CLINICAL STUDY

Microemboli are not a prerequisite in retinal artery occlusive diseases

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Abstract

Purpose **Retinal artery occlusion (RAO) is caused by arterio-arterial or cardiovascular emboli in about 50% of all cases, but the role of non-embolic causes remains unclear.**
Subjects and methods **We studied 27 patients with amaurosis fugax (AFX), branch retinal artery occlusion (BRAO), central retinal artery occlusion (CRAO) and anterior ischaemic optic neuropathy (AION). Patients underwent an evaluation of cerebrovascular and cardiovascular risk factors, measurement of haemorheological parameters, and Doppler/duplex sonography including ultrasound detection of cerebral microembolic signals and echocardiography.**
Results **Forty-one per cent of the patients had internal carotid atherosclerosis but only one patient had microembolic signals, probably due to a cardiac thrombus. Vascular risk factors, especially hypertension, were present in 82% of the patients correlating with abnormal haemorheological parameters such as increased thrombocyte reactivity.**
Conclusions **Our results indicate that altered haemorheological parameters, especially increased thrombocyte reactivity and vascular risk factors such as arterial hypertension, are non-embolic causes of vascular disease in a significant number of patients with RAO. This should guide diagnostic and therapeutic considerations concerning RAO in cases without proven embolic sources.**

Key words Doppler sonography, Embolus detection, Haemorheology, Retinal artery occlusive disease, Vascular risk factors

Acute loss of visual acuity or unilateral visual field loss due to arterial occlusive diseases may be transient or permanent. Clinicians usually differentiate acute prolonged arterial occlusion such as central retinal artery occlusion (CRAO), branch retinal artery occlusion (BRAO)[1,2] and non-arteritic anterior ischaemic optic neuropathy (AION)[3–5] from amaurosis fugax (AFX).[6–10] Risk factors for RAO include hypertension,[1,11,12] potential embolic sources from carotid atherosclerosis[4,13–21] and cardiac embolising diseases[11,22,23] in about half the patients.[8,11] A wide variety of systemic disorders associated with haemorheological abnormalities have also been described.[2,8,9,11,16,24,25]

While an embolic occlusion of the retinal arteries in AFX often does not last long enough to be visible during fundoscopy intravenous fluorescein angiography might detect remnants of embolic material or could show details of abnormal retinal circulation in CRAO or BRAO[2,8] and, rarely, in non-arteritic AION also.[3,5,17] Detection of embolic material flowing within the large brain-supplying arteries has become possible by means of ultrasound techniques.[26–30] In RAO of embolic origin, arteriosclerotic plaque and stenosis of the carotid arteries can be detected by Doppler and duplex sonography.[12,13]

We studied patients with RAO and AFX to evaluate the incidence of microembolic signals detectable by Doppler sonography, their possible sources and other non-embolic causes.

Subjects and methods

Twenty-seven patients with unilateral impairment of visual acuity underwent neurological and ophthalmological examination 1–28 days after onset of symptoms. Diagnosis was based on clinical presentation, symptoms and signs. Five patients were excluded because of inflammation of the optic nerve, arteritic AION and systemic disease.

Twenty-two patients received ultrasound examinations of the extracranial arteries by Doppler/duplex ultrasound and of the transcranial arteries by transcranial Doppler (TCD), including the ophthalmic arteries. Plaque characterisation and the extent of carotid atherosclerosis were determined. TCD detection of microembolic signals was performed with an EME Pioneer TC 4040 system for a duration of at least half an hour in both middle cerebral arteries through a thin region of the temporal bone (ultrasound window). Where bilateral insonation was impossible (due to an absent temporal ultrasound window) only the symptomatic side was insonated. Analysis of hyperintense transient (microembolic) signals (HITS) was performed during on-line recording by means of digital audio tape, followed by a

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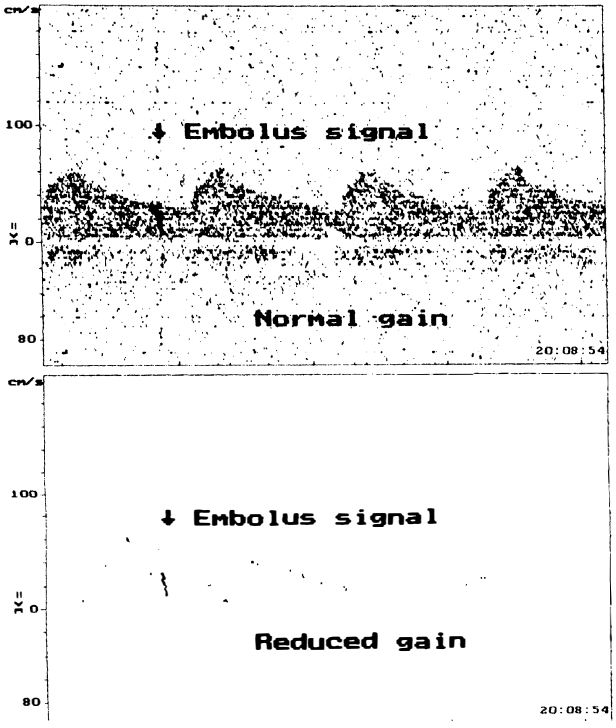

