ANGIOID STREAKS AND OSTEITIS DEFORMANS*

THEODORE L. TERRY, M.D.
Boston

The typical appearance of angioid streaks is so definite that, from the ophthalmoscopic examination, the ophthalmologist has no doubt of the accuracy of the diagnosis. Nevertheless, a discussion of the condition would not be complete without a consideration of the differential diagnosis. First, one should consider the typical picture of angioid streaks. As a rule, there is a more or less circular streak around or almost around the disc and quite close to it. From this streak, other branching streaks appear to radiate, but there may be other completely detached streaks which proceed in other directions. The streaks vary in width, but they do not always decrease in width after branching has occurred. The streaks do not run in straight lines. The changes in direction are characterized by obtuse angles rather than by gentle curves. The color of the streaks varies from dark brown to red. Some cases show white or grayish as well as colored streaks. Around the disc there is a "halo."† In Verhoeff's case unilateral streaks were present. Although in all other reported cases the disease is bilateral, it does not involve the two eyes to the same extent. It is therefore to be expected that the condition may appear to be unilateral in its early phase, since in some cases the process would be more advanced in one eye than in the other. Retinal and choroidal hemorrhages, colloidal excrescences, and macular lesions, consisting of choroidal changes, retinal hemorrhages, or circinate retinitis, are present at times.

Two types of pigmented streaks that must be distinguished

* Candidate's thesis for membership accepted by the Committee on Theses.

† The term "halo" is used to refer to the condition seen around the disc in many cases of angioid streaks in which there have been a loss in pigment and a degeneration of the choroid.

from angioid streaks are found in the fundus. One type consists in black, granular, straight or slightly wavy lines of various lengths. These streaks may branch. They are most numerous in the periphery of the fundus, and may extend to the limit of the ophthalmoscopic field. They are more or less meridional in direction, and tend to be parallel. They seldom extend nearer to the disc than from 2 to 3 mm. These streaks result from separation of the choroid, and Verhoeff[1] has shown that they are due to proliferation of pigment epithelium within the furrow-like creases that are produced in the separated choroid. The thickened epithelium remains after the choroid has become reattached to the sclera, thus producing the streaks.

The other type of pigmented streaks of the ocular fundus was first described by Siegrist.[2] Although the clinical and microscopic appearance of these streaks is more or less identical with that of the streaks produced by separation of the choroid, these result from sclerosis of the choroidal vessels. They are never found over completely sclerosed vessels. In his discussion of Verhoeff's paper Brown[3] suggested that these streaks may result from inward pressure of certain of the larger choroidal vessels against the pigment epithelium with a bending of the lamina basalis inwardly. Verhoeff suggested that the streaks may result from pulsation of the choroidal vessels. One may assume that the sclerosing choroidal vessels may pulsate to an unusual degree for a time. This abnormal pulsation may stimulate the local proliferation of pigment epithelium. Vos[4] reached practically the same conclusion.

In 1927 Holloway[5] published a report of two cases of angioid streaks of the ocular fundus, together with an exhaustive review of 58 cases collected from the literature. Since 1927 there have been about* 41 cases (Table I)

* It is impossible to give the exact number of cases reported, since in some instances it is not clear if the cases with pseudoxanthoma elasticum had been reported at an earlier date.

TABLE I

A. CASES OF ANGIOID STREAKS REPORTED IN THE LITERATURE SINCE THE REVIEW MADE BY HOLLOWAY

No. of Cases	*Reported by*	*Reference*	*Remarks*
1	Berliner[11]	Discussion of Newman's report	Osteitis deformans
1	Rowland	Unpublished paper read before New Eng. Ophth. Soc.	" "
2	Verhoeff[7]	. .	" " in one case
1	Batten[12]	Juler's case	" "
1	Vail[13]	Reported in discussion of Verhoeff's paper	" "
3	Gronbald[6]	. .	Pseudoxanthoma elasticum
1	Marchesni and Werz	Arch. f. Augenh., 1931, civ, p. 522.	" "
1	Poos	Klin. Monatsbl. f. Augenh., 1931, lxxxvii, p. 734.	" "
2	Hartung	Klin. Monatsbl. f. Augenh., 1932, lxxxviii, p. 43.	" "
2	Brill and Weil	Ztschr. f. Augenh., 1927, lxvi, p. 131.	" "
6	Clay	Arch. Ophth., 1932, viii, p. 335.	* " "
1	Newman[10]	. .	
1	Bönnet	Arch. d'opht., 1933, l, p. 721.	
1	Ishikawa	Acta Soc. Ophth. Jap., xxxvi, p. 1197. Abstracted in Zentralbl. f. d. ges. Ophth, 1933, xxviii, p. 380.	" "
2	Dykman	Arch. Ophth., 1934, xi, p. 283.	
2	Porter and Montgomery	Proc. Staff Meeting, Mayo Clinic, 1934, ix, p. 109.	
(2)	Weil	Klin. Monatsbl. f. Augenh., 1931, lxxxvii, p. 826.	These two cases are possibly the same as those reported by Brill and Weil (see above)
1	Ormund	Tr. Ophth. Soc. U. Kingdom, 1931, l, p. 258.	
3	Batten[12]	. .	
1	Batten[12]	. .	
1	Batten[12]	Percival Hay's case	
1	Batten[12]	Humphrey Neame's case	
1	Batten[12]	Williamson Noble's case	
1	Batten[12]	Muiehead's case	
1	Koppl	Ztschr. f. Augenh., 1927, lxvi, p. 131.	
1	Higaski	Abstracted in Zentralbl. f. d. ges. Ophth., 1930, xiii, p. 792.	
1	Jablonski	Arch. f. Augenh., 1930, ciii, p. 665.	
1	Meesman	Ztschr. f. Augenh., 1931, lxxiii, p. 294.	
1	Sobhy Bey	Bull. Ophth. Soc. Egypt, 1926, p. 78.	

