusions occurred in only one patient (Figures 1 to 3); however, five of the six remaining patients had inflammatory signs (eg, vitreous cells, disc swelling) (Figures 4 and 5) or white retinal lesions in both eyes (Table 2). Two patients had mul-

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PATIENTS AND METHODS

A retrospective review of those patients who were diagnosed as having branch retinal arterial occlusion and multifocal retinitis with or without disc edema from 1982 to 1993 was performed. The medical records were supplemented by contacting patients or their referring physicians for further follow-up information.

The criteria for inclusion were ophthalmoscopic and photographic evidence of at least one branch retinal arterial obstruction (**Figure 1** through **Figure 5**). In addition, each patient had at least two superficial white retinal lesions in the eye with the branch retinal arterial occlusion. Four patients were excluded who had only one white spot or had a white spot with an adjacent chorioretinal scar because of the possibility that these patients had toxoplasmic retinitis that caused a branch retinal arterial occlusion.[7,8] Patients were also excluded who had recurrent branch retinal arterial occlusions more than 1 month after their initial examination because of the possibility that they could have idiopathic recurrent branch retinal arterial occlusion.[9,10]

The following data were analyzed: age; gender; associated systemic illness; infectious exposures (ie, a cat scratch); presenting ocular symptoms; visual acuity at presentation; pupillary and vitreoretinal examinations; status of the optic nerve; laboratory data and blood pressure; durations of active retinitis and white spots; and final visual acuity. Fundus photographs of all patients were reviewed. Fluorescein angiograms of six patients were reviewed.

tiple occlusive events in a single eye. The number of retinal white spots varied from none to 27 per eye (median, two). In the six patients who were examined within 1 week of the onset of visual symptoms, vascular occlusive events occurred where the white spots overlapped major vessels.

Laboratory workup was directed by the presenting complaints (**Table 3**). A rapid plasma reagin was nonreactive, and the blood pressure was normal in each patient. The three patients who were tested for cat-scratch disease had serologic evidence of exposure.

The final visual acuity was excellent in all patients (**Table 4**). Three patients were treated medically. Antiinfective agents were used in treating two patients, and aspirin was prescribed for one patient with anticardiolipin antibodies. Follow-up ranged from 1 to 47 months, during which time no recurrent branch retinal arterial occlusions were documented.

COMMENT

These seven patients with branch retinal arterial occlusions associated with multifocal retinitis and optic nerve edema had clinical features that resembled the following conditions: embolic branch retinal arterial occlusions,[11] idiopathic recurrent branch retinal arterial occlusions,[9,10] multiple cotton-wool spots,[12] optic neuritis,[13] Leber's idiopathic stellate neuroretinitis,[3,14-19] and acute multifocal inner retinitis.[1,2] Although the cases reported in this article are not easily pigeonholed into any of these categories, they most closely resembled Leber's idiopathic stellate neuroretinitis and acute multifocal inner retinitis (**Table 5**).

Most branch retinal arterial occlusions are caused by emboli.[11] Branch retinal arterial occlusions in children and young adults are rare. They are most commonly associated with migraine.[20] None of our patients had evidence of emboli, and only one of our patients described a history of migraine (patient 4).

Healthy young patients can also experience idiopathic recurrent branch retinal arterial occlusions that are not associated with any evidence of systemic infection or inflammatory diseases.[9,10] These patients do not exhibit vitritis, and when they do have white retinal spots, the spots do not correspond to the sites of arterial occlusions.[9,10] In addition, unlike the patients in this report, patients with idiopathic recurrent branch retinal arterial occlusion experience recurrent arterial occlusions for a period that ranges from 3 months to 10 years.

The white retinal lesions in these patients are probably infiltrates and not cotton-wool spots. Cotton-wool spots are caused by nerve fiber layer infarcts and can be seen in patients with acquired immunodeficiency syndrome, diabetes mellitus, hypertension, collagen vascular disease, giant cell arteritis, radiation-induced retinopathy, and other systemic disorders.[12] Cotton-wool spots are usually associated with systemic causal factors.[12] Although one of our patients had acquired immunodeficiency syndrome, the remaining six patients did not have a systemic disor-

Table 1. History of Patients With Retinitis and BRAOs*

Patient No./ Age, y/Gender	Systemic Association	Interval to Ocular Symptoms	Exposures	Presenting Ocular Symptom
1/39/F	Fever, tinnitus, stiff neck	2 wk	Cat scratch	Blurred vision
2/32/M	Fever	2 wk	None	Visual field loss, floaters
3/14/F	Sinusitis	2 mo	Cat scratch	Visual field loss
4/21/F	Fever, flulike episode, migraine	3 wk	Cat scratch, 8 wk pregnant	Blurred vision
5/31/F	None	None	Cat scratch	Visual field loss
6/28/M	Headache	3 y (HIV)	HIV	Visual field loss
7/26/M	Flulike episode	1 wk	None	Visual field loss

*BRAOs indicates branch retinal arterial occlusions; HIV, human immunodeficiency virus.

