the evaluation for CTX to support early definitive therapy. Moreover, the measurement of cholestanol levels when a subject is initially seen with presenile cataracts of questionable etiology could be a valuable clinical tool.

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Familial Retinal Arterial Tortuosity Associated With Tortuosity in Nail Bed Capillaries

Familial retinal arterial tortuosity (fRAT) is characterized by marked tortuosity of second- and third-order retinal arteries with normal first-order arteries and venous system. Patients have variable transient vision loss owing to retinal hemorrhages after minor stress or trauma. Prognosis is usually excellent. Whether there is systemic involvement is controversial. We report 3 cases of fRAT associated with a high degree of tortuosity of capillaries at nailfold capillaroscopy as an indication of systemic vascular pathology.

Report of Cases. *Case 1*. A woman was first seen at age 19 years because of blurred vision after a minor car accident. Best-corrected visual acuity (BCVA) was 0.9 OD and 0.8 OS. Ophthalmologic examination revealed marked tortuosity of second- and third-order retinal arteries and multiple intraretinal and preretinal hemorrhages in both eyes (**Figure 1**A). The patient was observed. Four weeks later, BCVA was fully restored in both eyes and the hemorrhages had almost resolved.

Five years later, the patient reported frequent episodes of migraine. Tortuosity of the retinal vessels and BCVA remained unchanged, but the macular reflex appeared duller, and mild thickening of the inner limiting membrane was noted in both eyes (Figure 1B). No hemorrhages were observed.

Seven years after she was first seen, the patient had decreased visual acuity of 0.4 OD and 0.8 OS. She was in her 18th week of pregnancy and had undergone amniocentesis 2 days previously. Fundus examination showed several preretinal, foveal hemorrhages in both eyes. Four weeks later, BCVA returned to 1.0 OU and hemorrhages had resolved.

Twelve years after she was first seen, the patient reported episodes of blurred vision once per year, usually following minor exercise. Best-corrected visual acuity had always fully recovered. At this ophthalmologic examination, thickening of the inner limiting membrane was stable and there was 1 asymptomatic preretinal hemorrhage inferotemporal to the macula (Figure 1C). The patient still experienced 5 to 6 episodes of migraine per year but was otherwise healthy.

In visual field tests, scotomas were noted that corresponded to the locations of the hemorrhages. Fluorescein angiography demonstrated no leakage, staining, hypoperfusion, or capillary dropout. Neurologic examinations, including cranial magnetic resonance imaging, yielded normal findings. Extensive examinations in internal medicine, explicitly, tests for serologic factors including virus and bacteria antibody titers and for rheumatologic and autoimmune factors, coagulation tests, and serum electrophoresis, also yielded normal findings. The patient was not taking any systemic medication that would alter coagulation, and blood pressure was within normal limits.

At nailfold capillaroscopy, which was performed at the second and fourth visits, tortuosity of capillaries was highly increased in all fingers of both hands (Figure 1D and E). Minor rarefication and 1 avascular zone, but no microhemorrhages, were detected. Sodium fluorescein video nailfold capillaroscopy showed normal inflow and outflow, demonstrating absence of capillary spasm; normal transcapillary and interstitial diffusion of fluorescein; and normal halo. No other dermatologic disease, including Raynaud syndrome, was observed.

Case 2. The older sister of patient 1 reported a slight decrease in BCVA when first seen at age 28 years. However, BCVA was 1.0 OU. We found marked tortuosity of second- and third-order retinal arteries in both eyes but no hemorrhages. The patient had a history of 1 episode of transient microhematuria of unknown origin, but otherwise reported that she was healthy.

Seven years later, extensive ophthalmologic (**Figure 2**A), neurologic, and medical examinations were performed, analogous to those in patient 1. All findings were normal with the exception that antinuclear antibodies were 2-fold positive. Findings at dermatologic examination and nailfold capillaroscopy were identical to those in patient 1 (Figure 2B and C).

Case 3. The father of patients 1 and 2 was first seen at age 56 years and reported that he had never experienced any visual disturbances. He had a stroke with speech disturbance 8 years earlier, but reported no residual adverse effects. Best-corrected visual acuity was 1.0 OU. Marked tortuosity of second- and third-order retinal arteries was found in both eyes, without hemorrhages.

