Retinal Fluorescein Angiographic Evidence For Atheromatous Microembolism

Demonstration of Ophthalmoscopically Occult Emboli and Post-Embolic Endothelial Damage After Attacks of Amaurosis Fugax

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SUMMARY There is evidence that microemboli responsible for amaurosis fugax may be atheromatous but it can elude ophthalmoscopic confirmation, because such emboli quickly fragment and disappear from view in the retinal vessels. This report documents 2 patients in whom fluorescein angiography of the retina provided evidence of microembolization after an attack of amaurosis although the fundus appeared normal. In one patient the angiogram revealed intraluminal material; in the other it showed fluorescein leakage from patent arteriolar bifurcations.

ATHEROMATOUS MICROEMBOLISM is frequently the cause of amaurosis fugax, but ophthalmologic proof of this diagnosis is often difficult to obtain. Such emboli tend to fragment and disappear from view shortly after they become lodged in branches of the retinal artery. Ophthalmoscopic evidence of their atheromatous nature can be obtained only when the examiner fortuitously sees them in transit, or when their crystalline components (bright plaques) remain at the arteriolar bifurcations.

This report describes 2 patients whose atheromatous microembolism was heralded by an attack of amaurosis fugax; in both of them fluorescein angiography of the fundus provided evidence of embolization several days after the attack when ophthalmoscopic appearance of the retina was normal.

Patient 1. Occult Intraluminal Embolic Fragments

A 62-year-old man who had experienced several brief attacks of amaurosis fugax in his right eye suddenly became blind while his eye was being examined ophthalmoscopically by one of us (R.M.-M.). His attack lasted 15 minutes, after which he recovered vision over a period of about 5 minutes.

Immediately after the onset of blindness, a white embolus appeared in the main stem of the retinal artery. Two bright, atheromatous plaques were seen at bifurcations of the superior and inferior retinal arterioles. The embolus did not extend into adjacent arterioles nor did it cause complete obstruction of blood flow, although the flow in the blood column overlying the embolus was sluggish. At its distal end, the embolus moved synchronously with the pulse. From moment to moment, small fragments detached from the distal end of the embolus. These fragments temporally lodged in arterioles downstream from the embolus, but each quickly fragmented and disappeared from view. Each time a fragment occluded the lumen of an arteriole, the blood column in an adjacent vein became segmented and each time the fragment moved onward, the venous column again became continuous. Over the following 24-hour period this fragmentation occurred with diminishing frequency, with no report from the patient that his vision intermittently dimmed or blacked out.

Four days later, fluorescein angiography of his retina showed 2 intraluminal, hyperfluorescent areas at bifurcations of the inferior temporal arteriole of the right eye (fig. 1A, B). The size of these focal areas of hyperfluorescence remained unchanged during all the phases of angiography, but in the late phases, as fluorescein disappeared from the vessels, fluorescence of the embolic material was more conspicuous (fig. 1C, D). A second fluorescein angiographic study 15 days later showed no abnormalities.

This patient had systemic hypertension and type IV hyperlipoproteinemia. He had been treated with anticoagulants for 3 years following an operation for a right femoral-popliteal thrombosis. At the time of the attack of amaurosis fugax, his blood pressure was 120/80, and ophthalmic artery pressures were equal in both eyes. An electrocardiogram revealed an old posterior myocardial infarction. Angiograms of the aortic arch and carotid arteries showed ulcerated atheromatous plaques in the proximal portion of the innominate artery.

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FIGURE 1. Fluorescein angiogram (Patient 1). A to D. Two hyperfluorescent areas are seen in the central retinal artery and its inferior temporal branch (arrows). The size of these areas remain unchanged during the angiogram, but in late phases, when the fluorescein has disappeared from the vessels, their fluorescence is even more conspicuous.

Patient 2. Postembolic Fluorescein Leakage at Arteriolar Bifurcations

A 76-year-old man with systemic hypertension and minor signs of parkinsonism experienced a single attack of amaurosis fugax in his left eye. His eye was blind for 15 minutes, after which the upper field of vision returned; 5 minutes later the lower field was also clear. Three hours later, his ophthalmologist examined him and found a single bright plaque in his superior temporal arteriole. The patient reported no previous symptoms of transient neurologic deficit or cardiovascular disease, but 2 of his brothers had severe occlusive atherosclerotic vascular disease.

Two days after this attack of amaurosis, his left ocular fundus appeared normal except for a moderate narrowing and irregularity of retinal arterioles (fig. 2A). Fluorescein angiography of the fundus showed no abnormalities in the arterial phase (fig. 2B), but in the early venous phase showed 4 areas of focal hyperfluorescence, each at bifurcations of the superior nasal arteriole. In following phases of angiography these areas of hyperfluorescence increased in size and intensity, and a wedge-shaped zone of hypofluorescence was evident in the area supplied by the same arteriole (fig. 2C). In the late phases of the study, the hyperfluorescent arteriolar walls and adjacent retina contrasted sharply with the dark arteriolar blood column (fig. 2D). Two months later, fluorescein angiography of the fundus showed no abnormality (fig. 3).

An atheromatous plaque at the carotid bifurcation was confirmed by carotid angiography and removed by endarterectomy (fig. 4).