* Clay found pseudoxanthoma elasticum in a case reported previously by Calhoun, and included in those cases reviewed by Holloway.

B. REFERENCES OF OCULAR LESIONS IN OSTEITIS DEFORMANS

Vergne: Les Lesions Ocularis dans la Maladie de Paget, Ann. d'ocul., 1908, cxl, p. 321.
Glaessner: Zur Kenntnis der Pagets Knochenerkrankung, Wien. klin. Wchnschr., 1908, xxi, p. 132.
Coppez: Complications Ocularis de la Maladie Osseuse de Paget, Arch. d'opht., 1912, xxxii, p. 529.
Wylle: Two Cases of Optic Atrophy in Osteitis Deformans, Proc. Roy. Soc. Med., Sect. Ophth., 1923–1924, xi.

reported in the literature, and with the five new cases recorded here the total is brought up to 106. These more recent reports have added two outstanding contributions to our general knowledge of this condition; namely, the co-existence of angioid streaks with pseudoxanthoma elasticum, and the histopathology of the angioid streaks.

The coexistence of angioid streaks and pseudoxanthoma elasticum was discovered in three cases by Gronbald,[6] and other observers have since reported 20 additional cases (Table I, A). In most of these cases the diagnosis of pseudoxanthoma elasticum was confirmed by biopsy and microscopic study.

The histopathology of angioid streaks was reported by Verhoeff.[7] There has been a hesitancy on the part of some investigators to accept Verhoeff's case as one of true angioid streaks, because the streaks were not seen before enucleation; as there was a dense corneal scar which made an ophthalmoscopic examination impossible, and because the remaining eye showed no typical streaks. On December 16, 1933, five years after the enucleation, the patient was examined again by Dr. Verhoeff and myself. At this visit the following observations were made: The vision in the left eye was 6/15. The pathologic change around the disc, as originally described by Verhoeff, had altered somewhat. It was more extensive (fig. 1). There were some short pigmented streaks at the margin of the lesions. The choroidal vessels were less numerous than are usually seen in a blond fundus. This was highly suggestive of fibrosis of the choroid. *X*-ray examination showed osteitis deformans of the skull. There was no clinical or microscopic evidence of pseudoxanthoma elasticum. The hearing was definitely impaired.

I am of the opinion that the right eye contained angioid streaks, and that Verhoeff's report gives the first accurate explanation of the pathology of this condition. My reasons for this belief are:

1. If this was not a case of angioid streaks, then it was one of a still more rare and completely unknown ocular disease.

2. The pathologic findings explain perfectly the ophthalmoscopic appearance and every clinical feature of the disease.

3. All observers are of the opinion that the streaks are well below the retinal vessels. Although some investigators as-

sume that the streaks are due to pathologic changes deep in the retina, in the pigment epithelium of the retina, in Bruch's membrane, or in the choroid, no one except Verhoeff has demonstrated any such lesion histologically. The pathologic observations of Magitot[8] and of Lister[9] have not been accepted as of significance, since in all probability neither were true cases of angioid streaks.

4. The patient had osteitis deformans. The association of osteitis deformans and angioid streaks will be discussed later.

5. Pathologic changes were taking place in the choroid of the other eye. These may be early stages in the formation of angioid streaks. Similar fundus changes were present in one of my cases with streaks, and in another case in which no typical streaks were found. In our textbooks no description or diagnosis is given that regards this fundus change as a disease entity. In this eye the lack of a typical ophthalmoscopic picture of streaks may be due to the small amount of pigment present in the pigment epithelium of the retina.