He was seen 7 years later, and extensive ophthalmologic (**Figure 3**A), neurologic, and medical examinations revealed atrial fibrillation, and

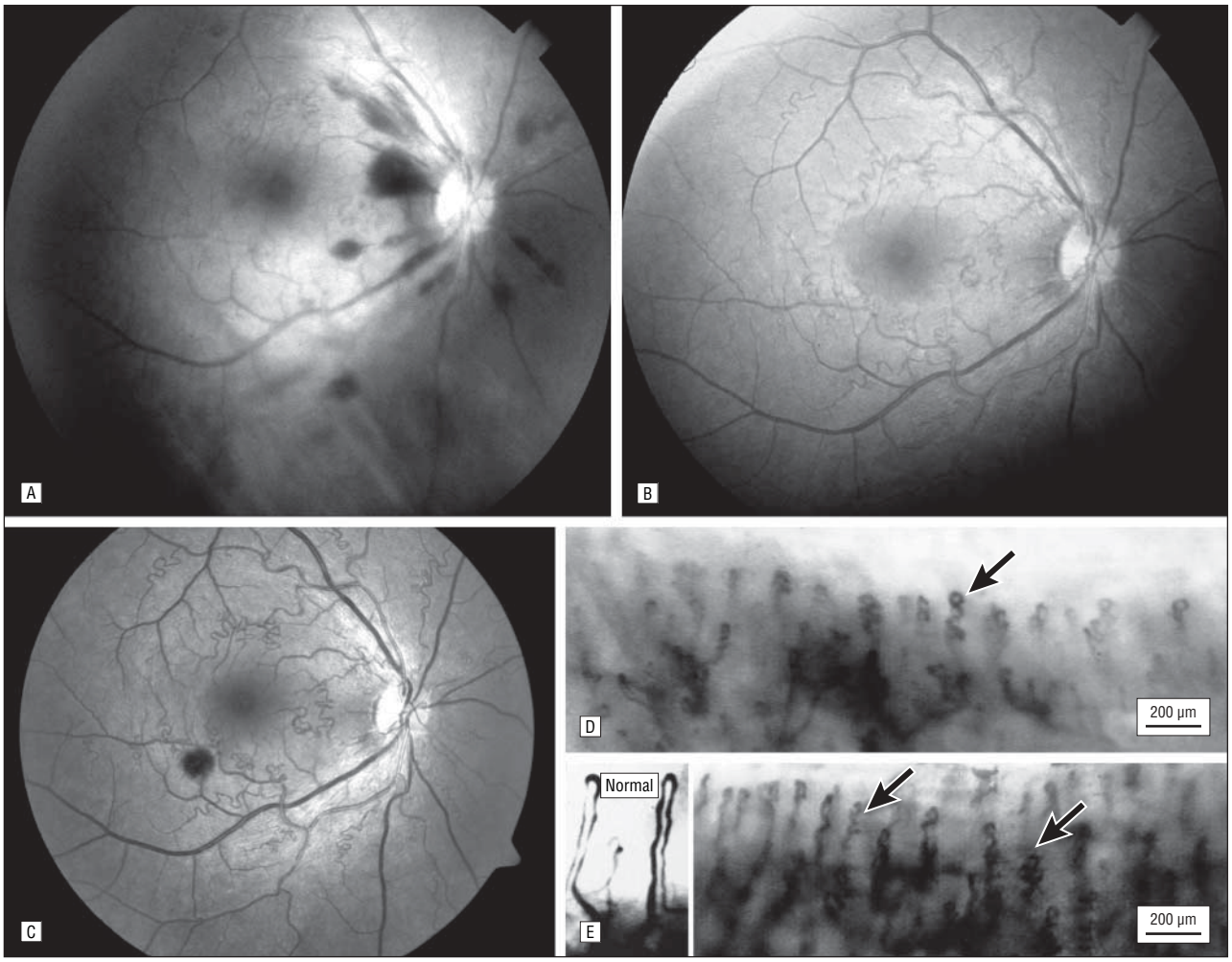

Figure 1. Patient 1. Views of the fundus and findings at nailfold capillaroscopy. A, When the patient was first seen after a minor car accident at age 19 years, multiple small hemorrhages were noted. She exhibited all of the typical features of familial retinal arterial tortuosity, with tortuosity in second- and third-order retinal arteries and normal large arteries and retinal veins. B, Five years later, no hemorrhages were seen and the retinal vasculature remained unchanged. C, Twelve years later, there was 1 preretinal hemorrhage inferotemporal to the macula; the retinal vasculature otherwise remained unchanged. D and E, Nailfold capillaroscopic findings in the right third and fourth fingers. Except for the high degree of tortuosity (present in approximately 