Table 2. Examination at Presentation*

Patient No.	Visual Acuity at Presentation		APD	Vitreous Cells		No. of White Spot(s)		Disc Swelling		Vascular Occlusion
	R Eye	L Eye		R Eye	L Eye	R Eye	L Eye	R Eye	L Eye	
1	20/15	20/20	None	2+	2+	27	8	Yes	Yes	L-sided superotemporal BRVO, L-sided macular BRAO, R-sided macular BRAO 2 times
2	20/20	20/20	None	No	No	1	1	Yes	Yes	R-sided inferotemporal BRAO
3	20/20	20/20	None	No	No	1	1	Yes	No	R-sided inferotemporal BRAO
4	20/15	2/200	L eye	No	2+	3	3	No	No	L-sided superotemporal BRAO
5	20/20	20/20	R eye	1+	1+	1	3	No	No	R-sided superotemporal BRAO
6	20/20	20/20	L eye	1+	1+	None	2	Yes	No	L-sided inferotemporal BRAO
7	20/25	20/20	None	1+	No	6	None	No	No	R-sided superotemporal BRAO, R-sided superotemporal BRVO, R-sided inferonasal BRAO

APD indicates afferent pupillary defect; BRVO, branch retinal vein occlusion; and BRAO, branch retinal arterial occlusion.

