Inherited Retinal Arteriolar Tortuosity With Retinal Hemorrhages

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Background: Familial arteriolar tortuosity is an autosomal dominant disorder affecting the retinal arterioles. 

Objectives: To report a pedigree with this disorder and describe a systemic workup to determine whether this vascular abnormality is limited to the eye.

Results: A 58-year-old woman referred for retinal hemorrhages was found to have retinal arteriolar tortuosity of both eyes, especially in the macular area. Her 63-year-old brother had a history of retinal hemorrhages beginning at age 18 years and had similar fundoscopic examination findings. The proband had an extensive systemic workup, including magnetic resonance imaging, and cardiac and renal angiography, that failed to demonstrate any other sequelae of this inherited ocular syndrome. However, each member of the family expressing this phenotype did have hypertension.

Conclusion: Inherited retinal arteriolar tortuosity is an autosomal dominant disorder limited to the eye, at least in this pedigree, within the sensitivity of the systemic workup we used.


A 58-YEAR-OLD woman referred for retinal hemorrhages was found to have retinal arteriolar tortuosity of both eyes, especially in the macular area. Her 63-year-old brother had a history of retinal hemorrhages beginning at age 18 and similar findings on fundoscopic examination. The proband had an extensive systemic workup, which included magnetic resonance imaging (MRI) and cardiac and renal angiography, that failed to demonstrate any other sequelae of this inherited ocular syndrome. However, each member of this family expressing the abnormal phenotype did have hypertension (Figure 1).

Retinal arteriolar tortuosity is reported to be an autosomal dominant disorder characterized by tortuous small retinal arterioles, frequent occurrence of superficial intraretinal hemorrhages, and the progressive expression of this abnormal vascular phenotype beginning in adolescence. This report describes an additional pedigree and details an extensive systemic workup that the proband underwent because of complaints of headache and fatigue.

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PATIENTS AND METHODS

The proband complained of intermittent blurred vision and dark spots in both eyes. She noted that her brother had had 2 similar episodes. Informed consent was obtained from all family members after which complete ophthalmic examinations of family members were performed and findings from systemic examinations reviewed. Fluorescein fundus photographs were taken with a Zeiss fundus camera (Carl Zeiss, Oberkochen, Germany) of the proband. Fundus photographs were obtained on all of the family members.

diac catheterization and ultrasonography to investigate complaints of weakness and vertigo. Blood pressure at the time of catheterization was 175/78 mm Hg with a mean of 110 mm Hg. Catheterization demonstrated elevated diastolic dysfunction with mild left ventricular hypertrophy, aortic regurgitation (1+), mitral valve regurgitation (1+), and an ejection fraction of 55%. The coronary arteries were normal as were the results of a pharmaco-logically induced coronary artery spasm test. The study also revealed normal renal arteries. Ultrasound confirmed the angiographic findings and did not demonstrate a source of emboli from valve leaflet calcification to explain the prior MRI and CT scan findings. Findings from Ml laboratory studies, which included antiphospholipid antibody, lupus anticoagulant, clotting parameters, and complete blood cell count were normal in the past. Medications currently being taken include naldolol, and clonazepam, and use of a beclomethasone dipropionate (Beconase) inhaler. Family history is noteworthy for a mother who died of hypertension and “vascular problems,” a brother with a history of retinal hemorrhages, and 2 daughters in good health. Review of systems did reveal that the patient had multiple areas of cutaneous nevi that were larger than 5 cm in diameter. Visual acuity was 20/30 OD and 20/30 OS. The entire arteriolar tree of both eyes was tortuous, especially in the macular area (Figure 2). There was no venous tortuosity, arteriovenous communications, or angiomas. There was no hemorrhage or exudate. Findings from fluorescein angiography showed no other abnormality (Figure 3). The patient returned 1 month later with a complaint of paracentral scotomas in both eyes. Results from retinal examination at that time demonstrated superficial ovoid macular hemorrhages in both eyes (Figure 4).

PATIENT II-c

A 63- year-old man had a history of retinal hemorrhages at ages 18 and 56 years. His medical history is noteworthy for hypertension and arthritis. His ocular history is notable for bilateral pseudophakia. His hypertension was controlled with verapamil. Visual acuity was 20/20 OD and 20/20 OS. Findings from slitlamp examination revealed centered pos-
terior chamber lens implants within an intact capsular bag in both eyes. Dilated funduscopic examination findings demonstrated tortuous retinal arteriolar vessels, especially in the macular area (Figure 5). The left optic disc was surrounded by a myelinated nerve fiber layer that extended for 1 disc diameter nearly 360° around the disc. There were no retinal hemorrhages or exudate.

