Chorioretinal Vascular Abnormalities Associated With Angioid Streaks and Pseudoxanthoma Elasticum

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Objective: To analyze the retinal and choroidal vascular abnormalities in eyes with angioid streaks (AS) associated with pseudoxanthoma elasticum (PXE).

Methods: Color photographs and fluorescein angiograms of 54 eyes of 27 consecutive patients with AS and PXE were examined retrospectively.

Results: Four (7%) of the 54 eyes had a major vascular abnormality at the level of the disc; this took the form of a large vascular loop corresponding to an arteriovenous communication between retina and choroid in 3 eyes (6%) and an anastomosis between 2 retinal arteries in 1 eye (2%).

Conclusion: Analysis of the vascular network in these eyes showed several vascular abnormalities, among which chorioretinal arteriovenous communications appear to be the most dramatic.


WHAT CAME to be known as angioid streaks (AS) were first described by Doyne1 in 1889, but this designation was not used until 1892, when Knapp2 applied the term to reflect the supposed vascular nature of these streaks. Angioid streaks are broad, irregular, reddish-brown or gray lines that radiate from the area around the optic nerve head and whose number, extent, and age at onset are variable. Their clinical significance lies in that they are related to breaks in the elastic layer of Bruch membrane,3 due to an abnormal fragility of the lamina basalis4 caused by a degenerative process combined with calcium deposits.5

Angioid streaks have been described in association with numerous systemic disorders involving elastic tissue, including pseudoxanthoma elasticum (PXE). The association of AS with PXE was first reported by Groenblad6 and Strandberg7 in 1929. The reported incidences of PXE-associated AS vary tremendously, depending on the diligence with which patients are scrutinized. Therefore, an incidence based on the observation of patients with PXE who have been followed up for less than several decades cannot be considered valid, as it appears that AS will eventually develop in virtually all patients with long-standing PXE.8

Pseudoxanthoma elasticum is a rare disease of the connective tissue with a prevalence of 1:160 000 and autosomal recessive and dominant inheritance patterns. Both forms of PXE were recently mapped to chromosome 16p13.1.9 It is a multisystem disorder that can involve arterial walls, cardiac valves, skin, gastrointestinal tract, and eyes (Bruch membrane, lamina cribrosa).10 In time, all patients tend to manifest a classic phenotype that involves all of these systems, with considerable variation in extent of involvement.

Due to calcification of the internal elastic lamina, which results in secondary narrowing of vessel lumina, coronary11 and peripheral vascular diseases12,13 are the most common and severe complications. Other as yet unexplained vascular manifestations have been reported to be associated with PXE; these include intracranial arteriovenous malformations14 and orbital varices.15

Based on the known systemic vascular changes associated with PXE, we wished to define the incidence of retinal or chorioretinal vascular abnormalities in patients with PXE.
**RESULTS**

A total of 54 eyes of 27 patients were examined. Patients ranged in age from 24 to 68 years (median, 46 years); there were 11 men and 16 women, which is in accordance with the higher incidence of PXE in women.

Optic nerve head drusen were clinically apparent in 20 eyes (37%), but disc excavation was consistently absent. Mottling of peripheral retinal pigment epithelium was present in all eyes. Neovascularization was noted in 35 eyes (65%). Obstruction of the central retinal artery was seen in 1 eye (2%).

The most obvious vascular abnormality was a large vascular loop at the level of the optic disc, observed in 3 (6%) of the 54 patient eyes (Figure 1), but in none of the control group. Using ICG in 2 of these 3 eyes, this loop was shown to be an arteriovenous communication between the central retinal artery and a large choriocapillary vein. Both of these eyes had dilated and beaded choriocapillary vessels. In 1 eye (Figure 2, A), the drainage vein appeared to divide, with 1 branch coursing toward the temporal inferior vortex vein and other toward the nasal inferior vortex vein. In the second eye (Figure 2, B), the vein seemed to course around the optic nerve head. The diagnosis of PXE had been confirmed by results of skin biopsy.

**SUBJECTS AND METHODS**

Among all eyes with AS that were examined from July 30, 1980, to February 2, 1997, at the Hôpital Jules Gonin, Lausanne, Switzerland, only those that met the following criteria were included in this study: (1) AS documented with color photographs and fluorescein angiography; (2) diagnosis of PXE based on results of clinical examination (yellow macules, papules, or plaques in commonly affected sites such as the neck, axillae, popliteal fossae, and antecubital areas) and/or skin biopsy (fragmentation and calcification of elastic fibers in the middle and lower third of the dermis); and (3) no concomitant intraocular or intraorbital disease except choroidal neovascularization.

We analyzed characteristics of the vessels and their embranchments. The level (prelaminar or post-laminar) of the first division of the central retinal artery was noted, as were the numbers of multiple branchings of the central retinal artery and abnormal arteriovenous communications. We recorded the numbers of additional arteries and abnormally coursing arteries (crossing over the raphe). Using the Fisher exact test, we performed a statistical comparison of the incidence of these vascular abnormalities with a control group. The control group consisted of 50 consecutive eyes that sustained indirect traumatic choroidal rupture and in which fluorescein angiography was performed in our retina department; $P < .05$ was considered statistically significant.

