The Relation of Retinal Artery Occlusion and Carotid Artery Stenosis

Michael P. Merchut, MD, Sudha R. Gupta, MD, and Mohammed H. Naheedy, MD

We retrospectively studied 46 patients with symptomatic retinal artery occlusion and assessed the pattern and extent of carotid artery disease ipsilateral to the retinal artery occlusion. Ipsilateral internal carotid artery atherosclerotic lesions were virtually limited to the cervical arterial segment; 50% of such lesions were plaques or stenoses of ≤60%, whereas 15% of the angiograms were normal. No clinical features were significantly associated with a flow-limiting carotid stenosis of >60%. Contrary to previous reports, the type of retinal artery occlusion, whether branch or central artery occlusion, was not predictive of severe underlying carotid stenosis or occlusion. Likely mechanisms of retinal artery occlusion include in situ thrombosis and emboli from carotid, and possibly cardiac, sources. Extension of thrombus from an occluded carotid artery into the ophthalmic artery did not appear to be a mechanism of retinal artery occlusion. (*Stroke* 1988;19:1239–1242)

Retinal artery occlusion (RAO) can be a central retinal artery occlusion (CRAO) or a branch retinal artery occlusion (BRAO). Since von Graefe first described CRAO in 1859,[1] the appearance of RAO has been well known.[2–4] There are various causes of RAO, including orbital trauma, coagulopathies (especially sickle cell disease), vasculopathies (systemic lupus erythematosus, temporal arteritis and other vasculitides, hairy cell leukemia), migraine, intravenous drug abuse, oral contraceptive use, cardiac disease (especially valvular disorders, myxoma), carotid artery disease, and procedures such as carotid angiography or endarterectomy.[5–9]

We reviewed the 17-year experience with RAO at our institution, attempting to define the pattern and extent of ipsilateral carotid artery disease associated with RAO. We examined various clinical features to see whether they would be predictive of severe carotid artery stenosis. The clinical features included the type of RAO (BRAO or CRAO), preexistent cardiovascular risk factors, a history of ipsilateral amaurosis fugax, transient ischemic attack (TIA) or stroke, and blood and coagulation parameters.

Subjects and Methods

We retrospectively studied 46 patients with symptomatic BRAO or CRAO seen at Loyola University Medical Center and Hines Veterans Administration Hospital from 1971 to early 1987; all patients had an ophthalmologic evaluation to confirm the diagnosis. We did not include cases of only amaurosis fugax and asymptomatic or incidental retinal emboli. The presence of cardiovascular risk factors or related clinical features such as diabetes mellitus, congestive heart failure, smoking, hypertension, angina, hyperlipidemia, cardiac arrhythmia, peripheral vascular disease, and myocardial infarction was determined by the recorded medical history, physical findings, and laboratory data. These risk factors or clinical features were evaluated as possible predictors for a flow-limiting carotid artery stenosis, defined as a cross-sectional stenosis of >60% present on an angiogram.

Hemoglobin content, prothrombin time (PT), partial thromboplastin time (PTT), and platelet count were recorded, when available, from the investigation closest in time to the occurrence of the RAO. These laboratory values were compared among different patient groups using analysis of covariance. Since blood was not uniformly drawn on the date of the RAO, the time of each blood test relative to the RAO was used as a covariate. We used Tukey's multiple comparison test to analyze mean platelet count since time could not be used as a covariate for that analysis.

All angiograms were reviewed with a neuroradiologist. It was desirable to depict the condition of the carotid arteries at the investigation closest in time to the occurrence of the RAO since atherosclerotic lesions change over time; therefore, we excluded patients who had angiography >2 months from the time of the RAO. Angiography had been performed

From the Departments of Neurology (M.P.M., S.R.G.) and Neuroradiology (M.H.N.), Loyola University Medical Center and Hines Veterans Administration Hospital, Maywood, Illinois.

Address for reprints: Dr. Merchut, Department of Neurology, Loyola University Medical Center, 2160 South First Avenue, Maywood, IL 60153.

Received December 22, 1987; accepted May 27, 1988.

a mean of 11 days from the time of the RAO. Arterial lesions were classified as total occlusion, stenosis of >60%, stenosis of ≤60%, and plaque with or without ulcer. Arterial segments specifically studied were the common carotid, extracranial (especially cervical) internal carotid, intracranial internal carotid, and ophthalmic arteries. The status of the contralateral, asymptomatic, cervical internal carotid artery was also noted.

Results

General Features of Retinal Artery Occlusion

Of the 46 patients, 33 were men, with an age range of 40–87 (mean 62) years; 19 men from Hines Veterans Administration Hospital accounted for the male preponderance. There were 13 women, with an age range of 30–81 (mean 61) years. There were 25 cases of CRAO (14 right, 11 left; mean age 64 years) and 24 cases of BRAO (13 right, 11 left; mean age 62 years). With BRAO, the arterioles occluded were usually temporal (18 of 24, 75%) and were less often nasal (two), macular (three), or multiple (one). One patient had a bilateral BRAO, while another had one CRAO and two BRAOs. These two patients were counted as two and three cases of RAO, respectively.