On the basis of Verhoeff's findings, the appearance of streaks is due to infolding of the inner layer of the choroid, which results from the contraction that ensues as fibrosis progresses in the outer layers of the choroid. Verhoeff found that some of the projections pointed inward and that some were bent sidewise. The ophthalmoscopic appearance of such folds depends on several factors. One of these is the obliquity of the line of vision to the pigment epithelium of the fold. One would be looking at several superimposed layers of pigment epithelium. If the streaks were bent sidewise, in addition to the piling-up effect on one side, one would actually be looking at three layers of pigment epithelium of the retina (fig. 2). Such streaks in the brunet fundus would appear to be dark brown. If, on the other hand, the pigment in the pigment epithelium was sparse or absent, there would be a piling-up effect or duplication of the choriocapillaris and the streaks would appear to be reddish. If, however, in a

blond fundus the choriocapillaris was not evident, one would see white streaks due to the scar tissue in the choroid, or light reflexes due to wrinkling of the retina, or both. If the fold was broad or not very high, there might not be sufficient piling up of pigment epithelial cells or of the choriocapillaris to give a pigmented or a reddish streak. In this case the wrinkle or fold in the retina would probably give a light reflex which would appear as a whitish or light line. Ruptures of the choroid would naturally appear as white streaks.

Verhoeff[7] mentions the coexistence of osteitis deformans and angioid streaks in a patient whom he had observed clinically. The following is a more complete report of this case:

Mr. J. H. P., aged fifty-two years, was first seen at the Massachusetts General Hospital October 28, 1927, at which time it was found that he had an advanced osteitis deformans.

The patient first noticed an increase in the size of his head twenty-two years previously. During the past seventeen years his height had decreased from 67 to 61 inches. He complained of severe pain in his legs. He had been deaf in the left ear for four years and in the right ear for two years. His complexion had been very fair but within the last five years there had been a darkening, until he came to have the general complexion of an Italian.

Examination of the ears showed calcium deposits in both tympanic membranes, and "there appears to be a dead labyrinth on the right side." There was sufficient thickening of the skull to account for this deafness on the basis of pressure atrophy of the nerve.

V.R.E. = 6/60; L.E. = 6/6. Except for the central scotoma in the right eye, the visual fields were normal. The patient was examined by Dr. Verhoeff, who made the diagnosis of angioid streaks, with a hemorrhage in the macular region of the right eye. I saw the patient at that time. Many streaks were present in each eye, and a "halo" was observed around each nerve head. The streaks were distributed more or less radially, and showed numerous branches which radiated from a somewhat circular streak around each disc.

In 1929 the patient died of bronchopneumonia. No autopsy was obtained.

In 1929 Rowland reported to the New England Ophthalmological Society a case of angioid streaks with osteitis deformans. This paper has not been published, but Rowland informed me that he had recently re-examined the patient and had found no evidence of pseudoxanthoma elasticum.

Berliner,[11] in a discussion of a paper by Newman, states: "In this connection I should like to report a case of angioid streaks that occurred in a woman aged seventy who was being treated for Paget's disease. I believe that another case of angioid streaks in association with Paget's disease was reported last spring in Boston. In both these cases there was no evidence of pseudoxanthoma. After seeing this case I examined the fundi in 28 other cases of Paget's disease and did not find any that showed angioid streaks in the retina. However, in three of these cases there was marked sclerosis of the choroidal vessels."

Batten[12] reported a case of angioid streaks coexistent with osteitis deformans.

Vail,[13] in his discussion of Verhoeff's paper, reported a case of angioid streaks. At my suggestion he has recently had the patient examined for osteitis deformans. The *x*-ray films showed irregular bone thickening, and bone rarefaction in the left occipital region that is characteristic of Paget's disease. In a personal communication Vail states: "I think there is sufficient evidence in the left occipital bone to warrant a diagnosis of beginning Paget's disease."

Several papers concerning ocular lesions associated with osteitis deformans have been published (see Table I–B for bibliography). Pigmented spots, and even streaks of pigment, arteriosclerosis, and retinal and choroidal hemorrhages were noted in the fundus. In several instances cataracts were present. Several observers have found a concentric contraction of the visual fields. The field changes are apparently due to pressure atrophy of the optic nerve produced by narrowing of the optic foramen by the bone disease. In his original paper on osteitis deformans Paget[14] gave an ex-

haustive study of the condition. His work was so thorough that considerable time elapsed before much was added to his observations. Paget originally reported 28 cases. In over half the patients in this series the hearing and vision were defective. Many patients exhibited discoloration or increased pigmentation of the skin. Four were "blind" due to "chorioretinitis and hemorrhages." At the time of Paget's report no clear-cut differentiation between osteitis deformans and osteitis fibrosa cystica was made. Since then the latter condition has been conclusively established as a separate disease entity with a known etiology (hyperparathyroidism).[15] It is possible to diagnose osteitis deformans before clinical signs and symptoms arise. The *x*-ray findings form the chief basis for such diagnoses. The disease is often discovered in the study of *x*-ray films taken during the investigation of some other condition. It has been possible to detect osteitis deformans of a single bone—the so-called monosteic type of Schlesinger. The serum phosphatase is increased in osteitis deformans. Other laboratory findings are of questionable value. Eosinophilia and basophilia have been reported. Disturbances in sulphur, calcium, and phosphorus metabolism have been observed.