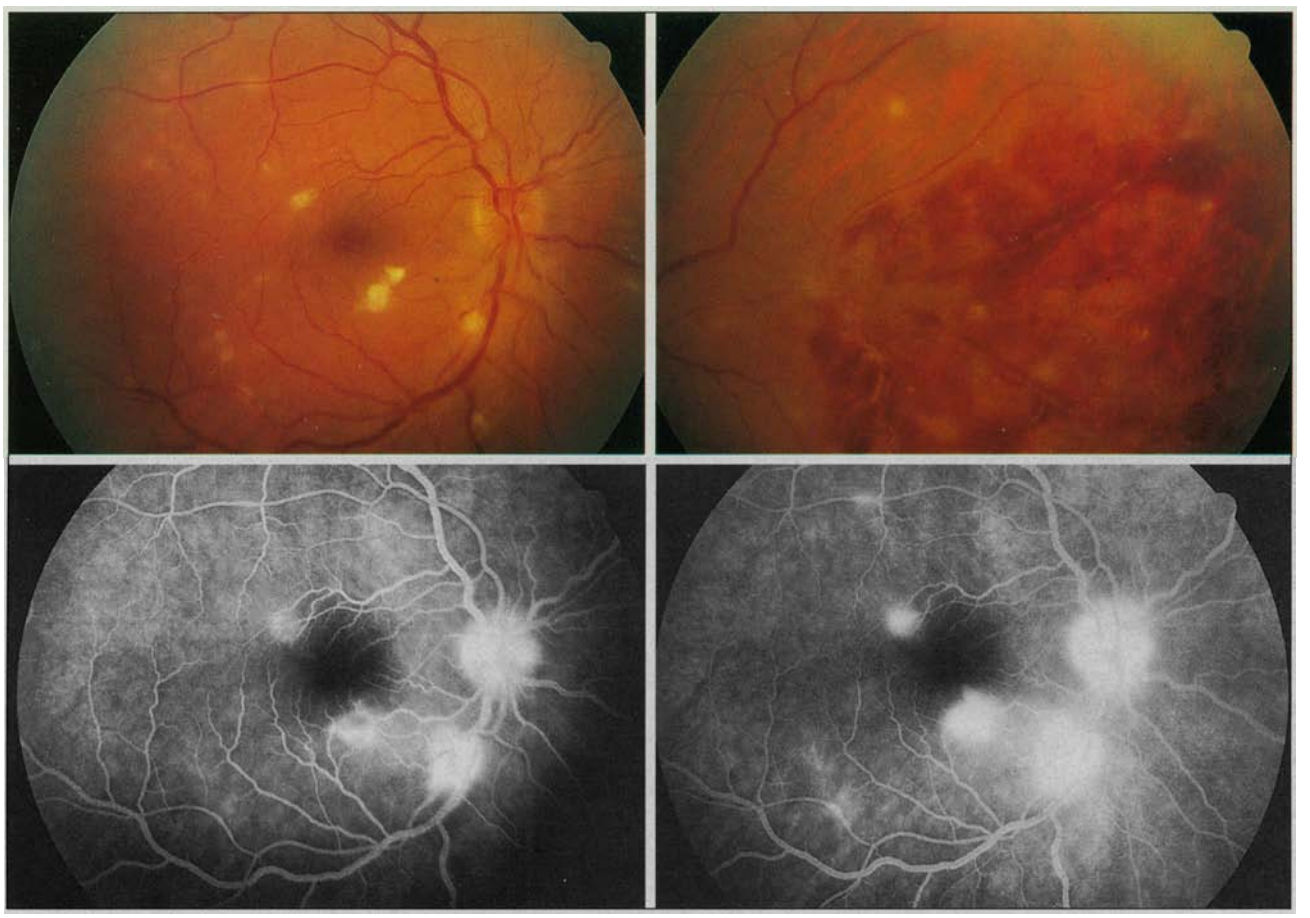

Figure 1. *Top, Patient 1 exhibited a 2-week history of fever, stiff neck, and tinnitus. Visual acuity was 20/15 OD and 20/20 OS. Fundus photographs show bilateral multifocal white spots. In the left eye, there was also a superotemporal branch retinal vein occlusion in the distribution of a vein that was adjacent to a white spot. Bottom, Early and late frames of a fluorescein angiogram that was taken of patient 1 shows leakage from the larger white spots and from the optic nerve. Not all of the lesions caused fluorescein angiographic abnormalities.*

der associated with cotton-wool spots. In addition, cotton-wool spots are usually not associated with vitritis and branch retinal arterial occlusions. Finally, two patients in this study developed white spots that grew into larger lesions, suggesting that the white spots were caused by inflammation or dividing organisms and not nerve fiber layer infarcts (Figures 1 to 3).

Optic nerve edema developed in four of the patients described in this series. A common cause of optic nerve swelling in young patients is optic neuritis. Unlike the patients in this series, patients with optic neuritis commonly have pain and a decrease in visual acuity.[13] Furthermore, vitreous cells and retinal lesions occur in less than 5% of patients with optic neuritis.[13]

These cases are probably closely related to Leber's idiopathic stellate neuroretinitis and acute multifocal in-

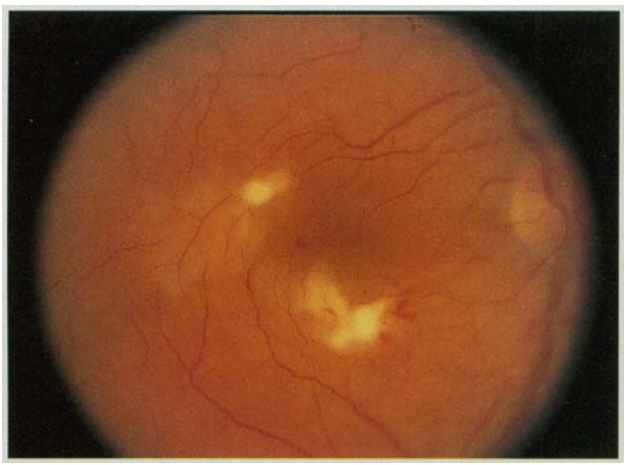

Figure 2. *Ten days after presentation and after the photographs in Figure 1 were taken, a decrease in visual acuity developed in the right eye of patient 1, and she noted paracentral scotomata. Visual acuity was 20/60 OD and 20/40 OS. The fundus photograph shows two macular branch retinal arterial occlusions in the distribution of vessels that are adjacent to the white spots. Some of the white spots appear larger than they were in Figure 1.*