Fig. 1. *Hyperintense transient signal (embolus signal) in the right middle cerebral artery (depth 50 mm) of patient no. 20 with normal and reduced gain.*

second off-line analysis of tapes. Criteria based on international consensus[27] were: (1) duration <0.1 s, (2) irregular appearance during cardiac cycles, (3) intensity >8 dB above background noise, (4) unidirectional signal and (5) characteristic acoustic sound (Fig. 1). Twelve patients underwent transthoracic and/or transoesophageal echocardiography to rule out cardioembolic sources.

Haemorheological testing (own laboratory standard) included platelet reactivity (normal value: 0.98 ± 0.09; mean +3 standard deviations (SD) = 1.25), erythrocyte aggregation with high shear (normal value: 5.9 ± 1.4) or low shear (normal value: 10.0 ± 2.2), fibrinogen level (normal value: 298 ± 67 mg/dl), plasma viscosity (normal value: 1.25 ± 0.07 cP), serum viscosity (normal value: 1.21 ± 0.06 cP) and haematocrit (normal value: 0.46 ± 0.06) (Table 1).

Results

Data of 14 men and 8 women, aged 65.4 ± 11.1 years, are summarised in Table 1. Four patients had AFX, 6 suffered from AION, 9 patients had BRAO, and 3 patients had CRAO.

Vascular risk factors were present in 18 of 22 (81%) patients, including arterial hypertension (HT) in 16 of 18 (89%), hypercholesterolaemia (HC) in 8 (45%), diabetes mellitus (DM) in 1, obesity (O) in 8 (45%), nicotine abuse (N) in 4 (22%) patients and cardiac diseases (CD), including a history of myocardial infarction and coronary artery disease in 6 (33%).

Ipsilateral to the diseased eye ultrasound examinations of the carotid arteries revealed internal

Table 1. *Pathogenic parameters in arterial occlusive diseases of the eye*

Patient no.	Age (years)	Sex	Type[a]	Doppler[b]/rate of emboli[c]	Risk factors[d]	Haemorrhage[e]	TTE/TEE[f]
1	62	M	AFX-os	0/0	HT, CD	F, HK	
2	81	M	CRAO-os	0/0	HT, HC, CD	F, PV	TEE
3	60	M	CRAO-od	0/0	HT, O	Normal values	
4	80	M	BRAO-os	80%/0	HT, HC, CD, N	TA	TTE
5	75	F	BRAO-od	0/0	None	F, TA, HS, LS	
6	69	M	BRAO-od	30%/0	HT, HC, CD	TA	
7	59	F	BRAO-os	0/0	HT, HC, O	F, PV	
8	50	M	BRAO-od	0/0	HT	F, TA, HS, SV, PV, HK	TTE
9	55	M	BRAO-os	0/0	HT, HC, N, O		TTE
10	62	M	AION-od	0/0	N, O	TA, HK	TEE
11	48	F	AION-os	70%/0	HC	HS, LS, SV	TTE/TEE
12	74	F	AION-od	0/0	HT, HC, O, CD	F, TA, HS, SV	
13	69	F	AION-od	0/0	HT, DM, O	TA, HS, SV, LS	
14	62	M	AION-os	30%/0	HT, O		
15	44	M	AFX-os	0/0	HT, HC, O	TA, SV, HK	TTE
16	57	M	AFX-od	0/0	HT	TA, HK	TTE
17	60	M	AFX-od	90%/0	None	TA	TTE
18	80	F	BRAO-od	30%/–	HT, CD	TA	
19	80	F	BRAO-od	< 30%/–	None		
20	73	M	AION-od	< 30%/R 14/h; L 10/h–	HT, N		TTE/TEE
21	59	M	BRAO-os	0/0	HT		TEE
22	80	F	CRAO-od	70%/–	None		TTE