The investigations of Schmorl[16] have added much to our knowledge of the condition. This observer made a very careful study of the results in 4,614 autopsies performed on patients over thirty-nine years of age, and found definite microscopic evidence of osteitis deformans in 3 per cent. of the cases. Thus, although clinical evidences of the disease are rare and are manifested late in the course of the condition, osteitis deformans is a relatively common disease. It is interesting to note that the previous conception of frequent involvement of the tibia is erroneous (Table II).

The figures in Table II are based on findings in the 138 cases of osteitis deformans that Schmorl found in 4,614 autopsies on patients over thirty-nine years of age.

Jaffe[15] observes that the fibula seems to show practically no predisposition to the disease. He also stresses the point that

there can be a variety of "irregular" forms of the disease, depending on the proportion of absorption to reformation of the bone. He states that the microscope will show definite osteitis deformans before the diagnosis can be made by *x*-ray.

TABLE II.—FREQUENCY OF INVOLVEMENT OF THE VARIOUS BONES IN OSTEITIS DEFORMANS

(According to Schmorl)

Bone	*Frequency*	*Per cent.*
Sacrum	78	56
Spine	69	50
Right femur (in most people subject to more trauma than the left)	43	31
Cranium	39	28
Sternum	32	23
Pelvis	30	21
Left femur	21	15
Clavicle	18	13
Tibia	11	8
Ribs	10	7
Humerus	6	4

The characteristic microscopic pathologic change of osteitis deformans is a combination of two main factors. On the one hand, osteoclasts are actively destroying bone and, on the other, the bone is being reconstructed. Changes, probably secondary in nature, take place in the bone-marrow and in the periosteum. The bone-marrow loses its usual hematopoietic character and becomes fibrosed. There may be hemorrhages into this new abnormal marrow, just as in angioid streaks there are hemorrhages into the fibrosed choroid. Later the abnormal bone-marrow may become fatty, and still later, after more or less healing of the part, it may reassume a more or less hematopoietic character. The periosteum becomes injected in places and forms bone. Jaffe states further: "Thus it is now established that the thickening of a tubular bone in Paget's disease is a matter of periosteal thickening." It would appear to be a relatively simple process, but no one has been able to produce the complete picture of osteitis deformans experimentally, although somewhat similar processes have been produced by

regulating the calcium and phosphorus intake and by feeding parathyroid extract.

Verhoeff[7] points out that the essential pathologic change of angioid streaks is a fibrosis corrigans of the choroid. Pseudoxanthoma elasticum is essentially a degeneration of the elastic tissue of the skin. There is therefore no obvious similarity in the pathology of these three conditions, but there are more or less secondary points in common. Some factor has altered the bone and the choroid. The bone regenerates abnormally; the choroid heals by scar formation; both reactions being somewhat characteristic of repair in the respective organs. Hemorrhages are seen in the fibrous bone-marrow and in the choroid. The factor which destroys the bone could be the factor which alters the choroid. Many theories have been advanced as to the etiology of the eye and bone conditions, several of which are obviously improbable.

Walker[17] has suggested a similarity between the choroid of the eye and the vascular portion of the organ of Corti. Calogero[18] and Soriano[19] find auditory disturbances in sympathetic ophthalmia, and suggest a type of pathologic change in the organ of Corti similar to that found in the choroid of the eye. In retinitis pigmentosa auditory nerve deafness occurs frequently.[20] There are, therefore, some reasons for believing that a part of the organ of Corti and the choroid may be composed of similar tissues which are susceptible to the same diseases. If angioid streaks are a manifestation of choroidal disease, then it is possible that in some of these cases one might find pathologic changes in the organ of Corti. Whether such an ear lesion would cause deafness is highly debatable. In osteitis deformans deafness is a common occurrence. It is generally believed—and no doubt correctly so—that the bony changes of Paget's disease, encroaching on the auditory nerve, produce pressure atrophy of the nerve. Other changes in the ear, such as stapes anklyosis,[21] osseous labyrinth capsule,[22] and otosclerosis[23,24] have been noted. However, if one can detect a nerve deafness before

the auditory nerve is sufficiently involved to cause a pressure atrophy, then this finding would support so theoretical a concept of "angioid streaks" of the inner ear.