30% of capillary loops; arrows depict typical examples), the capillaries were normal, a finding that was confirmed at sodium fluorescein video microscopy. For comparison, the inset in E shows enlargement of normal capillary loops at nailfold capillaroscopy in a healthy person. Note parallel arrangement of inflow and outflow arms.

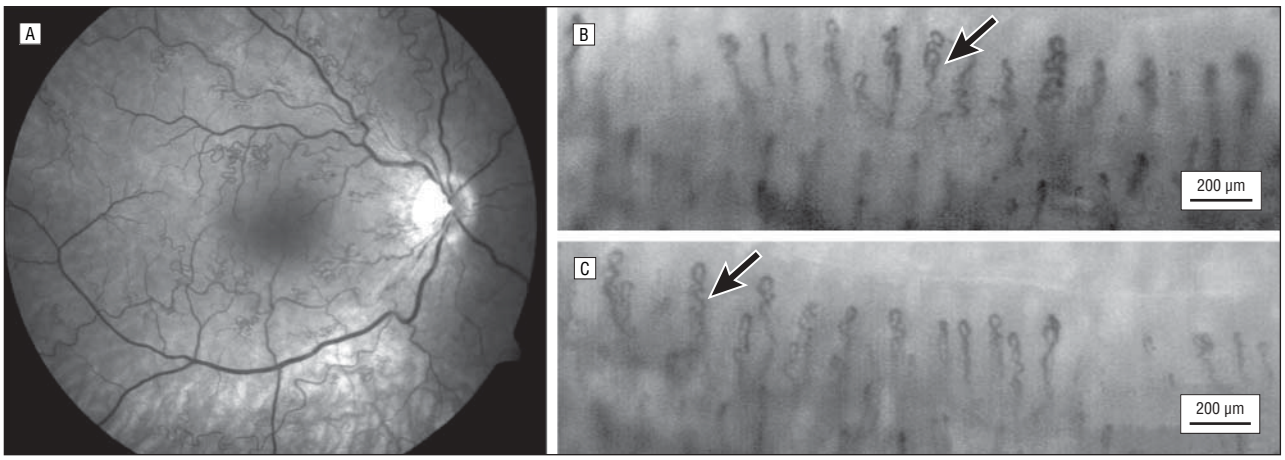

Figure 2. Patient 2. Views of the fundus and findings at nailfold capillaroscopy. A, At age 35 years, the patient demonstrated all of the typical findings of familial retinal arterial tortuosity. She had never experienced visual disturbances, although the degree of tortuosity was higher than in patient 1. B and C, Nailfold capillaroscopic findings in the left third and fourth fingers. Also in this patient, approximately 30% of capillary loops showed a high degree of tortuosity (arrows depict typical examples), while all other findings were normal, analogous to those in patient 1.

