ANGIOID STREAKS AND ELASTORRHEXIS*†

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ANGIOID streaks are thought to be due to breaks in the elastic lamina of Bruch's membrane. Ophthalmoscopically they present a jagged peripapillary ring which may be incomplete and from which radiate irregular spokes of width similar to retinal vessels. With time, they may progress, or become less distinct. Their colour varies from reddish-brown to dark brown according to the density of the overlying retinal pigment. But they may be pale grey or even in parts white, owing to proliferation of scar tissue.

Elastorrhexis is a systemic disease which commonly presents with a skin disorder known as pseudoxanthoma elasticum (PXE). The sites of predilection for PXE lesions are the neck, axillae, perineum, antecubital and popliteal fossae, abdomen, and oral mucosa. The skin is easily stretched and may hang in folds. Yellowish waxy papules varying in size from a pinpoint to a pea may give rise to a "plucked chicken" appearance.

PXE and angioid streaks have been reported in all races and in all decades of life although the peak age lies between 25 and 50. They are frequently associated as the Grönblad-Strandberg syndrome. This is often complicated by systemic vascular disease and as a systemic condition it is termed elastorrhexis. Other ocular manifestations include a mottled or *peau d'orange* appearance at the posterior pole of the fundus, drusen, and a disciform maculopathy. Choroidal and retinal haemorrhages often precede the maculopathy, and together with it are the most important cause of ocular symptoms.

Solar (or actinic) elastosis (SE) is an elastic disorder of skin not unlike PXE, but as it may occur only in areas of skin exposed to the sun any relationship with other diseases has generally been regarded as purely incidental. However, it is stated that senile elastosis (a synonym of solar elastosis) may be associated with angioid streaks (Duke-Elder, 1966).

It is the object of this paper to provide a short review of elastorrhexis, to present several cases of both SE and elastorrhexis manifesting in the same family, to assess the relevance of SE, and to attempt a classification of angioid streaks.

History

The skin lesions of elastorrhexis were first described by Balzer (1884) and again by Chauffard (1889). Darier (1896) redescribed Chauffard's patient and called the disorder PXE, giving elastorrhexis as an alternative name because of its histological nature. But in the early years only the former name was used as this gave a better clinical description of the skin.

Doyne (1889) presented to the Ophthalmological Society of the United Kingdom the first case of angioid streaks. In each fundus he described irregular jagged lines, nearly all deeply pigmented,

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whose jagged borders appeared exactly complementary. They were also associated with choroidal haemorrhages, and in each eye had followed ocular trauma. Plange (1891) reported a second case, and Knapp (1892) named the condition. It is interesting that Plange described a shallow radial pulse in his patient, a finding which he explained as being due to reduced elasticity of the arterial wall.

Grönblad (1929) described two cases with angioid streaks in which Strandberg had demonstrated lesions of PXE. Since then the association has been confirmed in 85 per cent. of all cases of PXE (Sandbacka-Holmström, 1939; Connor, Juergens, Perry, Hollenhorst, and Edwards, 1961) and in about 62 per cent. of all cases with angioid streaks (Scholz, 1941; Connor and others, 1961). The true figure for the latter may in fact be much higher, for in several reports of angioid streaks of unknown aetiology no biopsy of skin was undertaken, and in the occasional report there may be some doubt as to the true nature of the streaks.

Holloway (1927) collected 59 cases of angioid streaks and reported the striking incidence of systemic vascular disease in 23.3 per cent. Böck (1938) noted at *post mortem* the systemic nature of the Grönblad-Strandberg syndrome and so named the condition elastosis dystrophica. The term elastorrhexis was revived by Touraine and James (1940) and by Témime (1940). This implies a systemic disorder whereby elastic tissue becomes fragmented, but clinically there is particular involvement of the skin, the walls of blood vessels, and of Bruch's membrane. This name is a considerable improvement on the purely dermatological name PXE which is still used to describe internal disorders. The most important systemic complications include gastric haemorrhage, intermittent claudication, angina of effort, absent peripheral pulses, calcification of vessels, and hypertension (Wolff, Stokes, and Schlesinger, 1952; Eddy and Farber, 1962; Goodman, Smith, Paton, Bergman, Siegel, Ottesen, Shelley, Pusch, and McKusick, 1963; Foucault, 1963), any of which may occasionally lead to a presenting symptom or sign. A particular feature of the gastric haemorrhage is that several authors have remarked on its occurrence during pregnancy. Cerebral ischaemia has been well documented, and intracranial aneurysms have been described by Dixon (1951), McKusick (1956), and Scheie and Hogan (1957). Epistaxis and haematuria may be prominent (McKusick, 1956), and Foucault (1963) listed the importance of menorrhagia and Raynaud's phenomenon in women. There is a significant incidence of psychiatric disturbance, which may be attributed to cerebral vascular disease (Revell and Carey, 1948; McKusick, 1956; Gibbs, 1964). Rare systemic associations are epilepsy, thyrotoxicosis, and diabetes mellitus (Revell and Carey, 1948; Eddy and Farber, 1962), but their occurrence is most probably coincidental.

Histology

Kofler (1917) first suggested that angioid streaks might be due to fissures in Bruch's membrane. This is now the accepted view, and has been confirmed histologically by Böck (1938), Hagedoorn (1939), Klien (1947), Verhoeff (1948), and others. All their histological studies were made on patients with elastorrhexis; the common ocular findings were:

- (1) A heavy basophilic staining of Bruch's membrane with in several cases positive differential staining for calcium;
- (2) Numerous ruptures of the membrane in positions corresponding to *ante mortem* streaks, the choriocapillaris and pigment epithelium being intact at the site of each gap;
- (3) Hyaline excrescences at the disc margins.