To summarize the problem: 1. Is the coexistence of osteitis deformans and angioid streaks and of pseudoxanthoma elasticum and angioid streaks, a result of chance, or are these combinations the manifestations of disease entities? 2. Does the association of these conditions give any clue to their etiology? 3. Is there a nerve deafness in osteitis deformans before the advent of bony changes around the auditory nerve?

In order to attempt to answer these questions I have made a study of all available cases of osteitis deformans. Through the cooperation of Dr. Fuller Albright and Dr. A. Hampton, of the Massachusetts General Hospital, and of Dr. Henry Christian, of the Peter Bent Brigham Hospital; and through the kindness of Dr. E. B. Dunphy, who permitted me to see one of his private patients, I have been able to study 22 cases of osteitis deformans. Of this number, three showed definite angioid streaks. Four patients exhibited a "halo" around the disc and changes almost identical with those found in the left eye of Verhoeff's patient. Another patient of this group with a blond fundus showed a decrease in the number of choroidal vessels. This was suggestive of choroidal fibrosis. This patient also showed a typical "halo" around each disc. Three patients of this group exhibited numerous colloidal excrescences. In five patients retinal arteriosclerosis was present; in two, retinal hemorrhages were observed, and in three, choroidal hemorrhages. One patient had a closure of the central retinal vein and typical hemorrhagic retinitis, and one showed immature cataracts in each eye. With the exception of the case of hemorrhagic retinitis, the vision in each case was normal. The hearing was tested in only three cases, two of which showed nerve deafness. However, Case 5 showed definite pseudoxanthoma elasticum. In this case osteitis deformans was not demonstrable by *x*-ray, and

Dr. Albright did not find an alteration of the serum phosphatase. By personal communication, Dr. Grady Clay, of Atlanta, has informed me that he has two cases of angioid streaks not associated with osteitis deformans. *X*-ray examinations were made of some of the long bones and the spine, but not of the entire skeleton. The serum phosphatase was not determined. Clay's patients did have pseudoxanthoma elasticum. Although osteitis deformans is not completely ruled out in these cases, the question arises as to whether there is more than one type of angioid streaks; that is, a type that is part of a general disease which includes osteitis deformans, and another type that is a part of a general disease including pseudoxanthoma elasticum.

In addition to these cases I have studied six others in which the diagnosis of osteitis deformans was questionable. In this group angioid streaks were not present. One patient had numerous colloidal excrescences, and another had marked arteriosclerosis of the retinal vessels. Nerve deafness was present in one patient. None of this group showed clinical evidence of pseudoxanthoma elasticum.

REPORT OF CASES

CASE 1.—227362—G. L., female, aged fifty-one years, came to the ear department of the Massachusetts Eye and Ear Infirmary July 14, 1933, complaining of ringing in the left ear. A nasal spray was prescribed. Her head was considerably enlarged, and her legs were bowed. *X*-ray examination showed marked osteitis deformans of the skull, pelvis, femora, and tibia. She was referred to the medical clinic of the Massachusetts General Hospital, where the following findings were recorded:

History.—During the past five years the patient had had difficulty in procuring hats large enough for her head. A ringing in the left ear had begun four months previously. Three years ago a gangrenous appendix was removed.

Examination.—The patient was a small woman with the typical bowing of the legs and enlargement of the head characteristic of Paget's disease. Moist râles were heard at the right apex. The blood-pressure was 165/100. There was a loud systolic murmur at

the base of the heart. Red blood count, 5,210,000; hemoglobin, 75 per cent.; serum calcium, '11.8; serum phosphatase, 4.01; plasma phosphatase, 39.2 (normal from 3 to 5).

I saw the patient October 21, 1933, in my investigation of the fundus in osteitis deformans. Vision, each eye, =6/6. In each fundus there were typical, but not numerous, branching angioid streaks. There was a typical "halo" around each disc. No evidence of pseudoxanthoma elasticum was found. The visual fields were normal. The hearing test disclosed deafness of middle ear type.

CASE 2.—268321—W. H., male, aged fifty-nine years, came to the eye clinic of the Massachusetts Eye and Ear Infirmary May 26, 1933. His complaint was defective vision. The vision in each eye was 6/60, unimproved by glasses. In each eye there were moderate retinal arteriosclerosis and large macular hemorrhages. The patient was referred to the medical department to be examined for hypertension and arteriosclerosis. The medical department's report was as follows:

History.—The patient had always been healthy, and until he was forty-five years of age was able to obtain life insurance. During the past five or six years the legs had become bowed and shortened. In the last two years his head had increased in size one-eighth of an inch. For several years he had been suffering from pain shooting up and down the legs.

Examination.—The patient was a thin, old-looking man with a large head and with marked anterior and lateral bowing of the legs. The peripheral vessels were tortuous and markedly sclerosed. *X*-ray examination showed advanced osteitis deformans of the skull and tibia.