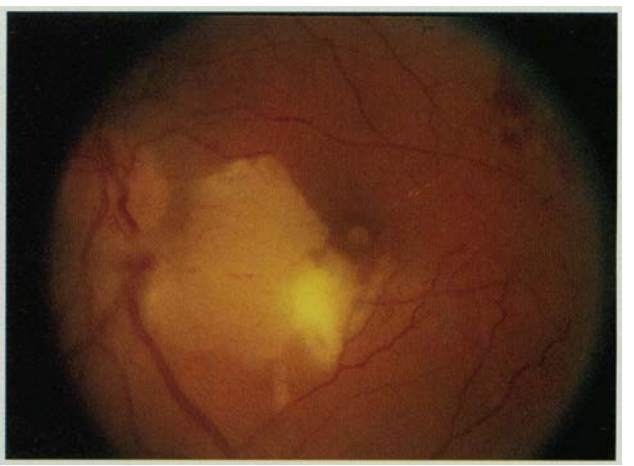

Figure 3. *Three days after the photograph in Figure 2 was taken, patient 1 noted a decrease in visual acuity in her left eye, and she exhibited yet another macular branch retinal arterial occlusion.*

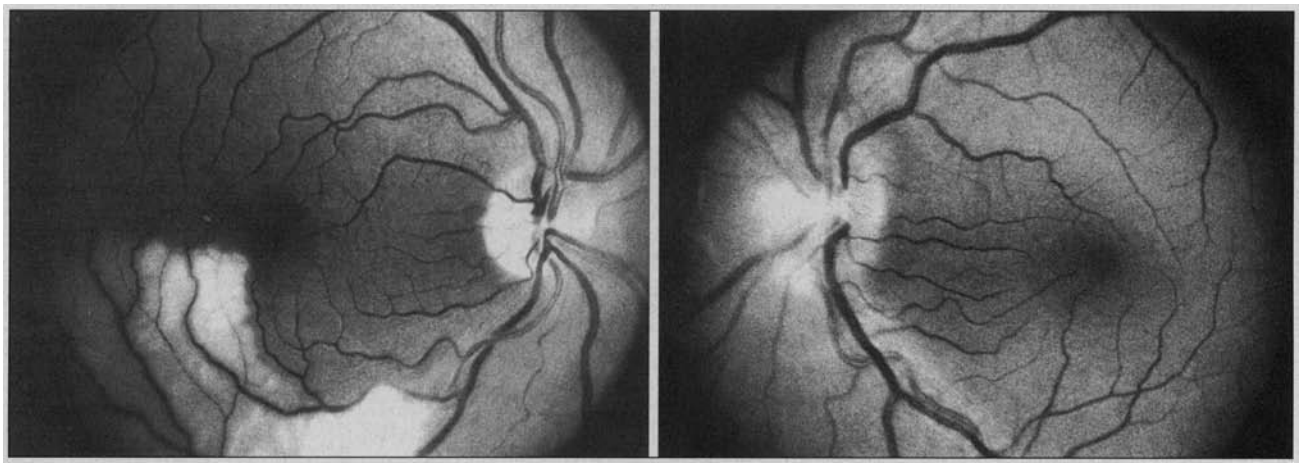

Figure 4. *Left, One month after the development of fevers and shaking chills, patient 2 noted a peripheral loss of vision in his right eye. The fundus photograph of the right eye shows a branch retinal arterial occlusion that is adjacent to a large white spot. Right, Fundus photograph of the left eye shows optic nerve edema; an inferonasal white retinal infiltrate in the midperiphery is not shown here.*

ner retinitis.[1,2,4,14-19] Although none of our patients had a macular star, four patients had optic nerve edema, which was bilateral in two. These seven patients had several similarities to patients with neuroretinitis and to patients with acute multifocal inner retinitis. These patients were young and exhibited good visual acuity, and their optic nerve edema resolved in less than 8 weeks with or without steroid therapy. Some of these patients also had a preceding viral illness, cat-scratch exposure, positive cat-scratch titers, an afferent pupillary defect, posterior vitreous cells, an elevated erythrocyte sedimentation rate, an elevated white blood cell count, and elevated white blood cell counts in the cerebrospinal fluid; all of these factors and laboratory findings can be seen in neuroretinitis and acute idiopathic multifocal retinitis.[1-4,14-18]

The six patients in this series who presented for examination within 1 week of the onset of their ocular symptoms had a white retinal infiltrate at the site of their branch retinal arterial occlusion. The occlusion of a branch retinal artery by a focus of retinitis has previously been reported in one case of acute multifocal inner retinitis[2] and in several cases of toxoplasmic chorioretinitis.[7,8] In this series, some of the larger lesions resembled toxoplasmic retinitis. Importantly, none of these lesions appeared to be adjacent to a chorioretinal scar as one would expect to see in patients with toxoplasmic chorioretinitis. In addition, all of these patients had multifocal white retinal lesions that were bilateral in five of seven. The multifocality of these lesions distinguishes them from toxoplasmosis, which is typically unifocal or occurs in a small region of the retina with localized satellite lesions. Also, unlike toxoplasmic chorioretinitis, the white spots in these patients rarely left any underlying retinal pigment epithelial abnormalities.

