ATROPHIA GYRATA CHOROIDEAE ET RETINAE*

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IN 1871 Mauthner published the report of an eye-condition, named choroideremia, and in 1896 E. Fuchs described a similar case under the term of atrophía gyrata choroideae et retinae. Later about 35 investigators have reported some 50 similar cases, trying to classify them as belonging to the one or other of these two clinical pictures first described.

It is evident from their information, however, that they have not always succeeded, and on reading the reports one receives an impression of great confusion.

Mainly, however, two divergent conceptions are prevalent, namely :

1. The two clinical pictures described both belong to the same condition, choroideremia forming the ultimate stage in the development of atrophía gyrata.

2. They are seen as different diseases, choroideremia being a defect or malformation, and atrophía gyrata an acquired progressive degeneration (atrophy) of retina and choroid.

Duke-Elder (1946) does not try to conceal the confusion around these conditions, writing : " In view of our unsatisfactory knowledge of both conditions and in the complete absence of pathological studies, the question must be left open ; indeed it is questionable whether either condition forms a homogeneous group," and he goes on : " It will also be remembered that no case of choroideremia has been seen younger than 14 years, but at the same time no one has yet seen a case of gyrate atrophy develop into this condition."

Another writer, Bedell (1937) declares : " The cases are too few to warrant dogmatic statements."

The variation in description of different symptoms in these conditions is not so great as to prevent a review of their main common features.

The condition is often familial. Consanguinity has been demonstrated in some cases. The hereditary character of the disease has been mentioned, the recessive modus being specially discussed. But especially on this point the information is unsatisfactory.

Night-blindness is one of the first and commonest symptoms.

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Most patients state that their night-blindness has lasted a long as they can remember, others have noticed the symptom first in the twenties. Determination of the commencement of the disease on this basis is therefore difficult.

The actual changes in the fundus oculi have been observed at various ages, down to 10 years (Mori, 1914; Werkle, 1931). Most publications, however, deal with patients of 20 years or more. Central vision becomes affected in an advanced stage, considerably reduced vision or amaurosis then occurring at a relatively early age.

The initial symptoms are usually vague, and this is probably the reason why no one has yet been able to determine just when and how the changes in the fundus take place.

The conditions have in several cases been associated with myopia, sometimes to a considerable degree. The accompanying myopia has even been considered decisive for the diagnosis: choroideremia or atrophía gyrata (Beckershaus, 1926).

The visual fields are in most cases contracted, in a great number of cases to within 10° .

Descriptions of the changes in the fundus vary. No two cases seem alike. In his work Bedell expresses the same opinion when saying: "At the beginning of this discussion I wish to say that practically no two cases are alike in regard to the distribution of pigment, the size and shape of the retained choroid about the macula or the modifications of the retinal and choroidal circulation. Many cases are similar but none are identical."

The changes vary in the different cases as well as in the two eyes of the same patient (Wernicke, 1909). Varying types have also been described within the same family (Böhm, 1932; Werkle).

The changes in the fundus have been described as a more or less extensive defect or atrophy, essentially of the central part of the fundus. The area round the macular region, however, seems to retain its normal appearance for a long time. Pigment and choroidal vessels become reduced and vanish from the atrophic part, which ultimately shows a whitish, glistening field with a few scattered pigment masses. This defect or atrophy may in some cases spread as far as to the periphery of the fundus. In other cases a rim of comparatively normal appearance is seen. This rim, or the remains of it, has been described in choroideremia and in gyrate atrophy.

Most authors claim that normal appearance of the retinal vessels is retained, whereas others, *inter al.* E. Fuchs, that they may be contracted almost to invisibility.

The optic discs have in most cases been described as normal, whereas E. Fuchs and Beckershaus state them to be yellow as in retinitis pigmentosa, and Bencini (1938) to be rose-coloured.

The earlier published records thus offer several common features: familial occurrence, night-blindness, reduction of central vision, defect of the visual field and defect or atrophy of the central part of the fundus, an area around the macular region and a peripheral rim excepted.

The varying descriptions of these conditions in different publications make it difficult to classify them. The characteristics which have been thought to distinguish the two conditions, atrophía gyrata and choroideremia, from one another are not always convincing. The efforts of the various text-books to describe the clinical picture of the two conditions give clear evidence of this difficulty.