Diagnosis.—Osteitis deformans and arteriosclerosis.

The patient consulted Dr. Verhoeff January 26, 1934, at which time the diagnosis of angioid streaks of the ocular fundi and hemorrhages in the maculas was made. The patient was referred to me for further study.

Examination showed numerous typical, branching angioid streaks in each eye. Some of the streaks were white and quite free from pigment. Around each disc was a "halo." Numerous colloidal excrescences were present throughout the fundus. At the periphery of the retina, where the pigment epithelium contained very little pigment, the choroidal vessels were markedly reduced in number and the fundus reflex was unusually pale.

Except for the central scotoma due to the macular hemorrhages, the visual fields were normal.

There was no evidence of pseudoxanthoma elasticum. This patient's skull was sufficiently diseased to account for his nerve deafness.

CASE 3.—294651—H. L., aged fifty-five years, came to the medical department of the Massachusetts General Hospital complaining of nausea and vomiting when tired.

History.—During the past three years the patient would vomit when she became tired or exhausted. The vomitus was bitter and free from blood. Recently the attacks had been more frequent, and the patient noticed that she would tire more easily. At the time of these attacks she observed a yellowish color of her skin. From ten to twelve years ago the left leg became shorter during an attack of "rheumatism."

Examination.—The patient was a well-nourished, apparently healthy woman. Her head was larger than normal, presenting the characteristic appearance of osteitis deformans. Her teeth were carious; some had been extracted. The venous pulsation on the right side of the neck was more marked than on the left. The pulse was regular and full. The apex beat was felt in the fifth interspace, 7 cm. from the midline. There was a suggestion of a systolic thrill. The heart sounds were of good quality, with a soft systolic murmur heard best at the apex. The edge of the liver was palpable. Vaginal examination revealed a cystocele. *X*-ray examination showed advanced osteitis deformans of the skull, the sacrum, the lumbar spine, and of both femora. Blood count: red cells, 3,090,000; white cells, 10,250; hemoglobin, 70 per cent.; serum calcium, 10.7; phosphorus, 4.44; serum phosphatase, 49.00.

There were many white branching angioid streaks of each fundus (fig. 3). Dr. Verhoeff confirmed my diagnosis. There were "halos" around the discs. The pigment epithelium of the retina contained no discernible pigment. The choroidal vessels were markedly decreased in number, which was highly suggestive of fibrosis of the choroid. Vision, each eye, =6/6. The visual fields were normal. There was no evidence of pseudoxanthoma elasticum. There was not sufficient involvement of the bones of the skull to account for the slight nerve deafness of which the patient was unaware.

The ear examination was made by Dr. Philip Meltzer. The right ear showed sclerotic changes marked with a small healed perforation just below the umbo. The patient had had a discharge

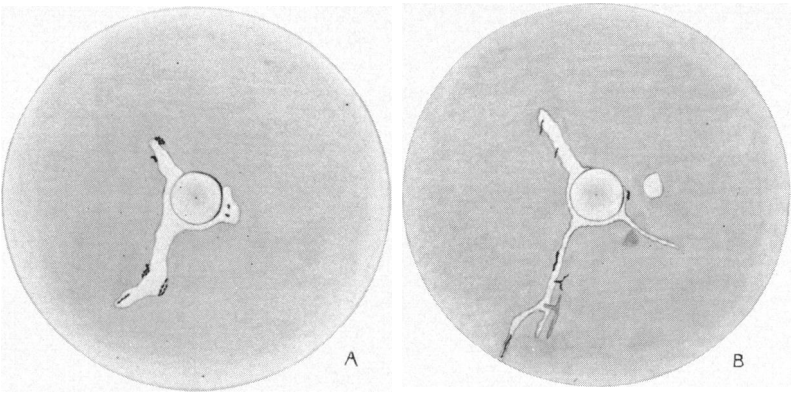

Fig. 1.—A, Appearance of the left fundus of Verhoeff's case soon after right eye was enucleated. B, Appearance of the left fundus five years later.