Patient Characteristics

Twelve patients (26%) had possible causes of RAO that were clinically obvious to their physicians. A carotid artery lesion was suspected in one patient with previous surgery and irradiation for a parotid carcinoma. All other patients were presumed to have noncarotid causes, such as valvular heart disease or other systemic illnesses (Table 1), of RAO. In general, these patients were believed to have nonatherosclerotic causes of RAO. Their average age was 58 years, and their physicians rarely ordered carotid angiography or ultrasonography.

The remaining 34 patients lacked such clinically obvious causes of RAO. With an average age of 64 years, this group was suspected of having atherosclerotic carotid disease. Carotid angiography and ultrasonography was often done.

Various characteristics of these groups were compared in an attempt to find clinical predictors for ipsilateral carotid stenosis of >60% (Table 2). Among several cardiovascular risk factors, diabetes mellitus prevailed in the atherosclerotic subgroup with ipsilateral carotid stenosis of ≤60% and congestive heart failure occurred more often in the nonatherosclerotic group. Other trends were not significant. Ipsilateral amaurosis fugax tended to occur more frequently in the atherosclerotic subgroup with carotid stenosis of ≤60%. Neither ipsilateral TIA or stroke, the type of RAO, nor the presence of cholesterol retinal emboli were predictive of carotid stenosis of >60%. To investigate possible rheologic or coagulation factors, we also compared mean hemoglobin content, PT, PTT, and platelet counts among the groups. No significant difference was found. χ^2 analysis may not be valid for all these significant trends, however, due to the distribution of the expected counts.

TABLE 1. Nonatherosclerotic Etiologies of Retinal Artery Occlusion in 12 Patients

Attributed causes	No.
Valvular heart disease	4
Systemic lupus erythematosus	1
Wegener's granulomatosis	1
Temporal arteritis	1
Hairy cell leukemia	1
Migraine	1
Migraine, postoperative blood loss	1
Pulmonary hypertension, paradoxical embolus	1
Previous neck irradiation, calcified carotid with clot	1
Total	12

Angiographic Data

Conventional arteriography via femoral artery catheterization was performed in 31 patients, and digital subtraction arteriography (DSA) in two. Angiography was rarely done in the nonatherosclerotic group, but findings from one of the two performed were abnormal: a 37-year-old patient with previous neck irradiation for a parotid carcinoma had intraluminal clot in the ipsilateral, calcified carotid artery.

Overall, common carotid artery disease was infrequent, occurring in only one patient, in whom an innominate artery occlusion was found. Internal carotid artery lesions prevailed in the cervical segment and were less striking on the contralateral, asymptomatic side (Table 3). Ipsilaterally, half of those angiographed had plaques or stenoses of ≤60%, while 15% were normal. Ulcerations were seen in five patients, four of whom had mild (0–30%) stenosis; one had 80–90% stenosis. No ulcerations were deep, ragged, or harbored a thrombus. No flow-limiting, stenotic, intracranial disease was noted between the cervical internal carotid artery and its ophthalmic branch, although mild plaques were noted there in 15% of the angiograms. Ophthalmic arteries ipsilateral to the RAO were visualized 76% of the time; none looked stenotic.

One RAO occurred ipsilateral to an occluded internal carotid artery and a stenotic external carotid artery, where retrograde external carotid emboli may have caused the RAO. Two patients suffered RAO in relation to angiography for amaurosis fugax and mild stroke/TIA. The former occurred during the procedure (99% carotid stenosis), the latter 2 days later (total occlusion).

Discussion

Carotid angiography is infrequently performed in patients with RAO attributable to valvular heart disease or various other systemic illnesses. However, it may be possible, especially in older patients, that atherosclerotic carotid lesions coexist. Younger patients, with less atherosclerosis, may rarely have

TABLE 2. Characteristics of 46 Patients With 49 Cases of Retinal Artery Occlusion