We also recorded other clinical findings, such as cup-disc ratio, peau d’orange, and choroidal new vessels.

To differentiate arteries from veins, and to determine the direction of blood flow in the case of ill-defined vascular abnormalities, indocyanine-green angiography (ICG) was performed whenever possible. Patients were contacted and asked to return specifically for this examination. All patients for whom informed consent was obtained underwent rapid-sequence ICG with emphasis on the choroidal and early arterial filling. To determine the presence or absence of optic nerve head drusen, B-scan echography was also performed on all of these eyes.
biopsy in both patients. No evidence of drusen was seen on results of B-scan echography in these eyes. In the third eye (patient unavailable for follow-up), ICG was not performed, but a similar-appearing retinochoroidal anastomosis was partially visible on the color photographs (Figure 1, C).

A retinoretinal arterial anastomosis (anastomosis between 2 retinal arteries) was present in 1 eye (2%) (Figure 3). In this case, the direction of the blood flow was not clear on results of ICG. Some irregularity of diameter was present in the anastomotic segment of the artery. As in the other cases, B-scan echography failed to show any drusen of the optic nerve head.

Minor vascular abnormalities were also recorded. Forty-four eyes (81%) of patients with PXE and AS had a postlaminar division of the central retinal artery, compared with only 12 eyes (24%) in the control group (P < .005) (Figure 3). The presence of arteries crossing over the raphe in 5 patient eyes (9%) vs none in the control group was also significant (Figure 3 and Figure 4).

The other vascular features recorded were not significantly associated with AS and PXE, although they were more common in patients than in controls. Additional arteries were noted in 21 patient eyes (39%) vs 13 control eyes (26%), and multiple branchings were noted in 9 patient eyes (17%) vs 5 control eyes (10%).

Various types of congenital and acquired vascular anastomoses involving the retina, the choroid, or both have been described previously.  Acquired retinoretinal arteriovenous communications are recognized manifestations of ischemic diseases such as diabetes, proliferative sickle cell retinopathy, and occlusive disease of the carotid artery. Following ischemic obstruction or destruction of physiologic vessels, these communications develop to allow blood to flow from obstructed arteries to patent veins.  Acquired retinochoroidal arteriovenous communications have been described also in the late stages of age-related macular degeneration, 26 in vascularized retinal epithelial detachments in age-related macular degeneration, 27 in recurrent toxoplasmosis, 28 and subsequent to the development of disciform lesions secondary to traumatic choroidal ruptures. 29 These arteriovenous communications need to be differentiated from the opticociliary shunts that represent dilated venous collateral channels in cases of primary or secondary retinal venous obstruction.
The vascular loops described herein may be congenital, as are cirrroid aneurysms and preapillary vascular loops. Furthermore, although extremely unlikely, the association of these preapillary vascular loops with AS and PXE could be coincidental. However, since elastic fibers are constituents of Bruch membrane and the walls of retinal arteries, the presence of such abnormalities in these eyes should not be surprising. Their more marked presence at the level of the optic disc and in the peripapillary area could be explained by the much greater amount of elastic tissue in the central retinal artery compared with that in the smaller and more peripheral retinal arteries. Although our findings suggest that these vascular abnormalities are associated with PXE, their congenital or acquired origin has not been determined. We suggest that these abnormalities, possibly related to secondary hemodynamic changes, could be a manifestation of progression of this disorder.

Unusual branching of vessels on the optic disc and the adjacent retina have been described in association with optic disc drusen. This phenomenon has been interpreted to be a response to complete interruption of blood flow at the level of the lamina cribrosa. The association of optic nerve head drusen and AS is not new, and mechanical compression by the drusens of vessels located in front of the lamina cribrosa could explain, at least in part, the vascular abnormalities seen in such cases.

In our cases, however, results of B-scan echography did not demonstrate any optic nerve head drusen. Nevertheless, the absence of physiologic excavation observed in all cases might suggest the presence of some noncalcified material at this level; therefore, mechanical compression of the vascular tree at the level of the optic disc could play a role in the formation of these vascular loops, possibly through a decrease in central venous blood flow.

In regard to the other vascular abnormalities that we noted, the postlamellar division of the central retinal artery was significantly associated with AS and PXE, as was the presence of arteries crossing the raphe. Although the other vascular abnormalities seen were not significantly associated with this disorder, it is interesting that they were seen more commonly in patients than in the control group, suggesting that some calcification of the elastic tissue of the media of the medium and small arteries might be associated with their pathogenesis. Additional follow-up of these eyes may well provide more information on the evolution of this process.

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REFERENCES


A look at the past...

In 1889, CLABORNE made experiments with sponge and cotton as a filling for the cavity of the eye after evisceration, but they were not satisfactory. Later he experimented with glass, wool, and asbestos as a filling, but found that they were not tolerated by rabbits any better than the sponge or cotton. On the whole he deems the ordinary enucleation the safest and best method yet devised of dealing with eyes that require removal.