Verhoeff (1948) also concluded that, although the choroidal vessels appeared normal, the disciform maculopathy when present was produced by choroidal submacular haemorrhages which later became organized and replaced by glial tissue. Angioid streaks are considered to be a direct result of lines of force within the eye (Terry, 1934; Hagedoorn, 1939; Goodman and others, 1963). This is in keeping with the associated incidence of ocular trauma (Doyne, 1889; Scholz, 1941; Bedell, 1961; Gills and Paton, 1965).

Histological examination of PXE lesions reveals in the middle and lower thirds of the dermis an accumulation of fragmented and irregularly-clumped fibres with the staining properties of elastic tissue. Giant cells and macrophages have been noted in the involved areas, and may give the appearance of a foreign-body reaction (Berlyne, 1960; Smith, Malak, Goodman, and McKusick, 1962); telangiectasis may be present towards the edge of the lesions (Hannay, 1951; Loria, Kennedy, Freeman, and Henington, 1957). There is no evidence of lipid infiltration. The usual sites of PXE involvement are areas of flexural stress. However, the skin may look entirely normal and yet show histologically conclusive evidence of the disease (Loria and others, 1957; Paton, 1959; Connell, 1962; Goodman and others, 1963). Therefore a biopsy should be taken before elastorrhexis can be excluded as a cause of appropriate ocular or systemic lesions.

Although the vascular manifestations of elastorrhexis appear clinically to present a juvenile form of arteriosclerosis, microscopically the two are readily differentiated: arteriosclerosis originates in the intima with a deposition of fat, whereas elastorrhexis is located in the media with secondary deposition of calcium and no fat (Szymanski and Caro, 1955). Calcification and reduced pulsation have been noted in the aorta and peripheral vessels of children only 9 years old (Wolff and others, 1952). Fragmentation of the internal lamina elastica, and elastic degeneration of the media with thinning and microaneurysmal formation have been demonstrated in the arterioles of the gastric wall in patients who had undergone subtotal gastrectomy for recurrent haemorrhage (Woo and Chandler, 1958; Connell, 1962). Sometimes the vascular disease appears obliterative, but this has been shown to be due primarily to swelling of the media rather than intimal thickening (Scheie and Freeman, 1946; McKusick, 1964). However, Foucault (1963) demonstrated on biopsies of the superficial temporal arteries involvement also of the intimal and adventitial coats.

Pathogenesis

10 years ago it was generally considered that the abnormal material of PXE resulted from degeneration of collagen fibres (Hannay, 1951; McKusick, 1956). But the older view that the defect lies in the elastic tissue has now been reasserted (Goodman and others, 1963). However, the histogenesis of elastin itself is still obscure, and it is also possible that the material is the result of an abnormal generation of elastotic fibres *de novo* (Loria and others, 1957). The evidence supporting degeneration of elastic fibres is:

- (1) That electron microscopy shows selective alteration of elastic tissue (Loria and others, 1957; Fisher, Rodnan, and Lansing, 1958);
- (2) That the abnormal fibres are dissolved by elastase even though calcium deposition provides some protection and delay in action (Findlay, 1954; Fisher and others, 1958; Mehregan, 1965);
- (3) That in PXE skin the dry-weight elastin content is increased (Smith, Davidson, and Clark, 1962);
- (4) That *post mortem* examination of arterioles in systemic elastorrhexis shows ruptures in the internal lamina elastica (Kaplan and Hartman, 1954; and others).

Unfortunately, although many different staining reactions have been established for dermal connective tissue, the affinities in different conditions are notoriously variable (Hass, 1939; Fisher and others, 1958), so that no particular significance can be attributed to them.

The basophilia in elastorrhexis, whether of Bruch's membrane or of PXE material, is probably due to deposition of calcium salts (Finnerud and Nomland, 1937; Klien, 1947). As calcium metabolism is always normal, the calcium deposition is thought to be a secondary phenomenon occurring in already degenerated, and genetically abnormal, elastic tissue. Its forerunner is probably an acid mucopolysaccharide (Smith, Davidson, and Clark, 1962; Johnson, Graham, and Helwig, 1964), which has been demonstrated in increased quantities around degenerating elastic tissue. However, Goltz, Hult, Goldfarb, and Gorlin (1965), commenting on cutis laxa in which there is considerable excess of acid mucopolysaccharide in relation to elastolysis, encountered no calcification.

Goodman and others (1963) showed that in PXE minute foci of calcification occur along normal-looking elastic fibres, often adjacent to sweat glands; they therefore concluded that the calcification is the primary change.

Basophilia has been found at times not to take up stain for calcium even in well-established cases (Hannay, 1951), but this may be due to fixative acidity (Hagedoorn, 1939). It may also occur in other elastic disorders of skin where there is little or no calcification (Lansing, Cooper, and Rosenthal, 1953; Goltz and others, 1965). Verhoeff and Sisson (1926) and Scholz (1941) noted basophilia of Bruch's membrane in 10 per cent. of random autopsied eyes. This has been confirmed as an age change by Hogan (1967). The mere presence of basophilia is therefore not necessarily of pathological significance.