[a]*Type* of retinal artery occlusive disease (os, oculus sinister; od, oculus dexter): AFX, amaurosis fugax; AION, anterior ischaemic optic neuropathy; BRAO, retinal artery branch occlusion; CRAO, central retinal artery occlusion.
[b]*Doppler*: Doppler/duplex sonographic grade of stenosis ipsilateral to the diseased eye.
[c]*Emboli*: Detection and number of HITS/hour. –, no detectable ultrasound window on either side.
[d]*Risk factors*: HT, hypertension; HC, hypercholesterolaemia; N, nicotine abuse; DM, diabetes mellitus; CD, cardiac disease; O, obesity.
[e]*Haemorheology*: TA, increased thrombocyte reactivity; LS/HS, increased erythrocyte low/high shear; SVPV, increased serum/plasma viscosity; F, increased fibrinogen; HK, increased haematocrit.
[f]*TTE/TEE*: transthoracic/transoesophageal echocardiography.

carotid artery (ICA) stenosis in 9 of 22 patients (41%), including stenosis of <30% in 5 patients, <70% in 1 and >70% in 3 patients. Bilateral HITS with a rate of 14/h to the right and 10/h to the left middle cerebral artery were detected in only one patient (no. 20). In the other 18 patients no HITS could be found. In 3 additional patients no temporal ultrasound windows could be detected.

Twelve of 22 (55%) patients received transthoracic (TTE) and transosoesophageal (TEE) echocardiography; 10 patients refused the examinations. Eight patients had normal results without evidence of cardiac disease or cardioembolic sources. One patient (no. 10) had aortic valve sclerosis without stenosis, 1 patient (no. 2) had left vetricular hypertrophy and 1 patient (no. 11) had a septal aneurysm, all 3 without visible cardiac thrombi. One patient (no. 20) showed a mural aneurysm with a large thrombus adhesive to the ventricular wall.

Fifteen of 16 (94%) patients had abnormal haemorheological parameters: increased (2.8 ± 2.1, mean ± SD) thrombocyte aggregation reactivity in 11, elevated erythrocyte aggregation (high shear (8.3 ± 2.7) in 5, low shear (11.7 ± 4.6) in 3), elevated (1.46 cP) plasma viscosity in 1, elevated (1.3 ± 0.1 cP) serum viscosity in 5, elevated (476 ± 38 mg/dl) fibrinogen level in 6 and elevated (0.55 ± 0.01) haematocrit in 5 patients. One patient showed no haemorheological abnormalities; in 3 patients no haemorheological data were available.

Conclusions

Emboli causing transient or permanent blindness or visual field defects have been described as due to disease of the heart or carotid artery stenosis in up to 62% of patients with arterial obstructive disease of the eye.[1,2] Potentially pathogenic HITS measured by means of prolonged transcranial Doppler sonography of the middle cerebral arteries were reported in symptomatic and asymptomatic patients suffering from both carotid or cardiac disease. Origin and significance of these HITS differed. Time of ultrasound examination and criteria for distinguishing real embolic signals from artefacts differed as well.[10,17,26–30] Doppler and especially duplex sonographic examinations of carotid arteries including characterisation of plaque morphology and reduction of diameter, play an important role in the diagnosis of potential carotid artery diseases.[3,6,7,10,11,13,15,19,21,24,31]

Carotid artery and cardiac disease are associated with AFX.[6-10] Other conditions leading to embolus formation and causing CRAO and BRAO,[1,2,11,32] such as arterial hypertension, tumours, radiological procedures, intravenous drug abuse, coagulopathies and rheumatic disorders, have also been described, but the aetiology is often not clear.[1,2,11,12,23,31]

In our study HITS could be detected in only 1 patient with AION, who had combined potential arterio-arterial (inhomogeneous plaque in the ipsilateral internal carotid artery) and cardiac (TEE-proven mural aneurysm with large thrombus) embolic sources. In this case the cardioembolic cause became the more likely due to bilaterally detected HITS and only unilateral low-grade carotid stenosis. In the other patients neither HITS nor extensive carotid artery disease were found. In these patients we did, however, find vascular risk factors, especially arterial hypertension, which correlates with findings of previous studies.[1,11,30] Haemorheological parameters were also altered. In particular thrombocyte reactivity was increased, previously described in RAO.[25,32] In non-arteritic AION the embolic origin is controversial and despite single reports, as in our patient, mostly rejected by investigators.[2–5,17,19] The same holds true for CRAO and BRAO.[2,4,21,23,32] In AFX the majority of investigators support an embolic origin.[4,6–10,21,32]

Our study confirmed the importance of non-embolic factors, particularly arterial hypertension together with increased thrombocyte reactivity, in RAO. Only a minority of patients had potential carotid or cardiac embolic sources, and only one had proven HITS. Even in patients with a potential embolic source, the rate of HITS was probably so low that no signals could be detected during the period of insonation.[26–30]

Non-embolic causes should be taken into consideration in RAO, regardless of the patient's cardiovascular pathology. Drugs reducing cardiovascular risk factors, especially prevention and treatment of increased arterial systemic blood pressure, might be indicated.

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