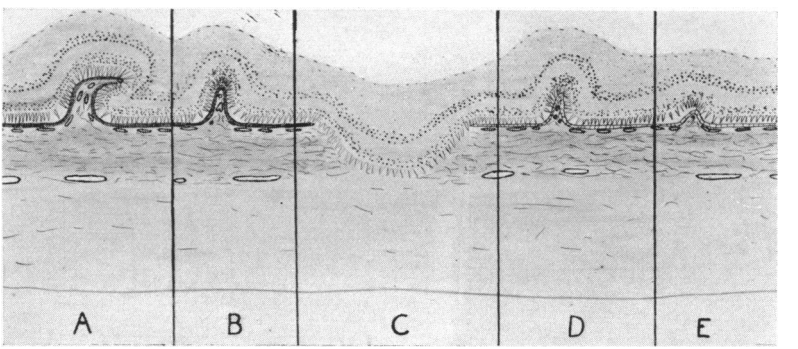

Fig. 2.—A schematic representation of the various microscopic findings in angioid streaks based on Verhoeff's case. In A and B the pigment in the pigment epithelium of the retina is very great—brunet fundus. In D and E there is little or no pigment in the pigment epithelium—blond fundus. A, represents a streak bent sidewise. On the left one would be looking obliquely at the pigment epithelium. This would give the effect of looking at several layers of pigment epithelium. On the right one would be looking at three layers of pigment epithelium of the retina and two layers of the choriocapillaris. B, represents a streak without a sidewise bend. C, represents a tear in the choroid. D, represents the piling-up effect of the choriocapillaris and explains the red color of some streaks. E, represents a very low streak without appreciable piling up of the choriocapillaris. Here one would see a light reflex due to a wrinkle of the retina.

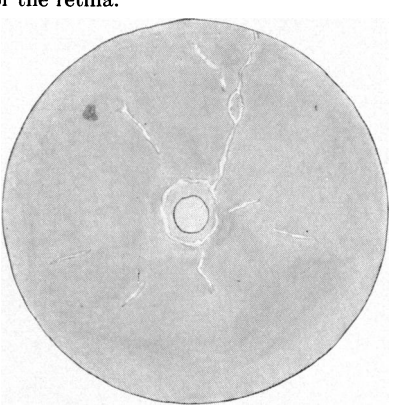

Fig. 3.—A sketch of the right fundus of Case 3, representing the appearance and distribution of the white streaks.

from the ear twenty years previously. The left ear showed sclerotic changes. The nose was essentially negative, and the Eustachian tubes were clear.

CASE 4.—D. C., male, aged sixty-six years.

History.—In 1909, while bowling, the patient broke his left hip. He had an extremely slow convalescence, and for some months he put most of the work on the right leg. In 1916 the right leg began to bow, and he grew shorter. During the past ten years his head had grown much larger. The patient was deaf in both ears, the deafness being first noted in the left ear fifteen years ago, and in the right ear five years ago. Mechanical auditory aids did not improve his hearing, which suggests that the deafness was due to nerve involvement.

One year previously due to hemorrhages in the macular region the vision in each eye had deteriorated. There was marked arteriosclerosis in each retina, and a "halo" was observed around each disc. In each eye, about three disc-diameters from the disc, there were a few short but typical branching angioid streaks. There was no evidence of pseudoxanthoma elasticum.

No *x*-ray examination was possible, but there was a typical clinical picture of advanced osteitis deformans. There were sufficient changes in the bones of the skull to account for the deafness.

The following case report concerns a patient who had angioid streaks and pseudoxanthoma elasticum. There was no evidence of osteitis deformans.

CASE 5.—275922—Female, aged forty-nine years. The patient came to the eye clinic of the Massachusetts Eye and Ear Infirmary July 25, 1933, complaining of defective vision. V. R. E. = fingers at two feet; L.E. = 20/70. A diagnosis of old chorioretinitis in both eyes was made. The patient returned to the clinic August 1, 1933, at which time fresh retinal hemorrhages were noted in the macular region. At her request she was referred to the medical department.

History.—For a period of from five to six years the patient had been troubled with blurring of the vision of both eyes. She had had frontal headaches four or five times a week. For several years she had had a dull pain in the back.

Examination.—The patient was an obese middle-aged female. The tonsils were enlarged and slightly reddened. There was a

systolic murmur of moderate intensity, loudest over the apex. The liver extended about the width of four fingers below the costal margin. The blood-pressure was 160/110. *X*-ray examination showed calcification and tortuosity of the aorta.

Diagnosis.—Hypertension and arteriosclerotic heart disease.

The patient was given a reducing diet, and digitalis was prescribed.

On January 17 the presence of a lump in the left breast was noted. This was considered to be a carcinoma. In view of the heart disease, it was thought best to treat the tumor with the *x*-rays rather than to resort to surgery.

The patient returned to the eye clinic January 29, 1934, at which time Dr. Frank Carroll discovered typical branching angioid streaks in each eye, in addition to the macular hemorrhages. The streaks were quite typical and somewhat numerous. There were two white streaks exactly like those observed in Case 3. There were "halos" around the discs.

Below each axilla was an orange-colored discoloration of the skin about 5 cm. in diameter. The color of these spots was almost identical with that seen in xanthoma. The skin in the region of these lesions was inelastic. In other parts of the body the skin had a normal elasticity. The patient would not permit a biopsy. Dr. E. L. Oliver, of the dermatologic clinic of the Massachusetts General Hospital, considered the lesions to be pseudoxanthoma elasticum. The patient was examined for osteitis deformans. *X*-ray examinations of the entire skeleton showed some decalcification of the bones, particularly of those of the skull, but there was no evidence of osteitis deformans.