Associated Conditions and Possible Genetic Linkage

Elastorrhexis is expressed as an autosomal recessive trait, and therefore manifests itself only in the homozygous state. The evidence for this is the occurrence in multiple members of individual sibships, the rarity in successive generations, and the increased frequency of parental consanguinity (Scholz, 1941; Berlyne, Bulmer, and Platt, 1961). The rare involvement of a second generation suggests that, unless the uninvolved parent happens to be a heterozygote, the disorder may be expressed in the heterozygous state by a variant gene acting as a dominant (Berlyne and others, 1961). The sex ratio is approximately equal.

The occasional association of PXE with Marfan's syndrome or the Ehlers-Danlos syndrome suggests a possible genetic linkage with other inherited disorders of connective tissue (Eddy and Farber, 1962; Adriaenssens, 1963). PXE has several times been associated with elastosis perforans serpiginosa (Fountain, 1965; Schutt, 1965). In fact Smith and others (1962) produced excellent evidence that elastosis perforans serpiginosa represents an abnormal foreign-body reaction in the skin to PXE tissue. Further, it is significant that, in their review of elastosis perforans serpiginosa, they found that over a third of cases are associated with other inherited connective tissue disorders, such as osteogenesis imperfecta, Marfan's syndrome, Ehlers-Danlos syndrome, and Down's syndrome. The Ehlers-Danlos syndrome was also reported with angioid streaks but without macroscopic PXE lesions by Green, Friedman-Kien, and Banfield (1966).

Angioid streaks are sometimes seen in patients with Paget's disease of bone (Ormond, 1931; Terry, 1934; Lambert, 1939). Scholz (1941) considered that Paget's disease (osteitis deformans) occurred in 9 per cent. of cases with angioid streaks, and that typical streaks could be detected in 8 per cent. of cases with Paget's disease. Several authors, including Szymanski and Caro (1955) and Keith (1956), have argued that Paget's disease and PXE may be aspects of the same disorder. The evidence is that both are inherited disorders of connective tissue, that systemic vascular manifestations with a predisposition to calcification of the media of arteries occur in both, that the angioid streaks are indistinguishable, that in both there may be a disciform degeneration at the macula, and that the triad of PXE, angioid streaks, and Paget's disease has been well documented in at least three cases (Woodcock, 1952; Larmande and Margailan, 1957; Shaffer, Copelan, and Beerman, 1957).

Evidence against this theory (McKusick, 1956; Cawley and Weary, 1962) is:

- (1) That elastorrhexis with its vascular manifestations is obvious at a much younger age than Paget's disease;
- (2) That while PXE is recessive in nature, Paget's disease is dominant and more common in men;
- (3) That patients with gross elastorrhexis usually have normal bones;
- (4) That angioid streaks occur early in elastorrhexis and between normal choroid and pigment epithelium, but occur late in Paget's disease (Paton, 1959) and often in association with choroido-retinal degeneration;

(5) That angioid streaks occur in 85 per cent. of cases of elastorrhexis but in only 8 per cent. of cases of Paget's disease;

(6) That it is unusual for affected siblings of patients with Paget's disease to have angioid streaks though it is common in the case of elastorrhexis;

(7) That the development of choroidal sclerosis is associated with disappearance of the streaks in elastorrhexis (Pearce, 1965), but not in Paget's disease.

It is therefore better at present to regard the two conditions as being unrelated. It is unlikely that the streaks in Paget's disease are due to a primary degeneration of Bruch's membrane, and points 4, 5, and 6 (above) also indicate their secondary nature.

More recently the Grönblad-Strandberg syndrome has appeared in Negroes with sickle-cell anaemia. Angioid streaks alone have also been reported (Paton, 1959; Geeraets and Guerry, 1960), though Welch and Goldberg (1966) surveyed 105 cases of sickle-cell disease without finding any streaks.

There may be in Negroes a genetic link between elastorrhexis and sickle-cell disease. The association has been recognised only since 1960, and several reports have now appeared (Geeraets and Guerry, 1960; Goodman and others, 1963; Charache and Richardson, 1964; Suerig and Seifert, 1964). This is quite a different matter from the relationship with Paget's disease. Perhaps it was not described in the past because it was rare for any sickle-cell patient to live long, and because the gravity of a sickle-cell crisis could easily mask a minor skin complaint. However, in sickle-cell disease without PXE angioid streaks are probably of a secondary nature, as it is difficult to relate primary elastic degeneration of Bruch's membrane, and Geeraets and Guerry (1960) found no basophilia or calcification of Bruch's membrane in this disease.

Case Reports

Case 1, a 40-year-old man, presented in April, 1965, with defective vision of the left eye. The onset had been rapid and was not related to trauma. He also suffered from cramp in the calves after walking for more than $1\frac{1}{2}$ miles, complained of giddiness, and had once had a blackout whilst under a car.

Examination.—The corrected visual acuity was 6/4 in the right eye and counting fingers in the left. The left fundus showed a circinate maculopathy with a star figure and hard exudates. At that time no other abnormality was noted.

By May, 1965, the left maculopathy had increased in size; there was a raised disciform area centrally, with surrounding exudation involving the whole of the posterior pole (Fig. 1, overleaf). The right macular area appeared granular with a few colloid bodies. Reddish angioid streaks were also noticed around both discs, but they were only small and no PXE of the skin was evident. It was considered that the left macular lesion might be a *Toxocara* cyst.

A full blood count, erythrocyte sedimentation rate, plasma proteins, and chest and skull x rays were all normal. Electrophoresis showed raised α_2 and β globulins. The serum cholesterol was 390 mg. per cent. Serological tests for syphilis were negative. The toxoplasmosis dye test was positive at 1:64.