The question will then be whether this difficulty can be explained on the basis of the available literature and the present material.

The conditions being rare, few students have had a chance to see many cases. If that should happen, they belong as a rule to the same family and the same generation and are of nearly equal age. It has, therefore, not been possible to observe the progressiveness of the disease. The insidiousness of the initial symptoms prevents an early diagnosis, and the condition has, therefore, never been followed from its beginning. The information given is often somewhat unsatisfactory, and one lacks illustrations of the findings. Therefore, a comparison between the individual cases is often impracticable. There is often no information as to whether the examination has been made in mydriasis and it is just in these cases that it is important to study the peripheral fundus findings in order to make a differential diagnosis between atrophía gyrata and choroideremia.

It has been mentioned that some of the cases are associated with myopia, and it is possible that enough attention has not been paid to the atrophic changes for which the myopic condition itself is responsible.

Further the pigmentation of the fundus is known to vary in light- and dark-complexioned individuals, so that even this factor has to be considered.

Accurate familial investigations are lacking. It is often merely mentioned that no other member of the family is suffering from the disease, or that no consanguinity has been found.

The close connection between these two conditions and retinitis pigmentosa has been a constant source of confusion. Thus Leber (1877) has classified Mauthner's case as an extreme retinitis pigmentosa.

Reports of the examination of the visual fields are seldom supplied with charts.

The presence of night-blindness has as a rule been reported, without any information as to how this has been demonstrated.

Accordingly the publication of every new investigation into these rare conditions seems justified.

First an attempt will be made to give a clinical picture, based on the present material, consisting of a family with 4 affected brothers, aged 27, 38, 44 and 46 years. Next this will be compared with the earlier descriptions to such an extent as is possible.

The present work will possibly contribute to the solution of some of the problems arising in connection with earlier publications with varying titles: choroideremia, atrophy of choroid, retinitis pigmentosa atypica, retino-choroidal atrophy, deficit of choroidea, congenital absence of choroidea with retinitis pigmentosa, congenital deficit of choroidea, etc.

On account of the familial examinations journeys have been made to Solör, the home of most members of the family. Investigations have also been made to the Public Register in Hamar and at the Parish Register.

Dark-adaptation has been examined by means of a biophotometer. The procedure has been: adaptation to dark for 20 min., then adaptation to light for 10 min.

The illustrations of the fundus oculi have been drawn by A. Scheen, Oslo. To include also the peripheral part of fundus, the picture of the central part has been somewhat condensed. The changes in the fundus being decidedly symmetrical in both eyes, the picture of more than one eye from each patient has been considered unnecessary.

Case reports

General examination of the members of the family in question has revealed no other disease nor defect that might be suspected of having a connection with the mentioned eye-condition. All members of the family seemed normally equipped mentally. They were well-built and healthy-looking. Wassermann reaction was negative in the four affected brothers. Neither did the information of causes of death in the family suggest any prevailing familial disease that might be connected with the eye-condition. General examination of the diseased eyes has offered no pathological finding, apart from those in the fundus. The lenses were clear in all the patients. Transpupillary illumination showed a glistening white reflex from the central part of the fundus. Tension was normal in all. All examinations have been made in maximal

mydriasis. The patients were dark-haired and with brownish complexion.

Case 1. I.H., born March 24, 1915, aged 27 years.—The first trouble noted by the patient was difficulty in finding his way home after dark. There was a marked difference between himself and his working companions. He felt inclined to believe this night-blindness to have been present ever since he was a child, but was sure it was there at twenty. He was an average pupil of the preliminary school and reading caused him no trouble. He served his military term as a common soldier. He was working in the woods, and in his work he had no inconvenience from his eyes. He had noticed a slight peculiarity, however, namely that when he was looking for any small object, the location of it took him a considerable time. He had in a way to search for it with his eyes. He had noticed no flickering nor photopsias. Vision, he believed, was still good during day-time, but the diminution of night-vision was troublesome.

Status praesens 5/1/43 :

Fundus o. dext. Plate I, Fig. 1.