Since no histopathologic findings are available for these cases, one can only speculate as to the origin of the white retinal infiltrates. First, a blood-borne bacterial infection (eg, cat-scratch disease) could cause bacterial emboli to lodge in the retinal capillaries. In addition, bacteria could reach the retina from the choroid or the vitreous cavity. After the bacteria become established in the retina, they could divide and form an infiltrate.

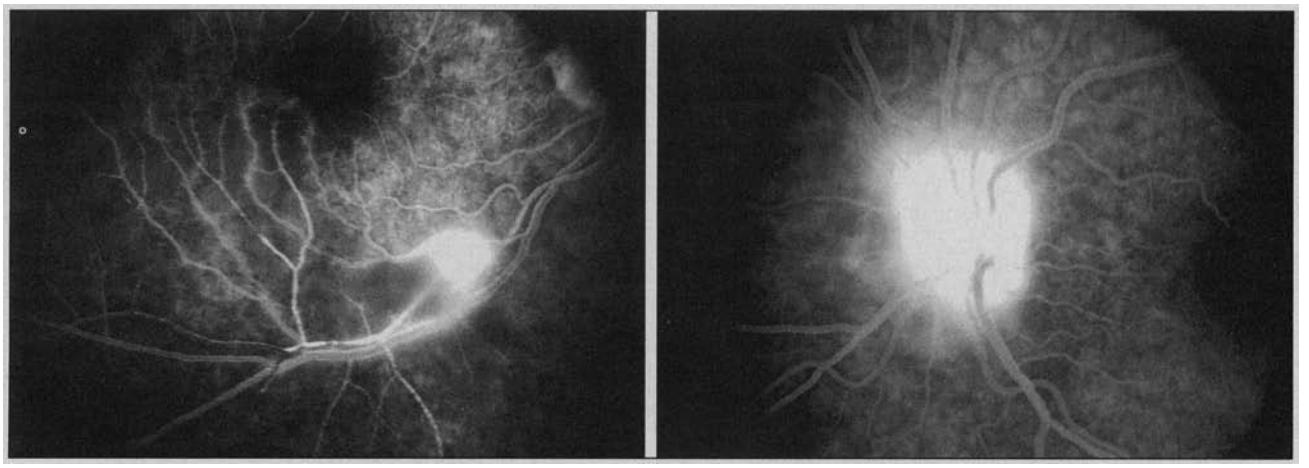

Figure 5. *Left, The fluorescein angiogram shows a region of leakage that is adjacent to a branch retinal arterial occlusion in the right eye. Right, In the left eye, there is leakage from the optic disc.*

Table 3. Blood Pressure and Results of Laboratory Studies*

Patient No.	BP, mm Hg	ESR, mm/h	WBC Count, $\times 10^9$/L	RPR, FTA-ABS	ANA	Anticardiolipin or Lupus Anticoagulant	Titer: Lyme	Titer: Cat Scratch	CT or MRI Finding	Other Studies
1	168/94	90	8.2	NR, NR	Negative	–, NR	Positive	Positive†	Abnormal‡	Lumbar puncture§ and blood culture, negative
2	110/70	8	11.3	NR, –	Negative	Medium high, NR	–	–	–	HIV-negative
3	110/70	25	10.3	NR, –	Negative	–	–	Positive‖	–	Toxoplamosis titer, negative
4	120/70	15	5.3	NR, –	–	–	–	–	–	Blood culture, negative
5	96/70	10	9.8	NR, NR	Negative	NR, NR	–	Positive	MRI, normal	HIV-negative
6	108/78	125	3.6	NR, NR	–	–	–	–	–	Chest x-ray film, normal
7	130/90	10	13.6	NR, NR	Negative	NR 2 times, –	NR	–	–	Anterior chamber tap,¶ negative; HIV- and ANCA-negative

**BP indicates systemic arterial blood pressure; ESR, erythrocyte sedimentation rate; WBC, white blood cell; RPR, rapid plasma reagin; ANA, antinuclear antibody; CT, computed tomography; MRI, magnetic resonance imaging; NR, not reactive; minus sign, not done; HIV, human immunodeficiency virus; and ANCA, antinuclear cytoplasmic antibody.*