In September, 1965, he complained of further faintness on tilting his head backwards, of intermittent claudication on walking quickly for half a mile, and of occasional nausea and dyspepsia after meals. His pulse situation was found to be disastrous: both carotids and subclavians were feeble, the femorals and radials were palpable, but the popliteals and all foot pulses were absent. The upper arm blood pressure was 100/70 mm. Hg.

Histology of a skin biopsy from the postero-lateral part of the neck was reported by Dr. E. H. Hemsted to show marked thickening and fragmentation of elastic fibres in the middle and lower thirds of the dermis, in keeping with PXE (Fig. 2, overleaf).

Diagnosis.—Grönblad-Strandberg syndrome, with arteriosclerosis affecting in particular the lower limbs and vertebral arteries. Under the care of Dr. J. D. Kidd, whose opinion was sought concerning the systemic vascular disorder, further investigations revealed the following: serum cholesterol 400 mg. per cent., lipids, 1,000 mg. per cent., β -lipoproteins increased; liver function tests, urine analysis, blood urea and

FIG. 1.—Case 1, left eye, showing exudative maculopathy.

FIG. 2.—Case 1, skin section, showing elastorrhexis in the middle third of the dermis. Haematoxylin and eosin. $\times 85$.

electrolytes, and serum vitamin A all within normal limits. An x ray of thighs indicated that both superficial femoral arteries were extensively calcified. Axillary root vertebral and basilar angiography (carried out by Dr. P. W. E. Sheldon) showed no intrinsic vascular abnormality. An electro-encephalogram was non-specific, and the electrocardiogram was normal at rest and after exercise. A barium meal showed a small but constant filling defect on the lesser curve, suggesting gastric ulceration.

Treatment.—He was given a diet free from animal fat, and when seen in October, 1966, was subjectively much improved, having experienced no further gastric or cerebral symptoms, but still suffered from intermittent claudication.

Examination.—The corrected visual acuity was 6/5 in the right eye and counting fingers in the left. The discs were normal, and angioid streaks in each eye were more obvious than before. At the left macula there was an inactive white scar with a pigmented border (Fig. 3), with slight pigment mottling of the surrounding fundus and also at the right posterior pole. There were no haemorrhages.

Puckered areas of skin with reduced elasticity were seen just above the supraclavicular fossae. The peripheral pulses were unchanged except that the left femoral also was now almost absent. Serum cholesterol was 445 mg. per cent.; plasma amylase 300 units per cent.

The electro-oculogram showed a light rise of 200 per cent.

FIG. 3.—Case 1, left eye, showing macular scar one year later than Fig. 1.

Family History.—As this patient displayed so many features of elastorrhexis, his relatives were invited to attend for examination; 22 members of the family were investigated (Fig. 4), and one of his sisters is presented below as Case 2.

Nine of the children in the family and two cousins of the proband were examined, and none was found to have any ocular or cutaneous abnormality.

FIG. 4.—Pedigree of the family of Cases 1 and 2.

Of the five members of the first generation examined, the three males had hypertrophic SE of the skin confirmed histologically by Dr. E. H. Hemsted, but no evidence of the Grönblad-Strandberg syndrome; two of them had a raised serum cholesterol level. Neither the mother nor the paternal aunt of the proband had any evidence of SE, hypercholesterolaemia, or the Grönblad-Strandberg syndrome; the total serum lipids in the mother were raised (2,200 mg. per cent.).

Three unaffected siblings and the 19-year-old niece of the proband were examined, and in three of them cervical skin biopsies were performed. The histology in each case, reported by Dr. E. H. Hemsted, showed a relative excess of elastic staining tissue, lightly basophilic in haematoxylin and eosin sections in the upper dermis suggesting solar elastosis. Stains specific for calcium were all negative.

The SE changes were not related to more than average sun exposure in any of the six cases, and their various occupations were considered to be unconnected.

Case 2, a sister of Case 1 aged 23, was free from symptoms.

Examination.—In November, 1965, the visual acuity was 6/4 in the right eye and 6/5 in the left. Classical dark brown angioid streaks (Fig. 5) were seen radiating from peripapillary rings in each eye. The maculae had a slightly mottled appearance. The skin at the sides of the neck looked puckered, and when it was stretched minute yellowish papules became visible, producing a “plucked” chicken appearance. The axillae, antecubital fossae, and both groins were similarly affected. The oral mucosa was normal. The histology of a skin biopsy, reported on by Dr. E. H. Hemsted, showed areas of fragmented elastic tissue in the middle third of the dermis.

FIG. 5.—Case 2, left eye, showing angioid streaks.

Diagnosis.—Grönblad-Strandberg syndrome.

Though her peripheral pulses were weak, all were present save the posterior tibials. The haemoglobin was 83 per cent., serum calcium 5.1 mEq/l., serum cholesterol 390 mg. per cent.

Follow-up.—A year later her only troubles were a slight cosmetic problem about her neck, and the complaint that her hands went white and dead very easily. There was no evidence of cramp, intermittent claudication, or internal haemorrhagic phenomena. The eyes were unchanged and the central fields were full.

Binocular examination of the angioid streaks under high-power magnification with a slit lamp and contact lens revealed that they were of a deep purple-brown hue, that their jagged borders were complementary, that they were deep to the retinal pigment epithelium, and that they were not associated with retinal folds. Irregularities in the retinal pigment could be seen to cross in front of the streaks, and in some places there was a degree of pigment atrophy at the sides of the streaks.