The optic disc is of normal colour and appearance. Temporally it is surrounded by a narrow white halo. The retinal vessels seem normal. Centrally in the fundus there is a somewhat irregular area measuring about 3 disc-diameters, striking because of its reddish colour in the otherwise whitish annular zone surrounding this area and the optic disc. The appearance of this macular area is practically normal. Temporally it has a somewhat irregular brownish pigment-border with some projections. Otherwise it shows some scattered pigment spots, somewhat more densely accumulated in macula proper. Peripherally there are some traces of choroidal vessels. The borders towards the disc are more diffuse with even transition into an atrophic area with fine pigment granules, specially above and below the disc. Several choroidal vessels are seen in the atrophic part between the disc and the macular region.

This maculo-papillary region is surrounded by a whitish annular zone, varying in width, and peripherally limited by an irregular pigment-border with long pigmented projections into the light annular zone. In turn these may communicate with irregular pigment-masses in the light zone, thus forming lagoon-like designs. Pigment is totally lacking in a great part of this annular zone, and the white sclera is seen shining through. Specially on the nasal side a great part of the choroidal vessels is obliterated, only a few contracted ones remaining in some places. Between the peripheral border in the fundus and the macular area, however, some thick choroidal vessels are seen crossing the white zone.

PLATE I

FIG. 1.

Atrophia gyrata choroideae et retinae. Fundus o.d. Case 1, I.H.,
aged 27 years.

FIG. 2.

Atrophia gyrata choroideae et retinae. Fundus o.d. Case 2, O.H., aged 38 years.

FIG. 3.

Atrophia gyrata choroideae et retinae. Fundus o.d. Case 3, S.H., aged 44 years.

FIG. 4.

Atrophia gyrata choroideae et retinae. Fundus o.d. Case 4, E.H., aged 46 years.

This whitish zone is surrounded by a rim of apparently normal fundus. It is somewhat wider temporally than nasally and centrally it is limited by the above mentioned pigment-border with its projections. The part immediately outside the peripheral border, however, is slightly greyish with irregularities of pigmentation and of atrophic appearance. Near the border the choroidal vessels from the whitish annular zone are distinguishable.

The picture of fundus o. sin. is practically the same. The optic disc and the retinal vessels must be described as normal. The reddish macular area is somewhat larger and more irregular, but otherwise showing the same properties as the right side. Except on the nasal side this area is everywhere surrounded by a pigment-border. The same whitish annular zone is seen surrounding the maculo-papillary region, that peripherally is limited by a pigment-border with projections, showing the same tendency to lagoon-formation. Scattered in the white zone, particularly around the optic disc and between the macular region and the disc, are some larger pigment masses and dust-like dots. The choroidal vessels are highly reduced, a few thick ones still persisting temporally in the zone, specially in connection with upper and lower part of the macular region. The peripheral rim is present, and is of the same appearance as on right side.

Visus : o.d. : 5/5, o.s. : 5/5.

Fields of vision : See Chart, Plate II, Fig. 1.

Sense of colour : Normal according to Ishihara.

Night-vision : See text-fig. 2, p.838. Reduced.

Case 2. O.H., born August 20, 1904, aged 38 years.—The first symptom of eye-trouble noticed by the patient was that his vision in the dark was not as good as that of his friends. He believed night-vision to have been reduced since his early youth, and was certain of it at twenty. He had served his military term, and at that time noticed nothing wrong with his vision. 5 years ago he noticed that his vision had become diminished also in day-time. This had gradually grown worse, so that now he was afraid he would have to give up working in the woods. He was able to read only for a short while at a time and by good light. He had never noticed flickering before his eyes nor photopsias.

Status praesens 7/1/1943 :

Fundus o. dext. See Plate I, Fig. 2.

Colour and appearance of the optic disc are normal. It is surrounded by an atrophic halo. The retinal vessels seem normal. Corresponding to the part around the macular region there is an oval, about 1 x 3 disc-diameters, greyish-red area. Appearance of its temporal part is that of normal fundus, whereas the nasal part

is greyish. Temporally this area has a brownish pigment-border. Corresponding to the macular region proper there is a somewhat denser accumulation of pigment. A bundle of thick choroidal

Plate 11

Visual Fields in *Atrophia gyrata*
Chorioideae et retinae. Obj. 5/330.