Discussion

In both these patients, distinctive focal arteriolar changes were demonstrated by fluorescein angiography several days after their attack of amaurosis fugax, even though the ocular fundi appeared normal ophthalmoscopically. The evidence that these changes were signs of atheromatous microembolism is indirect. Fortuitously, at the time of the attack of monocular blindness, retinal emboli were observed in
FIGURE 2. B & W picture and fluorescein angiogram (patient 2). A. Left ocular fundus shows moderate arteriolar sclerosis (black and white picture). B to D (fluorescein angiogram). No abnormality is seen during the arteriolar phase; however from the early venous phase, 4 hyperfluorescent areas are observed, each located in a bifurcation of the superonasal arteriole, increasing progressively in size during the study and spreading into the surrounding retina (C and D, white arrows). A wedge-shaped hypofluorescent area is observed at the course of the same arteriole (C, black arrows). In a later phase (D) two-point fluorescein leakage is seen at arteriolar bifurcation.
each patient's fundus; in each case the embolic material included bright plaques. Both patients had angiographic evidence of extracerebral atheromatous disease. In one patient an eroding atheromatous plaque was removed from the carotid bifurcation in the neck on the same side as the symptomatic eye.

In patient 1, the ophthalmoscopically occult embolus demonstrated by fluorescein angiography was discovered 4 days after the attack of amaurosis. It was intra-arterial and was lodged at a bifurcation; it did not impede the blood flow, and it absorbed fluorescein. We believe this embolus was an atheromatous aggregate of platelets, lipid, and fibrin (as described by McBrien, et al.\(^1\) and Warren and Lytton\(^2\)), and that it was a fragment of the larger embolus seen in the mainstem of the retinal artery during the amaurotic attack. This parent embolus was greyish-white and did not obstruct the blood flow; it moved at its distal end with each pulse beat and released fragments into the retinal vascular bed. This demonstrates that soft, atheromatous emboli can lodge at arteriolar bifurcations without causing occlusion, and can remain there for several days.

In patient 2, post-embolic, focal fluorescein leakage at several retinal arteriolar bifurcations was demonstrated 2 days after an attack of amaurosis fugax. This leakage indicates endothelial damage caused by microemboli, as Dollery and co-workers\(^3\) and Shakib and Ashton\(^4\) demonstrated in animals using fluorescein angiographic and electron-microscopical methods.

Our observation of bright plaques at corresponding arteriolar bifurcations immediately after a patient's attack is evidence that cholesterol crystals were probably the agents responsible for these fluorescein angiographic signs. Cholesterol crystals are the rigid component in atheromatous microemboli that lodge in arteriolar bifurcations; the soft components wash on downstream. As these wafer-like sharp-edged crystals impact in the lumen they may puncture the endothelium before shearing apart and disappearing from ophthalmoscopic view. We believe that the endothelial bifurcation leaks documented in the second patient can cause intramural plasma seepage and focal, greyish-white opacity of retinal arterioles of the type described by Dark and Rizk\(^5\) in patients with atheromatous microembolism.

Objective evidence of retinal microembolism is of obvious value in the management of patients with amaurosis fugax. Although we do not know how frequently fluorescein fundus angiography can provide such evidence, our experience shows that this diagnostic method can be useful when the retinal vascular bed appears normal ophthalmoscopically.
Embolization from a Fusiform Middle Cerebral Artery Aneurysm

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SUMMARY A 34-year-old man had a transient ischemic attack and subsequently a completed stroke. Arteriography revealed a large fusiform aneurysm of the left middle cerebral artery with intraluminal thrombus. At surgery, the thrombus was seen within the lumen of the aneurysm. Absolute evidence for embolization is lacking as no examination for this could be done.

Embolization from intracranial aneurysms seems to occur exclusively in large or giant aneurysms. Turbulent flow and a "stagnant zone" probably promotes thrombus formation. The reasons for the relative rarity of subsequent embolization are discussed.

Because embolization from intracranial aneurysms is so uncommon and because aneurysms usually produce focal deficit by other mechanisms, 4 criteria are presented to determine whether embolization is likely.

CEREBRAL ANEURYSMS generally produce neurologic deficit by means of hemorrhage, vasospasm or mass effect. Embolization from cerebral aneurysms is rarely mentioned in reviews of transient ischemic attacks (TIA), non-atherosclerotic causes of stroke, and the non-hemorrhagic consequences of cerebral aneurysm.1-9

Case Report

A 34-year-old, white, right-handed man was admitted with aphasia and a right hemiparesis. He had been in good health until 10 days previously, when he experienced lightheadedness and right hemiparesis lasting 5 minutes. Six days later, he had a similar attack from which he did not fully recover. There were no associated headache or other neurological symptoms. There was no history of diabetes, hypertension, or other significant medical diseases. Family history was also unremarkable.

Examination revealed an alert, cooperative man with a moderate Broca's aphasia. There was a mild, right central facial paresis and a right hemiparesis affecting the arm more than the leg. He had right-sided hyperreflexia with bilateral flexor plantar responses. The remainder of the neurological examination was normal. There were no ocular or cervical bruits.

Routine blood studies and a coagulation profile were normal as were plain skull radiographs. An EEG revealed 1½ to 3 c/s delta activity over the left hemisphere most marked in the temporal leads. Computed tomography (fig. 1) revealed an area of decreased density in the region of the left internal capsule. At the level of the suprasellar cistern on the left, there was an area of increased density which became enhanced with contrast injection. Arteriography revealed a fusiform aneurysm along the M-1 segment of the middle cerebral artery (fig. 2). There was a suggestion of thrombus within the aneurysm. The aneurysm measured 2 cm in length by 9 mm in height. A lumbar puncture was normal.

The aphasia and hemiparesis improved markedly and 11 days following admission, the patient underwent a left frontotemporal craniotomy. The aneurysm was dissected out using microsurgical technique and was much larger than it appeared on arteriography. Many vessels, clearly patent, were seen coming off the dome. Intraluminal thrombus was seen through the aneurysmal wall opposite the take-off of the small penetrating vessels. The aneurysm could not be clipped or trapped but was wrapped with muslin gauze.

In the immediate post-operative period, the aphasia and hemiparesis was slightly worse. However, he had no further attacks of TIA or stroke and was discharged from the hospital on aspirin 10 grains b.i.d.
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