As well as the posterior tibial pulses, the right dorsalis pedis and popliteal pulses were now also absent, and the right femoral was feeble. The blood pressure was 135/70. X rays of the chest, pelvis, and thighs showed no abnormal features. Plasma amylase 125 U., serum cholesterol 315 mg. per cent., total serum lipids 2,000 mg. per cent. The electro-oculogram showed a light rise of 268 per cent.

Case 3, a woman aged 76, represented the only possible case out of 2,000 random patients personally examined for the presence of angioid streaks.

Examination.—The corrected visual acuity was reduced to 6/36 in the right eye and 6/60 in the left by large areas of chorio-retinal degeneration adjacent to the discs and extending over both posterior poles. Choroidal sclerosis was present in each eye. Brown streaks were seen to be running over the areas of choroidal atrophy in a way characteristic of angioid streaks, and at a level between the choroidal and retinal vessels. However, examination under magnification with a slit lamp and contact lens revealed that the streaks were no more than linear accumulations of retinal pigment which tapered at their ends into normal pigment epithelium. The case was potentially interesting in that the patient also had both clinical and histological SE of the skin and that x rays showed well-marked Paget's disease of the right tibia and frontal hyperostosis of the skull. The ocular condition may therefore be ascribed to a possible association with Paget's disease, although the streaks were not true angioid streaks.

Comment

Two cases of elastorrhexis in siblings are presented, further confirming the recessive nature of the disease. In one of them the systemic vascular element is considerably more prominent than the cutaneous, again establishing the superiority of a general name such as elastorrhexis over the dermatological name PXE. The presence of hypercholesterolaemia and hyperlipidaemia is considered to be of a familial nature and unrelated to the elastorrhexis, although it undoubtedly aggravates existing arterial disease. There was no evidence to be found of pancreatic exhaustion as described by Kahán, Kahán, Tapasztó, and Bencze (1963). It is interesting to note in Case 1 the natural resolution of the disciform maculopathy without specific treatment; also, although his gastric ulcer is not necessarily related to elastorrhexis, it may be considered when active as a dangerous source of internal haemorrhage. Electro-oculogram studies relate to the function of the retinal pigment epithelium as a whole (Arden, Friedmann, and Kolb, 1962) and the normality of these recordings further supports the primary non-involvement of the pigment epithelium in angioid streaks. Binocular examination of the fundus with a slit lamp and contact lens was found to be a useful method of distinguishing the true streaks of Cases 1 and 2 from the pseudo streaks of Case 3.

Several members of the family showed evidence of SE. This was originally thought to be an age change provoked by weathering (Unna, 1896; Hass, 1939); the old name of senile elastosis is misleading and should be discarded in favour of solar or actinic elastosis,* since

* Actinic elastosis was preferred by the committee on nomenclature of the American Academy of Dermatology (cited by Smith, 1963).

the changes occur only in areas of skin exposed to the sun and are not related to age (Lund and Sommerville, 1957; Smith, 1963). Histologically there is, in the upper third of the dermis, a lightly basophilic mass of thick twisted amorphous fibres having the staining properties of elastin and, like PXE material, may be considered to be derived from elastic tissue (Lansing and others, 1953; Findlay, 1954; Smith and others, 1962; Mehregan, 1965).

I. W. Whimster (personal communication, 1966) considers that there are two forms of SE: atrophic and hypertrophic. The former is the more common in old people, and also includes those elastotic changes secondary to trauma, irradiation dermatitis, and lupus erythematosus. The cases described in this paper are of the hypertrophic type; the skin is thick, rather yellow, furrowed, and of firm texture. It is seen most distinctly at the back and sides of the neck as "cutis rhomboidalis nuchae". These changes may occur as early as the third decade if the subject is so predisposed, are often associated with a fair complexion, and may result from sun exposure unrelated to the patient's usual habitat and occupation.

With regard to the family presented, it is tempting to suggest therefore, that there is a predisposition to hypertrophic SE which is based on a genetic factor. This could even be related or linked to the heterozygous state of PXE, but it has not been possible to support the latter idea by observation of other PXE families. None of these possibly heterozygous patients displayed angioid streaks.

Any direct relationship between angioid streaks and SE now appears to be extremely doubtful. Only five cases of the association have been recorded (Clay, 1932; Scholz, 1941) and all come from the older literature. In several cases there was no specific examination for the coexistence of Paget's disease. There may also have been confusion with PXE, as distinction between this and SE of the neck may be extremely difficult (Weidman, 1931; Lewis and Clayton, 1933; Franceschetti and Roulet, 1936), and it has also been known for PXE to involve predominantly the upper third of the dermis (Finnerud and Nomland, 1937). Jacoby (1934) described a woman aged 27 with angioid streaks, in whom the dermatological report was of SE although the skin section had been taken from the axilla. This must have been a misdiagnosis, and a later physician did in fact describe this patient as a case of PXE.

Classification of Angioid Streaks

In the past there has been little constructive classification of angioid streaks, more a grouping together of conditions with which they are associated. Although the exact aetiology is still far from conclusive, it is reasonable to classify the angioid streaks of elastorrhexis (and of the Ehlers-Danlos syndrome) as PRIMARY, and of all other disorders as SECONDARY. Streaks that are formed in ways other than by breaks in Bruch's membrane may be regarded as PSEUDO. There are several theories as to the cause of SECONDARY streaks, but basically they are covered either by impaired nutrition or by metastatic calcification of the elastic lamina of Bruch's membrane. Klien (1947) regarded all angioid streaks in disorders other than the Grönblad-Strandberg syndrome to be due to a secondary defect in the elastic fibres of Bruch's membrane, resulting either from an increased availability of metal salts or from a pathological facility for their deposition. Impaired nutrition of Bruch's membrane may result from (a) sickle-cell anaemia, (b) choroidal sclerosis, or (c) retinal exsanguination.