Fig. I.- Case 1, I. H., 27 years.

Fig. 2.- Case 2, O. H., 38 years.

vessels lead to the upper and lower pole, and stand out sharply against the whitish sclera. Apart from this maculo-papillary region, the entire central fundus is occupied by a glistening white

annular zone, where, besides the mentioned choroidal vessels to the macular region, only scattered and contracted choroidal vessels and a few smaller or larger pigment-masses are seen. This whitish annular zone is peripherally limited by a border of pigment with irregular projections, capable of forming lagoon-like designs. The peripheral rim in the fundus is present. Close to the pigment-border the fundus contains rich amounts of small pigment-masses, and is somewhat greyish and pale. Otherwise it resembles the normal fundus. Width of the rim is about the same as in Case 1.

Fundus o. sin. The picture of the fundus is practically identical with that of the right eye, making a detailed description superfluous. Disc and retinal vessels appear normal. The macular area has an oval shape and greyish-red colour, with scattered pigment-masses, somewhat denser in the macular region proper, and a more closely-knit bundle of choroidal vessels lead to the upper and lower poles of the region. The central part of fundus is for the rest a glistening white with very few and contracted choroidal vessels. There are scattered masses of pigment. The zone is peripherally limited by a similar pigment-border as on the right side. The peripheral rim in the fundus is somewhat greyish and atrophic with some pigment-masses near the border, but otherwise apparently normal.

Visus: o.d.: 5/50, o.s.: Counting fingers at 3 m.

$0^\circ + 0.5 \div 3 \frac{5}{10}$; $0^\circ + 1 \div 3 \frac{5}{50}$.

Fields of vision: See Chart, Plate II, Fig. 2.

Sense of colour: Normal according to Ishihara.

Night vision: See Text-fig. 2, p. 838, Highly reduced.

Case 3. S.H., born July 19, 1898, aged 44 years.

The first eye-trouble noted by the patient was difficulty in seeing in the dark. He was unable to determine the time when this began nearer than to early youth. He had served his military term as a common soldier. At thirty-seven he knew for certain that his vision had become diminished also in day-light. Since then his eye-sight has steadily diminished. He worked in the woods, and his eye-sight was now interfering with his work. He had been an active hunter, but had to give it up 5 years ago. He could read big print only. He had never noticed flickering before his eyes nor photopsias.

Status praesens 5/1/43:

Fundus oculi dext. See Plate 1, Fig. 3.

Colour and appearance of the optic disc are normal. It is surrounded by a peripapillary halo. The retinal vessels are of normal appearance. Corresponding to the part around the macular region there is a triangular, faintly greyish area. By a projection

its temporal corner is connected with the peripheral rim of the fundus. This area has a slightly pigmented border, and scattered over the triangular space there are fine pigment-masses with a denser accumulation corresponding to the macula proper. The macular region is distinctly atrophic, the underlying choroidal vessels faintly visible. Some choroidal vessels enter this region from the periphery, especially to the upper and lower part. Below this triangular space there is a larger dark brown pigment-mass with several sharply outlined round holes, through which the white sclera is visible. At the bottom of these holes a few choroidal vessels are seen. Outside these areas the central fundus is occupied by partly glistening whitish areas with no or few and contracted choroidal vessels. Scattered over this whitish annular zone are small pigmented masses or greyish areas. Also some larger pigment-masses are seen, partly communicating mutually, partly with the peripheral pigment-border, thus forming lagoon-like designs. The peripheral rim, present also here, is centrally defined by a distinct pigment-border. Peripheral to the pigment-border the rim is greyish-brown with scattered pigment-masses and is distinctly atrophic. At the extreme periphery the rim is of a brighter reddish colour, but even here it cannot be described as normal.

Fundus o. sin. The picture seen here is mainly the same as on right side. The macula area is somewhat larger and more irregular with pigmented projections communicating with the pigment-border of the peripheral brim. The macular area is surrounded by a pigment-border and has a greyish-red colour and fine pigmented spots, densest in the macular region proper. A bundle of thick choroidal vessels is seen leading to the upper and lower parts of the macular region. Otherwise there is a similar central annular zone with glistening white parts and pigment-masses with lagoon-forming projections. The peripheral rim in fundus is like that in right eye.