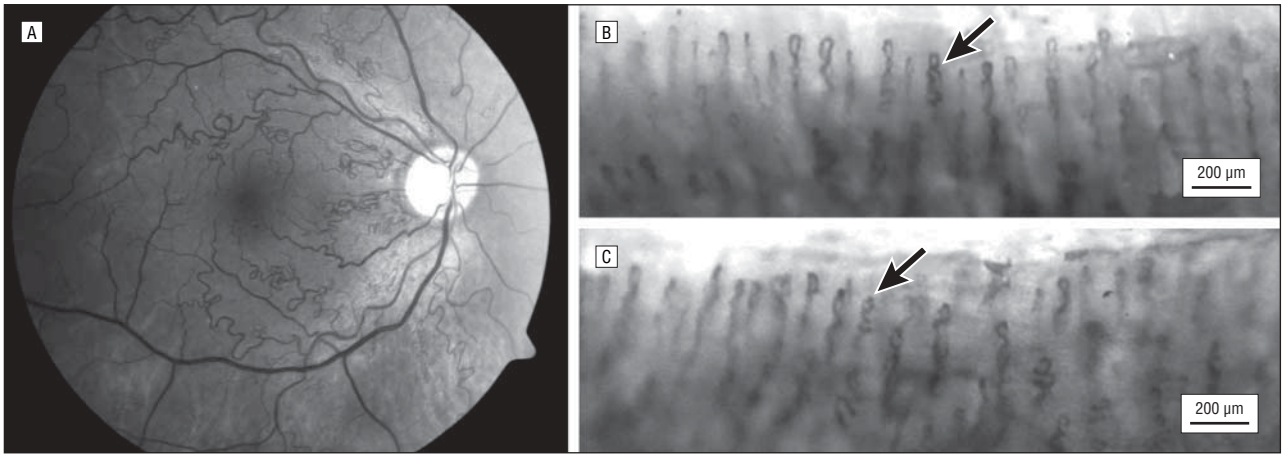

Figure 3. Patient 3. Views of the fundus and findings at nailfold capillaroscopy. A, When the patient was last seen at age 62 years, he demonstrated all of the typical findings of familial retinal arterial tortuosity. The patient had never experienced visual disturbances, although the degree of tortuosity was greater than in patients 1 and 2. B and C, Nailfold capillaroscopic findings in the patient's right second and fourth fingers. Approximately 30% of capillary loops showed a high degree of tortuosity (arrows depict typical examples), while all other findings were normal, analogous to those in patients 1 and 2.

warfarin sodium therapy was prescribed. As in patients 1 and 2, all other systemic findings were normal. Findngs at dermatologic examination and nailfold capillaroscopy were identical to those in patient 1 (Figure 2B and C).

Comment. All 3 patients had typical features of fRAT: only second- and third-order arteries were affected, while first-order arteries and the venous system were normal. The caliber, shape, and branchings of affected arteries were normal; no leakage or staining was observed at fluorescein angiography; symptomatic hemorrhages followed minor stress or trauma; visual prognosis was excellent; and no associated systemic disease was found in any of our 3 patients. These findings correspond well with the previously reported approximately 100 cases.[1,2] While in isolated cases systemic disease was found in patients with fRAT (malformation in the Kieselbach nasal septum, vascular mass in the spinal cord, sixth nerve palsy, simultaneous conjunctival hemorrhage, teleangiectasis of the bulbar conjunctiva), no consistent associated systemic disease has been reported and, thus, fRAT was generally believed to be an isolated retinal finding.[2,3] Our finding of marked capillary tortuosity at nailfold capillaroscopy favors systemic vascular disease in fRAT.

Recently, a syndrome has been reported consisting of features of fRAT with hematuria, muscular contractures, and sporadic other disorders such as cardiac arrhythmia.[4] This syndrome is distinct from the finding in our patients; only patient 2 had transient microhematuria and pronounced tortuosity in nail bed capillaries, in contrast to the unspecific findings at nailfold capillaroscopy found in patients with the newly reported syndrome, which is dominated by renal disease.

Nailfold capillaroscopy, as it was performed in our patients, is considered a mirror of systemic vascular processes, and a high degree of validity of correspondence and prognostic value is found, for example, in diabetes mellitus, systemic scleroderma, primary chronic polyarthritis, and systemic lupus erythematosus, and especially with ocular capillaries and in glaucoma.[5] Nailfold capillaroscopy demonstrated the identical features of capillary loops as retinal vessels in showing a high degree of tortuosity without any other pathologic findings such as leakage of dye, occlusion, or caliber abnormalities. A milder form of tortuosity at nailfold capillaroscopy has been described in patients with psoriatic arthritis,[6] but, to our knowledge, tortuosity of this magnitude has not been reported before. Considering that hemorrhages from retinal vessels are a hallmark of fRAT, manifestation in other tissues could be expected, although evidence for consistent systemic disease is thus far lacking in fRAT.

By demonstrating that capillary abnormalities are also found in nailfold capillaries of patients with fRAT, retinal vascular abnormalities can no longer be accepted as an isolated finding. We believe that, because of an increasing number of reports of this disease,[2] further investigation as to systemic involvement in patients with fRAT is warranted.

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