(a) In sickle-cell anaemia, where the streaks are usually associated with a sickle-cell

retinopathy, the impaired nutrition could be caused by low oxygen tension, intravascular sickling, and stasis in the choriocapillaris (Paton, 1959; Geeraets and Guerry, 1960).

(b) Choroidal sclerosis may be a localized feature of the eye, or associated with more widespread senile vascular disease. It may be associated with choroidal haemorrhages, with a disciform degeneration at the macula, with choroido-retinal atrophy, and with angioid streaks (*e.g.* Case VIII of Bedell, 1961). These are also all well-documented ocular complications of Paget's disease (Ormond, 1931; Terry, 1934; Mackie, 1956; Hugonnier and Royer, 1959), and it is very likely that choroidal sclerosis is an important factor in the cause of angioid streaks in this disorder.

Choroidal sclerosis may be the main aetiological factor in angioid streaks associated with senile vascular disease, as disciform exudation at the macula often coexists (McWilliam, 1955). However this group is not well documented in the literature, and it is important to exclude elastorrhhexis and Paget's disease, both of which are associated with vascular disease, and the presence of pseudo streaks. Hogan (1967) has shown that the appearance of choroidal sclerosis is due to an age change in the collagen fibres of Bruch's membrane which causes intercapillary fibrosis of the choriocapillaris, and that the choroidal vasculature may be otherwise normal. When this effect is severe enough to be associated with angioid streaks it is likely therefore that the breaks in the elastic lamina are due to a secondary effect of impaired nutrition on already ageing elastic tissue.

Ashton and Sorsby (1951) described the *post mortem* pathology of a familial dystrophy in two elderly sisters. They found choroidal sclerosis with choroidal atrophy and vascularized glial tissue associated with ruptures in a non-basophilic Bruch's membrane, but they considered the choroidal changes to be secondary to the changes in Bruch's membrane.

(c) That retinal exsanguination could later cause angioid streaks was first suggested by Yatzkan (1957). His examples were certain cases of severe gastric haemorrhage, in one of which both PXE and Paget's disease had been excluded. Paton (1959) also suggested that this in the form of a sickle-cell crisis might be a cause of angioid streaks in sickle-cell disease.

Metastatic calcification of Bruch's membrane is another possible explanation of angioid streaks in Paget's disease; it may also explain the occasional report of angioid streaks occurring in acromegaly (Howard, 1963; Paton, 1963) or familial hyperphosphataemia (McPhaul and Engel, 1961).

Important features of angioid streaks which may distinguish them from pseudo streaks are that they tend to involve both eyes to an equal extent, that the edges of their zigzag borders are complementary, and that they are not pigmented except when of long standing (when they may be associated with segments of choroido-retinal atrophy and pigment clumping).

PSEUDO streaks may be caused by:

- (1) Peripapillary streaks of pigment and choroidal atrophy which, though common in people of all ages, in a few eyes can simulate a picture of short angioid streaks;
- (2) Lines of pigment accumulation in or at the sides of areas of choroido-retinal atrophy (as in Case 3);
- (3) Radiating streaks of pigment arising after subsidence of a choroidal detachment (Scholz, 1941; McWilliam, 1955) or an exudative retinal detachment (Sivasubramaniam, 1958);
- (4) Traumatic tears in the choroid (Scholz, 1941);

- (5) Retinal folds which have collected pigmentary debris (Law, 1938);
- (6) Perivascular choroidal pigment atrophy which is said to occur in young patients without systemic vascular pathology (Scholz, 1941);

this contrasts with

- (7) Siegrist's condition of pearl-chain streaks of pigment along partly-sclerosed choroidal vessels, which is said to occur predominantly in elderly hypertensive males (Terry, 1934; Scholz, 1941).

Conclusions

(1) A skin biopsy is useful in the diagnosis of young or middle-aged patients who present with disciform degeneration of the macula. It should be emphasized that the skin may appear macroscopically normal.

(2) The term elastorrhesis is preferred to pseudoxanthoma elasticum, and better implies both the pathological and the systemic nature of the condition.

(3) The angioid streaks of elastorrhesis and the Ehlers-Danlos syndrome are considered to be due to primary, and those of other conditions to secondary degeneration of the elastic lamina of Bruch's membrane. In Paget's disease and in elderly patients without systemic disease, choroidal sclerosis may be an initiating factor. It is extremely doubtful whether there is more than a coincidental relationship between elastorrhesis and Paget's disease.

(4) There may, however, be a genetic link between elastorrhesis and sickle-cell anaemia in Negroes; but when angioid streaks occur without elastorrhesis, they are considered to be secondary to impaired nutrition of Bruch's membrane.

(5) The hypertrophic form of solar elastosis may be determined by a genetic factor. This could possibly be linked to the heterozygous state of elastorrhesis.

(6) Angioid streaks have no direct relation to solar (senile) elastosis, even though the latter may be prominent in other members of an elastorrhesis family.

(7) When angioid streaks are observed, it is important to look for elastorrhesis, especially if the patient is young, and for Paget's disease if the patient is old. A slit lamp and contact lens may be found useful in excluding the presence of pseudo streaks.