Visus: o.d. 5/20, o.s. 5/50.

Barely passing Schiötz reading test 1/20 with right eye.

Fields of vision: See Chart, Plate III, Fig. 3.

Sense of colour: Apparently good according to Ishihara.

Night-vision: See Text-fig. 2, p. 838. Highly reduced.

Case 4. E.H., born December 22, 1895, aged 46 years.

In early youth already the patient noted that his vision after dark was not so good as that of his friends, but he was unable to fix the time for the beginning. At twenty his vision was reduced also in day-light, and at thirty-five he was no longer able to read. Since the age of forty he has been blind. He has never noticed flickering before his eyes nor photopsias.

Plate '111

Fig. 3.- Case 3, S. H., 44 years.

Status praesens 5/2/43 :

Fundus oc. dext. Colour and appearance of the optic disc are normal. It is surrounded by an atrophic halo. The retinal vessels are possibly somewhat contracted. A greyish-brown, about disc-sized area is here seen around the macular region, with a few choroidal vessels to the upper and lower pole. Above and below this macular area there are some greyish-brown parts with some lighter streaks and lines, interpreted as remnants of atrophied choroidal vessels. The macular region is changed, having lost all its normal structure. Otherwise the entire central part of fundus is whitish and glistening, with scattered pigment-dots and a few larger masses, particularly in the vicinity of the optic disc. The choroidal vessels are mostly obliterated, leaving a few contracted ones in the extreme periphery of the white zone. The peripheral rim is present, but narrower than in the other patients, and more greyish-pale, atrophic. Centrally it is limited by a pigment-border, somewhat less prominent than in the others. The pigmented, lagoon-forming projections are seen also here.

Fundus o.s. The picture being identical to that of right eye; further description is considered unnecessary.

Visus : Reduced to mere perception of light o.u.

Family investigations (See pedigree, Plate IV)

The disease is demonstrated in 4 brothers in a family of 9 children, 6 men and 3 women. The brothers and sisters of the patients and all their children have been examined and found normal. The only child of one of the patients (2, O.H.), a boy of seventeen, was normal. Mother of the patients (M.H., Gen. IV) has been examined. She was 70 years old, and was not suffering from night-blindness. Central vision 5/5 o.u. Fields of vision

PLATE IV.

Pedigree demonstrating the family with four cases of atrophía gyrata choroideae et retinae.

⊙ examined. ● affected.

were normal. The optic discs were surrounded by white atrophic haloes with a few choroidal vessels (see Text-fig. 1). This finding was read as a senile atrophy, and is specially mentioned here because similar findings have been described in literature (Bencini), and it will presently be discussed.

Father of the patients (O.H., Gen. IV) was 69 years old and had normal eyes. His sister (O.F., 64 years old) and her 10 children have all been examined and their eyes found normal. M.H., Gen. IV, was one of a family of 5, of whom 3 are dead at 64, 25 and 26 years of age. None of these were known to have had eye-trouble. The surviving sister and all her descendants were normal.

The direct line of ascendants of M.H. and O.H. has been followed for 3 generations, information being sought in the parish

and public registers and from the living members of the family, without evidence of eye-diseases in any of these individuals being found. Neither has consanguinity of M.H. and O.H.'s families been demonstrated. The possibility of existing blood-relationship cannot be excluded, however, on basis of these investigations,

FIG. 1.

Atrophic halo around the optic disc. M.H., mother of the patients (drawing by the author).

specially including ascendants in direct line. But all members of the family denied the existence of such connection between the two families. M.H. and O.H. came from communities far apart.

Thus the disease has been demonstrated in 4 brothers, but neither in their ascendants nor descendants.

Clinical picture

Histories and clinical pictures of the 4 brothers are strikingly uniform. The first symptom of the condition is night-blindness. The patients are unable to fix the time for its beginning, but as a rule state that it has been present since early youth. The youngest patient (Case 1. I.H., aged 27 years) declares that his night-blindness probably commenced when he was a child, but he was sure of its presence at twenty. Table I below gives the time when night-blindness and diminished central vision were noticed by the patients, and vision at the time of examination.