Dr. Fuller Albright found the serum phosphatase to be 4.5−, well within normal limits.

The ears were examined by Dr. Philip Meltzer. Except for sclerosis of both tympani, the ears were normal.

The coexistence of osteitis deformans and angioid streaks has therefore been observed in nine cases, four of which have been discovered in this study. In the literature there are 106 cases of angioid streaks, including those reported here. Osteitis deformans was recognized in 8.49 per cent. of these. The coexistence of angioid streaks and osteitis deformans is of too frequent occurrence to be the result of chance. All my patients with osteitis deformans and angioid streaks ex-

hibited marked bony changes of the skull. This would indicate a close relationship between the skull changes and those of the choroid, but why this should be so is not obvious. It is possible that angioid streaks may develop before Paget's disease is demonstrable clinically. This probably was true in Verhoeff's case, in which acute Paget's disease was found by *x*-ray examination five years after the diagnosis of angioid streaks was made. This relationship cannot be settled by the age incidence of the diseases, since the conditions which lead to the diagnosis are so different. The possibility of fibrosis corrigans, to use Verhoeff's term, of the organ of Corti can be settled only by further exhaustive studies and by autopsies.

I believe that a marked decrease in the circulation, due to arteriolar sclerosis, and even actual closure of the small vessels could initiate the bone changes, the choroidal changes, and even the pseudoxanthoma elasticum. Locke[25] states: "More or less generalized arteriosclerosis, usually of a striking type, has been so commonly observed in these cases [osteitis deformans] that it may almost be regarded as a universal manifestation of the disease." No doubt some additional factor is needed to produce the condition, such as faulty diet, familial tendency, trophic nerve disturbance, and the like. In osteitis deformans, angioid streaks, and pseudoxanthoma elasticum a familial tendency is noted.

No discussion of the association of bone tumors and osteitis deformans is included in this report, since the points at issue in this communication have no direct bearing on such tumors.

Among ophthalmologists there has been a tendency to explain the distribution and etiology of angioid streaks on an anatomic basis. No anatomic basis is obvious; no vessels and no nerve fibers are distributed along the general course of the streaks. The embryology of the eye is apparently not a factor in the production of the streaks. On the other hand, the following experiment demonstrates easily that streaks can be produced by mere physical contraction of the choroid:

A small bladder of cargile membrane was distended with air and the end was closed by means of a rubber band. The pressure within the bladder was only sufficient to maintain its shape without tension. A small circular rod was held very lightly against the apex of the bladder to represent the optic nerve. A 25 per cent. solution of celloidin was then spread over the end of the bladder up to the rod. As it dried, the celloidin contracted. Folds appeared in the bladder of identical distribution and branching as are observed in angioid streaks. After the contraction was complete, pressure was applied by compressing the opposite end of the bladder, and tears were produced in the celloidin exactly analogous to the tears of the choroid observed in cases of angioid streaks.

CONCLUSIONS

1. Osteitis deformans and angioid streaks coexist in a sufficient number of cases to indicate that they are each local manifestations of a single general disease. To a slight extent this conclusion is supported by certain similarities in the histologic findings. Possibly the underlying cause of osteitis deformans can produce angioid streaks before it produces changes in the bone.

2. Arteriosclerosis alone is obviously not sufficient to cause either osteitis deformans or angioid streaks. It would seem undoubtedly to be an important factor, but some unknown additional factor must be necessary to produce these lesions.

3. Deafness is commonly associated with osteitis deformans. This has been attributed to the compression of the auditory nerve through bone changes, but it may be due, at least in some cases, to changes in the organ of Corti similar to those in the choroid in cases of angioid streaks.

4. Pseudoxanthoma elasticum has recently been observed in many cases of angioid streaks, but never in osteitis deformans. Pseudoxanthoma elasticum, however, is a condition that is unfamiliar even to most dermatologists, and in

its early stages osteitis deformans may be clinically unrecognizable. Further investigation is therefore needed to ascertain the exact relationship existing between these three conditions. Osteitis deformans, however, is associated with profound changes in the body, whereas pseudoxanthoma elasticum, so far as is known, is not; therefore, in regard to angioid streaks, the former would seem to be of far greater importance than the latter.

5. Changes in the choroid resulting in a shrinkage of that tissue can produce wrinkles and folds and tears similar in pattern to those found in angioid streaks.

6. A deficiency of pigment in the epithelium of the retina may prevent one from seeing the angioid streaks, or may cause the streaks to appear as white lines instead of as red or pigmented lines.

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