Summary

A family is described with an apparent genetic predisposition to solar elastosis in which there are two cases of elastorrhesis. The literature concerning the history, histology, and pathogenesis of elastorrhesis and angioid streaks is reviewed, and the relationship with solar elastosis is discussed. An account of primary, secondary, and pseudo streaks is given, and this classification is suggested to clarify some of the growing points of confusion.

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REFERENCES

- ADRIAENSSENS, A. (1963). *Belg. T. Geneesk.*, **19**, 1234.
 ARDEN, G. B., FRIEDMANN, A., and KOLB, H. (1962). *Lancet*, **1**, 1164.
 ASHTON, N., and SORSBY, A. (1951). *Brit. J. Ophthalm.*, **35**, 751.
 BALZER, F. (1884). *Arch. Physiol. (Paris)*, **3 ser.**, **4**, 65.
 BEDELL, A. J. (1961). *Trans. Amer. ophthalm. Soc.*, **59**, 111.
 BERLYNE, G. M. (1960). *Lancet*, **1**, 77.
 ———, BULMER, M. G., and PLATT, R. (1961). *Quart. J. Med.*, **30**, 201.
 BÖCK, J. (1938). *Z. Augenheilk.*, **95**, 1.

- CAWLEY, E. P., and WEARY, P. E. (1962). *Arch. Derm. Syph. (Chicago)*, **86**, 725.
- CHARACHE, S., and RICHARDSON, S. N. (1964). *Arch. intern. Med.*, **113**, 844.
- CHAUFFARD, A. (1889). *Bull. Soc. Méd. Hôp. Paris*, **3 ser.**, **6**, 412.
- CLAY, G. (1932). *Arch. Ophthal. (Chicago)*, **8**, 334.
- CONNELL, J. L. (1962). *Aust. N.Z. J. Surg.*, **32**, 78.
- CONNOR, P. J., JUERGENSEN, J. L., PERRY, H. O., HOLLENHORST, R. W., and EDWARDS, J. E. (1961). *Amer. J. Med.*, **30**, 537.
- DARIER, J. (1896). *Mhefte prakt. Derm.*, **23**, 609.
- DIXON, J. M. (1951). *Amer. J. Ophthal.*, **34**, 1322.
- DOYNE, R. W. (1889). *Trans. ophthal. Soc. U.K.*, **9**, 128.
- DUKE-ELDER, S. (1966). "System of Ophthalmology", vol. 9, pp. 722, 726. Kimpton, London.
- EDDY, D. D., and FARBER, E. M. (1962). *Arch. Derm.*, **86**, 729.
- FINDLAY, G. H. (1954). *Brit. J. Derm.*, **66**, 16.
- FINNERUD, C. W., and NOMLAND, R. (1937). *Arch. Derm. Syph. (Chicago)*, **35**, 653.
- FISHER, E. R., RODNAN, G. P., and LANSING, A. I. (1958). *Amer. J. Path.*, **34**, 977.
- FOUCAULT, J. P. (1963). *Arch. Ophtal. (Paris)*, n.s. **23**, 561.
- FOUNTAIN, R. B. (1965). *Proc. roy. Soc. Med.*, **58**, 1091.
- FRANCESCHETTI, A., and ROULET, E. L. (1936). *Arch. Ophtal. (Paris)*, **53**, 401.
- GEERAETS, W. J., and GUERRY, D. (1960). *Amer. J. Ophthal.*, **49**, 450.
- GIBBS, J. S. H. (1964). *Aust. J. Derm.*, **7**, 156.
- GILLS, J. P., and PATON, D. (1965). *Arch. Ophthal. (Chicago)*, **73**, 792.
- GOLTZ, R. W., HULT, A. M., GOLDFARB, M., and GORLIN, R. J. (1965). *Arch. Derm. Syph. (Chicago)*, **92**, 373.
- GOODMAN, R. M., SMITH, E. W., PATON, D., BERGMAN, R. A., SIEGEL, C. L., OTTESEN, O. E., SHELLEY, W. M., PUSCH, A. L., and MCKUSICK, V. A. (1963). *Medicine (Baltimore)*, **42**, 297.
- GREEN, W. R., FRIEDMAN-KIEN, A., and BANFIELD, W. G. (1966). *Arch. Ophthal. (Chicago)*, **76**, 197.
- GRÖNBLAD, E. (1929). *Acta ophthal. (Kbh.)*, **7**, 329.
- HAGEDOORN, A. (1939). *Arch. Ophthal. (Chicago)*, **21**, 746.
- HANNAY, P. W. (1951). *Brit. J. Derm.*, **63**, 92.
- HASS, G. M. (1939). *Arch. Path.*, **27**, 334 and 583.
- HOGAN, M. J. (1967). *Trans. ophthal. Soc. U.K.*, **87**, 113.
- HOLLOWAY, T. B. (1927). *Trans. Amer. ophthal. Soc.*, **25**, 173.
- HOWARD, G. M. (1963). *Amer. J. Ophthal.*, **56**, 137.
- HUGONNIER, R., and ROYER, J. (1959). *Bull. Soc. Ophtal. Fr.*, pp. 393.
- JACOBY, M. W. (1934). *Arch. Ophthal. (Chicago)*, **11**, 828.
- JOHNSON, W. C., GRAHAM, J. H., and HELWIG, E. B. (1964). *J. invest. Derm.*, **42**, 215.
- KAHÁN, A., KAHÁN, I. L., TAPASZTÓ, I., and BENCZE, G. (1963). *Klin. Mbl. Augenheilk.*, **142**, 1047.
- KAPLAN, L., and HARTMAN, S. W. (1954). *Arch. intern. Med.*, **94**, 489.
- KEITH, C. G. (1956). *Brit. J. Ophthal.*, **40**, 480.
- KLIEN, B. A. (1947). *Amer. J. Ophthal.*, **30**, 955.
- KNAPP, H. (1892). *Arch. Ophthal.*, (N.Y.), **21**, 289.
- KOFER, A. (1917). *Arch. Augenheilk.*, **82**, 134.
- LAMBERT, R. K. (1939). *Arch. Ophthal. (Chicago)*, **22**, 106.
- LANSING, A. I., COOPER, Z. K., and ROSENTHAL, T. B. (1953). *Anat. Rec.*, **115**, 340.
- LARMANDE, A., and MARGAILLAN, A. (1957). *Bull. Soc. franç. Ophtal.*, **70**, 206.
- LAW, F. W. (1938). *Trans. ophthal. Soc. U.K.*, **58**, 191.
- LEWIS, G. M., and CLAYTON, M. B. (1933). *Arch. Derm. Syph. (N.Y.)*, **28**, 546.
- LORIA, P. R., KENNEDY, C. B., FREEMAN, J. A., and HENINGTON, V. M. (1957). *Arch. Derm.*, **76**, 609.
- LUND, H. Z., and SOMMERVILLE, R. L. (1957). *Amer. J. clin. Path.*, **27**, 183.
- MACKIE, E. G. (1956). *Trans. ophthal. Soc. U.K.*, **76**, 267.
- MCKUSICK, V. A. (1956). *J. chron. Dis.*, **3**, 263.
- (1964). *Circulation*, **30**, 326.
- MCPHAUL, J. J., and ENGEL, F. L. (1961). *Amer. J. Med.*, **31**, 488.
- MCWILLIAM, R. J. (1955). *Brit. J. Ophthal.*, **39**, 298.
- MEHREGAN, A. H. (1965). *J. invest. Derm.*, **45**, 404.
- ORMOND, A. W. (1931). *Trans. ophthal. Soc. U.K.*, **51**, 258.
- PATON, D. (1959). *Arch. Ophthal. (Chicago)*, **62**, 852.
- (1963). *Amer. J. Ophthal.*, **56**, 842.
- PEARCE, W. G. (1965). *Trans. ophthal. Soc. U.K.*, **85**, 429.
- PLANGE, O. (1891). *Arch. Augenheilk.*, **23**, 78.
- REVELL, S. T. R., and CAREY, T. N. (1948). *Stth. Med. J. (Bgham, Ala.)*, **41**, 782.
- SANDBACKA-HOLMSTRÖM, I. (1939). *Acta dermat.-venereol. (Stockh.)*, **20**, 684.