†Afipia felis *IgG and IgM positive.*

‡*The MRI scan showed that bilaterally enhancing lesions in the caudate nucleus could be owing to inflammation or infarction.*

§*Cerebrospinal fluid cultures were negative, with a WBC count of 5.0×10⁹/L and 0.10 poly morphonuclear leukocytes and 0.90 lymphocytes.*

‖Rochalimaea henselae *IgG positive.*

¶*Intraocular toxoplasmosis IgG negative.*

Table 4. Treatment and Final Visual Acuity

Patient No.	Duration of Active Retinitis, wk	Treatment	Final Visual Acuity: R Eye	Final Visual Acuity: L Eye	Follow-up, mo
1	4	Ganciclovir, doxycycline monohydrate, prednisone	20/20	20/20	22
2	2	Aspirin	20/20	20/20	47
3	. . .	None	20/20	20/20	18
4	2	None	20/15	20/20	1
5	2	None	20/20	20/20	21
6	6	None	20/20	20/20	13
7	4	Prednisone, doxycycline monohydrate	20/20	20/20	13

Alternatively, the immune response to systemic bacterial infection could cause the formation of a white infiltrate. If a systemic illness causes activation of the immune system, immune complexes and inflammatory cells could form white infiltrates through deposition in retinal vessels.

Arterial occlusions at the site of retinitis could be from direct inflammatory infiltration of the vessel or from secondary effects of the inflammatory mediators on the vascular wall. Surrounding inflammation may invade the wall of a vessel and cause the vessel wall to thicken and disrupt blood flow. In addition, surrounding inflammation may compress a vessel and have the same effect. Even without direct invasion of the vessel wall, inflammatory mediators may cause edema of the vessel wall that could disrupt blood flow, and this could allow a thrombus to form. In the six patients who returned for long-term follow-up, after the retinitis was inactive, the retinal vessels did not

Table 5. Comparison of BRAO and Retinitis With Other Entities*

	Current Series	Idiopathic Recurrent BRAO[8,18]	Optic Neuritis[13]	Neuroretinitis[3,14-19]	Acute Multifocal Inner Retinitis[1,2]
Decrease in visual acuity	+	+	+++	+	±
Macular star	–	–	–	+++	–
White spots	+++	++	±	++	+++
Vitritis	++	–	±	+	+++
BRAO	+++	+++	–	–	±
Recurrent BRAOs	–	+++	–	–	–

**BRAO indicates branch retinal arterial occlusion; one plus sign, variable; three plus signs, characteristic; plus minus sign, minimal/rare; minus sign, not described; and two plus signs, common.*

resume a normal appearance at the site of occlusion. Instead, the vascular wall remained sclerosed, and fluorescein angiograms showed that the vessels remained occluded. This finding suggests that the inflammation caused permanent damage to the vessel wall. *Afipia felis*, one of the organisms possibly responsible for cat-scratch disease, could do this because it grows preferentially in vascular endothelial cells.[21]

All seven patients in our series had several findings that suggested that a systemic disorder caused their retinal inflammation. Six of seven patients had bilateral signs of ocular inflammation. Fever, flu, or aseptic meningitis preceded the ocular symptoms in five patients. Some patients had evidence for exposure to bacterial infections that were known to produce similar findings. The white blood cell count or erythrocyte sedimentation rate was elevated in several patients, and serologic tests were positive for cat-scratch disease in three patients and for Lyme disease in one.

When confronted with a patient with multifocal retinitis, optic nerve edema, and branch retinal arterial occlusion, evaluation for treatable infections (eg, cat-scratch disease, toxoplasmosis, syphilis, and Lyme disease) should be performed. Cat-scratch disease is usually self-limited.[21-24] Treatment with rifampin, ciprofloxacin, gentamicin sulfate, or a combination of trimethoprim-sulfamethoxazole is sometimes effective at limiting the duration of illness.[22] In addition, young patients with a branch retinal arterial occlusion should be evaluated for a possible coagulopathy or source of embolism. One patient in this study did have a positive anticardiolipin antibody, and this patient was treated with aspirin; in this patient, anticardiolipin antibodies may have developed in response to a systemic infection since the patient also reported a fever. In a young patient with other neurologic events and a high erythrocyte sedimentation rate, bacterial endocarditis and an atrial myxoma should be considered in the differential diagnosis.[25,26] We could not determine if treatment played any role in the modification of the course of this disease that, in untreated patients, is self-limited and has a good prognosis.

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