Risk factor or clinical feature	Group			p
		Atherosclerotic		
	Nonatherosclerotic ($n=13$)	Stenosis >60% ($n=13$)	Stenosis ≤60% ($n=23$)	
Diabetes mellitus	0	1	10	<0.01
Congestive heart failure	4	2	0	<0.05
Smoking	3	7	13	NS
Hypertension	7	11	15	NS
Angina	2	6	7	NS
Hyperlipidemia	1	3	4	NS
Cardiac arrhythmia	0	4	3	NS
Peripheral vascular disease	0	5	5	NS
Myocardial infarction	4	3	7	NS
Ipsilateral amaurosis fugax	0	3	9	<0.05
Ipsilateral transient ischemic attack/stroke	2	4	2	NS
Ipsilateral retinal cholesterol emboli	2	4	6	NS
Retinal artery occlusion (branch/central)	6/7	6/7	12/11	NS
Hemoglobin (mean ± SD g/dl)	12.0 ± 2.2	13.5 ± 3.6	13.8 ± 2.0	NS
Prothrombin time (mean ± SD sec)	12.1 ± 1.3	12.0 ± 1.0	11.8 ± 0.8	NS
Partial thromboplastin time (mean ± SD sec)	27.3 ± 3.5	33.5 ± 14.0	27.4 ± 7.9	NS
Platelet count (mean ± SD $10^3/mm^3$)	300 ± 184	241 ± 68	265 ± 67	NS

One patient had bilateral branch retinal artery occlusions, and one patient had one central retinal artery occlusion and two branch retinal artery occlusions. NS, not significant at $p<0.05$, χ^2 analysis.

RAO from other carotid lesions; the history or signs of neck trauma, tumor, or previous neck irradiation (see Table 1) may be indicators for carotid angiography in this patient group. Most patients with RAO have no clear-cut cause of RAO and frequently undergo angiography for suspected carotid artery disease. With this selection bias, more carotid lesions would be expected in these patients than in those with systemic, nonatherosclerotic causes of RAO. Referral bias probably exists in our retrospective study, too, if RAO patients came to a medical center specifically for carotid angiography and endarterectomy. The patients we studied, however, have a prevalence of cardiovascular risk factors and an average age similar to those of other RAO series.[15,16] The purpose of our report was to evaluate the carotid artery status in this specific patient group and to see whether there were predictors of severe carotid artery stenosis ipsilateral to the RAO.

A history of ipsilateral TIA or stroke was not a significant predictor of flow-limiting carotid artery stenosis, whereas ipsilateral amaurosis fugax was associated with normal or less stenotic carotid arteries. Other cardiovascular risk factors were not predictive, and hematologic or rheologic differences between patient groups did not exist (Table 2).

TABLE 3. Angiographic Cervical Internal Carotid Artery Lesions in Patients With Retinal Artery Occlusion

Series	Type		Stenosis									
			Total occlusion		>60%*		≤60%*		Plaque ± ulcer		Normal	
	Central	Branch	No.	%	No.	%	No.	%	No.	%	No.	%
Kollarits et al[10]	9	2	4	36	3	27	1	9	3	27	0	0
Sheng et al[11]	25	0	1	4	3	12	4	16	6	24	11	44
Tomsak et al[12]	13	0	0	0	6	46	4	31	0	0	3	23
Shah et al[13]†	14	15	1	3	5	17	4	14	3	10	16	55
Hedges et al[14]†	25	23	0	0	15	31	0	0	15	31	18	38
Current study	17	18										
Internal carotid artery												
Ipsilateral ($n=34$)			8	23	4‡	12	5	15	12	35	5	15
Contralateral ($n=30$)			3	10	1	3	8	27	7	23	11	37

*Criteria were stenosis "over 50%" and "50% or less" in the series of Kollarits et al and Sheng et al.
†Digital subtraction angiography.
‡These four patients actually had stenosis of ≥80%.

Wilson and associates[17] felt that the type of RAO predicted the underlying carotid artery disease; CRAO was more likely with a carotid artery occlusion, while BRAO indicated an operable carotid artery stenosis. Our experience differs in that BRAO and CRAO occurred with equal frequency in patients with flow-limiting carotid artery stenosis or occlusion, as well as in those with less severe or absent disease. Similarly, cholesterol emboli did not necessarily indicate a greater degree of stenosis (Table 2). In our study, certain embolic events, such as amaurosis fugax, occurred twice as often in patients with BRAO than in those with CRAO; TIAs occurred more often in CRAO patients. Wilson et al[17] found both amaurosis fugax and TIAs more frequently in patients with BRAO.

In our study, ipsilateral carotid artery disease of a degree less than flow-limiting occurred in 50% of those who underwent angiography, while 15% showed normal carotid arteries (Table 3). Mild to no ipsilateral carotid artery disease likewise was found in 54–84% of other RAO series.[11–14] An exception was the study of Kollarits et al,[10] in which 63% of the patients had ipsilateral severe stenosis or occlusion. Only 12% of our patients had flow-limiting stenoses of >60% in the cervical internal carotid artery. No stenotic lesions of this degree occurred distal to the cervical segment, and more proximal stenoses near the aortic arch were rarely found.