- SCHEIE, H. G., and FREEMAN, N. E. (1946). *Arch. Ophthal. (Chicago)*, **35**, 241.
 ——— and HOGAN, T. F. (1957). *Ibid.*, **57**, 855.
 SCHOLZ, R. O. (1941). *Ibid.*, **26**, 677.
 SCHUTT, D. A. (1965). *Arch. Derm.*, **91**, 151.
 SHAFFER, B., COPELAN, H. W., and BEERMAN, H. (1957). *Arch. Derm. Syph. (Chicago)*, **76**, 622.
 SIVASUBRAMANIAM, P. (1958). *Brit. J. Ophthal.*, **42**, 759.
 SMITH, E. W., MALAK, J. A., GOODMAN, R. M., and MCKUSICK, V. A. (1962). *Bull. Johns Hopk. Hosp.*, **111**, 235.
 SMITH, J. G. (1963). *Arch. Derm.*, **88**, 382.
 ———, DAVIDSON, E. A., and CLARK, R. D. (1962). *Nature (Lond.)*, **195**, 716.
 SUERIG, K. C., and SIEFERT, F. E. (1964). *Arch. intern. Med. (Chicago)*, **113**, 135.
 SZYMANSKI, F. J., and CARO, M. R. (1955). *Arch. Derm. Syph. (Chicago)*, **71**, 184.
 TÉMINE, P. (1940). Thèse de Paris. Jouve, Paris.
 TERRY, T. L. (1934). *Trans. Amer. ophthal. Soc.*, **32**, 555.
 TOURAINE, A., and JAMES (1940). *Bull. Soc. franç. Derm. Syph.*, **47**, 217.
 UNNA, P. G. (1896). "The Histopathology of Diseases of the Skin", trans. N. Walker, p. 976. Clay, Edinburgh; Macmillan, New York.
 VERHOEFF, F. H. (1948). *Brit. J. Ophthal.*, **32**, 531.
 ——— and SISSON, R. J. (1926). *Arch. Ophthal. (N.Y.)*, **55**, 125.
 WEIDMAN, F. D. (1931). *Arch. Derm. Syph. (Chicago)*, **24**, 954.
 WELCH, R. B., and GOLDBERG, M. F. (1966). *Arch. Ophthal. (Chicago)*, **75**, 353.
 WOLFF, H. H., STOKES, J. F., and SCHLESINGER, B. E. (1952). *Arch. Dis. Childh.*, **27**, 82.
 WOO, J. C., and CHANDLER, F. W. (1958). *Ann. intern. Med.*, **49**, 215.
 WOODCOCK, C. W. (1952). *Arch. Derm. Syph. (Chicago)*, **65**, 623.
 YATZKAN, D. N. (1957). *Amer. J. Ophthal.*, **43**, 219.