Angioid Streaks and PXE

Factsheet

Angioid streaks are broad, irregular, red to brown to grey lines which radiate from the area around the optic nerve head under the retinas of individuals with pseudoxanthoma elasticum (PXE). These streaks or striations are typically bilateral and vary in width from 50 to 100 microns, barely detectable by ophthalmoscopy, to 3-4 times the average retinal vascular width, dramatically visible to the casual ophthalmic observer. Their borders are irregular, serrated, and occasionally ill-defined, particularly when they are smaller than the blood vessels in that region. Their number and extent are variable, as are their age of onset. Their course tends to be more sinuous and angular than normal retinal blood vessels.

The first description of angioid streaks was provided in 1889 by Dr. Robert W. Doyne, an English ophthalmologist. He reported a male who had received injuries to both eyes: "In all directions throughout the choroid of both eyes, especially around the discs, are irregular, jagged lines, nearly all deeply pigmented . . .". "The irregularities and jags in their outline exactly correspond in most places and are probably due to rupture of the pigment layer of the retina . . .".

Dr. Herman J. Knapp, a German-born American ophthalmologist, who coined and introduced the term "angioid streaks" in 1892, felt that they represented "the conversion of extravasated blood into streaks of dark brown or black pigment in the retina . . ." .

Subsequently, in 1929, Groenblad, also an ophthalmologist, related the occurrence of angioid streaks with Pseudoxanthoma Elasticum, in the same year as Strandberg described them independently.

The reported frequencies of angioid streaks in pseudoxanthoma elasticum vary tremendously with the era of the observer, the specialty (dermatology, genetics, ophthalmology, etc.), and the diligence with which individuals and all family members are scrutinized. At least 50% of all individuals with PXE demonstrate angioid streaks. However, that "prevalence rate" typically reflects a "single encounter" and does not reflect the analysis of diligent observations of individuals with PXE followed sequentially over years and decades.

Angioid streaks are not present in newborns or infants but, in some individuals and families can, be identified before the age of 10 years. Retinal fundus photography documents their appearance and serves as baseline for future observations. Retinal fluorescein angiography will enhance recognition

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of the angioid streaks, because they are typically hyperfluorescent wherever the retinal epithelium is thinned or atrophic, thereby permitting their ready recognition in the contrast-enhanced presentation of monochromatic photography.

Just as the pathogenesis of PXE in the skin, gastrointestinal system, and cardiovascular systems is unknown, so the pathogenesis of angioid streaks is similarly in much debate. The best current information suggests a defect in elastic fibres, particularly in Bruch's membrane, the elastic layer between the retinal pigment epithelium and the choroid.

Histopathology shows premature basophilia and staining with increased amounts of calcium and iron, much as seen in older eyes in general. Both thinning and thickening of the basement membrane and Bruch's membrane are noted under the retinal pigment epithelium. The streaks present as ruptures in this elastic lamina of Bruch's membrane.

Angioid streaks are seen in a number of clinical disorders in addition to Pseudoxanthoma Elasticum: sickle cell anaemia, thalassemia, Paget's disease of bone, acromegaly and other pituitary disorders, and familial hyperphosphatemia. Occasionally, angioid streaks are noted with "no other disease", but they have also been seen in younger individuals with PXE who have no (current) cutaneous manifestations of the disease but develop them later. Therefore, the presence of angioid streaks should be considered indicative of an underlying systemic illness, even if the specific disorder cannot be identified or defined accurately at the time that the angioid changes are first noted. The patient must remain under continuing surveillance.

The most common retinal feature associated with angioid streaks is the presence of "peau d'orange", a mottled fundus appearance which classically precedes the appearance of the streaks. The French term persists as a description of the fine, relatively symmetrical, drusen-like, flat, yellow, and occasionally confluent lesions in the retinal pigment epithelium, extending throughout the posterior pole and out to the equator. Peau d'orange does not affect visual acuity, even when the fovea is involved. However, when readily identifiable in one individual, siblings and parents should be investigated for the presence of peau d'orange even in the absence of angioid streaks.

Other retinal changes in association with peau d'orange and angioid streaks include focal hemorrhages with or without scarring, salmon patches (which

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typically represent a healing subretinal hemorrhage), black dots, (the result of metaplasia of the pigment epithelium following focal or blot hemorrhages), and "pearls" (dead white or yellow-white foci typically 150-300 microns in size, again representing either the result of subretinal hemorrhage, subpigment epithelial hemorrhage, or a focal disciform scar with spontaneous resolution). Occasionally, peripheral hemorrhages under the retina, near the ora serrata, may evolve to discoid metaplasia of the retinal pigment epithelium simulating disciform degeneration.

Intrapapillary drusen, or drusen of the optic nerve head, have been seen in some individuals and in some families, typically but not universally with dominantly inherited PXE. The usual complications of intrapapillary drusen including juxtapapillary bleeding, juxtapapillary disciform disease, visual field deficits, and even advanced visual impairment, can occur in this association.

The most visually devastating complication of angioid streaks and peau d'orange is disciform degeneration of the central visual area. The mechanism of disruption of the pigment epithelium-Bruch's membrane barrier and the invasion of new blood vessel under the retina is not different from other causes of disciform disease. Historical initial attempts to apply laser photocoagulation with either green or red wavelengths met with limited success, giving laser treatment for this complication a variable and poor outlook. More recent technologies, to identify fully the extent of neovascular membranes with sequential fluorescein angiography and rapid retreatment of recurrences, have yielded a better outcome in many individuals. However, the risk of recurrence is real, presumably because of the widespread defects in the pigment epithelium Bruch's membrane interface.

Other historical references to visual impairment in PXE from "choroiditis" or "chorioretinitis" are probably misinterpretations of the disciform process. Occasional older individuals with peau d'orange and angioid streaks will develop geographic atrophy of the retinal pigment epithelium, simulating "central areolar choroidal sclerosis" and sometimes (incorrectly) called "age-related macular degeneration".

Individuals with PXE also have systemic vascular disease involving large arteries, such as the carotid artery in the neck. For this reason, they may have a slightly higher risk than the general population for retinal vascular occlusive disease and non-arteritic ischemic optic neuropathy.

Other historical ocular complications of PXE include "blue sclerae" and

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vulnerability to global rupture. These case reports are probably misinterpretations and misdiagnoses of osteogenesis imperfecta, a different connective tissue disorder, since no valid description of these associations has appeared in the last 15 years of ophthalmic and genetic literature. Although angioid streaks are listed historically as complications of the Ehlers-Danlos syndrome, those reports are also probably due to a misdiagnosis of PXE by a different eponym.

All individuals with angioid streaks, and especially all individuals with PXE, should undergo a diligent, complete ophthalmologic examination and annual surveillance for ocular complications of this disorder. by Richard Alan Lewis, MD, Baylor College of Medicine

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