Older pathologic studies suggested that BRAO is usually embolic, whereas CRAO is thrombotic.[18] The ophthalmic artery was visualized in 76% of our angiograms, as frequently in patients with BRAO as in those with CRAO. Of course, this does not rule out an in situ thrombosis of the central retinal artery but it implies that ophthalmic artery lesions appear unlikely as causes of RAO. However, ophthalmic artery occlusions might recanalize before angiography. Wilson and colleagues[17] wondered whether a carotid artery occlusion was likely to cause a CRAO by thrombus propagation into the ophthalmic artery. There were eight patients with carotid artery occlusion in our study, and the ophthalmic artery was seen angiographically in five of the eight.

In RAO patients with carotid artery disease limited to plaques or non–flow-limiting stenosis, in situ thrombosis or embolus might have caused the RAO. Fifteen patients with less severe or no carotid artery disease had two-dimensional echocardiography. Results from nine of these 15 were abnormal, showing valve thickening or dyskinetic/hypokinetic left ventricles. Whether the heart could be a source of embolus for RAO in these patients is a question for further study. The other six of these 15 echocardiograms were normal, including two from patients who had only plaques on carotid angiography. Retinal artery thrombosis may be the mechanism in such patients with fairly unremarkable carotid angiograms and echocardiograms. In situ thrombosis seems to be a likely mechanism for RAO from migrainous and vasculitic causes as well.

Acknowledgments

The authors thank Joyce Stallworth and Denise White for manuscript preparation, Jack Corliss and Shobha Srinivasan for statistical analysis, and Dr. Susan Trimble for patient referrals.

References

1. von Graefe A: Ueber embolie der arteria centralis retinae als ursache plotzlicher erblindung. *Graefes Arch Clin Exp Ophthalmol* 1859;5:136–140
2. Miller NR: *Walsh and Hoyt's Clinical Neuro-ophthalmology*, ed 4. Baltimore, Williams & Wilkins, 1982, pp 223–226
3. Henkind P, Chambers JK: Arterial occlusive disease of the retina, in Duane TD, Jaeger EA (eds): *Clinical Ophthalmology*. Philadelphia, Harper & Row, 1985, vol 3, pp 1–14
4. Arruga J, Sanders MD: Ophthalmologic findings in 70 patients with evidence of retinal embolism. *Ophthalmology* 1982; 89:1336–1347
5. Appen RE, Wray SH, Cogan DG: Central retinal artery occlusion. *Am J Ophthalmol* 1975;79:374–381
6. Brown GC, Magargal LE, Shields JA, Goldberg RE, Walsh PN: Retinal arterial obstruction in children and young adults. *Ophthalmology* 1981;88:18–25
7. Goodman GK, Winkler CF, Eiferman RA, Yam LT: Bilateral occlusion of the central retinal artery associated with hyperglobulinemia in hairy cell leukemia. *Can J Ophthalmol* 1982;17:124–127
8. Johnson LN, Krohel GB, Hong TK, Wood G: Central retinal artery occlusion following transfemoral cerebral angiography. *Ann Ophthalmol* 1985;17:359–362
9. Treiman RL, Bloemendal LC, Foran RF, Levin PM, Cohen JL: Ipsilateral blindness: A complication of carotid endarterectomy. *Arch Surg* 1977;112:928–932
10. Kollarits CR, Lubow M, Hissong SL: Retinal strokes I. Incidence of carotid atheromata. *JAMA* 1972;222:1273–1275
11. Sheng FC, Quinones-Baldrich W, Machleder H, Moore WS, Baker JD, Busuttil RW: Relationship of extracranial carotid occlusive disease and central retinal artery occlusion. *Am J Surg* 1986;152:175–178
12. Tomsak RL, Hanson M, Gutman FA: Carotid artery disease and central retinal artery occlusion. *Cleve Clin Q* 1979; 46:7–11
13. Shah HG, Brown GC, Goldberg RE: Digital subtraction carotid angiography and retinal arterial obstruction. *Ophthalmology* 1985;92:68–72
14. Hedges TR, Giliberti OL, Magargal LE: Intravenous digital subtraction angiography and its role in ocular vascular disease. *Arch Ophthalmol* 1985;103:666–669
15. Karjalainen K: Occlusion of the central retinal artery and retinal branch arterioles. *Acta Ophthalmol* 1971; 109(suppl):1–95
16. Savino PJ, Glaser JS, Cassady J: Retinal stroke: Is the patient at risk? *Arch Ophthalmol* 1977;95:1185–1189
17. Wilson LA, Warlow CP, Ross-Russell RW: Cardiovascular disease in patients with retinal artery occlusion. *Lancet* 1979;1:292–294
18. Cogan DG: *Neurology of the Visual System*. Springfield, Ill, Thomas, 1966

KEY WORDS • carotid artery diseases • embolism • retinal artery • thrombosis

The relation of retinal artery occlusion and carotid artery stenosis.

M P Merchut, S R Gupta and M H Naheedy

Stroke. 1988;19:1239-1242
doi: 10.1161/01.STR.19.10.1239
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628