PATIENTS III-a AND III-b
Two women aged 29 and 26 years have no history of retinal hemorrhages. Both patients have a medical history noteworthy for Marfan syndrome. Visual acuity and ocular findings were normal in each, including the absence of ectopia lentis.

PATIENT I-a
A 90-year-old man has had no history of retinal hemorrhages. His medical history is notable for rheumatoid arthritis. His visual acuity was 20/40 OD and 20/60 OS. He is bilaterally pseudophakic. The retinal vessels were attenuated but not tortuous and exhibited mild atherosclerotic changes. The macula had areas of retinal pigment epithelial rarefaction.

COMMENT
Familial retinal arteriolar tortuosity with superficial macular hemorrhages was first reported by Beyer in 1958.1 Since that original report, other families have been identified in Europe, North America, and Japan.2-11 These cases, like ours, are characterized by arteriolar tortuosity, competency of the retinal vessels on fluorescein angiography, intermittent superficial retinal hemorrhages, and autosomal dominant transmission. Venules are normal. The
single other syndrome that produces arteriolar tortuosity alone without venous involvement is coarctation of the aorta. Other congenital diseases, such as familial dysautonomia, or congenital storage diseases, such as Fabry or Marteaux-Lamy syndrome, can cause combined venular and arteriolar tortuosity. Congenital syndromes associated with classic phacomatosis are associated with vascular tortuosity secondary to arteriovenous shunts, as in Wyburn-Mason syndrome, or hemagiomas, as in von Hippel-Lindau syndrome. Although we were curious as to whether our patient’s nevi and history of MRI documented central nervous system vascular abnormalities might demonstrate that this autosomal dominant defect was a forme fruste of a phacomatosis, her affected brother had no similar skin pigmentation and the findings from his MRI did not demonstrate intracranial arteriolar tortuosity. Other syndromes that are associated with venous and arterial tortuosity include macroglobulinemia, cryoglobulinemia, leukemia, and polycythemia vera. The natural history of patients with familial retinal arteriolar tortuosity is favorable, demonstrating that once the diagnosis is established by physical examination findings of the propositus’ relatives, a benign prognosis can be offered to the patient. We cannot demonstrate that the intracranial lesions found by MRI were caused by abnormal vessels and therefore associated with retinal arteriolar tortuosity. It may prove worthwhile to determine whether there is a history of migraine or central nervous system abnormalities in existing pedigrees.

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REFERENCES


ARCHIVES OF NEUROLOGY

Paraneoplastic Cerebellar Syndrome and Optic Neuritis With Anti-CV2 Antibodies:
Clinical Response to Excision of the Primary Tumor

Vincent de la Sayette, MD; Françoise Bertran, MD; Jérôme Honorrat, MD; Stéphane Schaeffer, MD; Serge Iglesias, MD; Gilles Dejer, MD

Objective: To describe a patient with a paraneoplastic cerebellar syndrome and optic neuritis with circulating anti-CV2 antibodies and clinical improvement after excision of a small cell lung carcinoma.


Setting: A 62-year-old man simultaneously developed a severe cerebellar syndrome and a bilateral optic neuritis predominantly in the left eye (visual acuity, 20/23 in the right eye; <20/400 in the left eye; and bilateral swelling of the optic discs).

Main Outcome and Results: Anti-CV2 antibodies, recently described as associated with paraneoplastic neurological syndromes, were detected in the patient’s serum sample. These antibodies were demonstrated to react with the cytoplasm of a subpopulation of oligodendrocytes in the white matter of rat brain in the cerebellum, brainstem, spinal cord, and optic chiasm. The patient was found to have a small cell lung carcinoma, which was removed. After excision of the tumor, the cerebellar syndrome improved dramatically and the papilledema disappeared despite aftereffects of the optic neuritis.

Conclusions: These findings were consistent with the diagnosis of a paraneoplastic neurological syndrome, although both optic neuritis and remission of the cerebellar syndrome are uncommon patterns of paraneoplastic syndromes. CV2 antigen expression by the oligodendrocytes of the cerebellum, brainstem, spinal cord, and optic chiasm correlated with the clinical syndrome observed in our patient. However, the precise pathophysiological role of anti-CV2 antibodies is still unknown.

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