The table gives evidence that night-blindness is the initial symptom, being noticed by the patient before the reduction of central vision. Thus the 27 years old I.H. has still normal vision. The other patients have noticed diminished vision at 33 and 37 and

TABLE I

Age at time of examination—beginning of night-blindness and reduced vision—central vision in atrophía gyrata choroideae et retinae.

Case	Age	Patients noticed :—		Central vision
		Night-bl.	Red vision	
1.	I. H., 27 years	In childh.	Gives normal vision	O.d. : 5/5, o.s. : 5/5
2.	O. H., 38 years	At twenty	At thirty-three	O.d. : $0^{\circ} + 0.5 \div 3 : 5/10$ O.s. : $0^{\circ} + 1 \div 3 : 5/50$
3.	S. H., 44 years	In youth	At thirty-seven	O.d. : 5/20, o.s. : 5/50
4.	E. H., 46 years	In youth	At twenty	Amaurotic at forty

20 years. In case 2, O.H., diminished vision has been demonstrated objectively at 38 years, and in case 3, S.H., aged 44 years. He is now barely able to read big print, and is having trouble with his eyes when working in the woods. Case 4, E.H., aged 46 years, has been blind since the age of 40 years.

None of the patients has noticed flickering before his eyes nor photopsias.

Determination of the time for onset of the disease must essentially be based on the patients' statement that night-blindness commenced in childhood or early youth.

The actual changes in the fundus oculi show great uniformity in the 4 patients, the only variations demonstrable being supposedly due to progress of the disease. The changes are also mainly symmetrical for both eyes.

The optic discs are of normal appearance. So are the retinal vessels, Case 4 excepted. This patient is blind, and the retinal vessels are here somewhat contracted. The macular region seems to remain normal for a long time, presenting the picture of a more or less reddish island in the otherwise whitish and glistening central fundus. This macular area is in most cases surrounded by an irregular brown pigmented border. Within the area there are scattered pigment-dots, often somewhat denser in macula proper. With age it becomes concentrically reduced, gradually assuming a more greyish-brown colour, until, as in the 46 years old patient (Case 4, E.H.) merely an irregular greyish-brown patch remains.

In connection with the macular area there are some choroidal vessels, specially around the upper and lower part, and from here crossing the whitish atrophic zone toward the periphery. Number and calibre of these vessels decrease with age of the patient. In the eldest brother (see Plate I, Fig. 4) only a few thin ones remain. Near the macular region in this patient there are some whitish lines in a denser accumulation of pigment-masses. These lines are undoubtedly attributable to obliterated choroidal vessels.

The central part of fundus, apart from this macular area, is essentially changed into a more or less glistening, white annular zone, peripherally limited by a narrow retino-choroidal rim. Besides the above mentioned choroidal vessels, the younger patients show, specially in the macular region, also a few scattered ones in the whitish annular zone. These vessels become reduced with advanced age, until they show nearly complete obliteration in the oldest patient. Scattered pigment-dots and masses are found also in this zone. A number of pigmented projections from the peripheral rim show a tendency to lagoon-formation. The position of the pigment-masses and projections suggest an earlier connection between these. The described pigment formations present a highly irregular picture, different from the more regular "bone-corporuscle cells," of retinitis pigmentosa. Also the pigment-accumulations seem to become reduced with advance of the patient's age.

The retino-choroidal atrophic zone widens in the course of years, essentially through contraction of the macular area, but also at the expense of the peripheral rim.

This retino-choroidal rim is seen in the extreme periphery. In the younger patients the rim, close to the border, is somewhat greyish-atrophic with a few dots of pigment. Otherwise it is normal. In the oldest patients it is possibly all atrophied. Width of the rim is also somewhat reduced in the oldest patients. An estimation of this part, however, is admittedly difficult, even in good mydriasis.

Transpupillary illumination, as it has been mentioned, gives a white reflex corresponding to the annular zone in the fundus. The lenses are clear in the 4 patients.

Sense of colour is normal.

Adaptation to dark is greatly reduced. (See Fig, 2, demonstrating curves for the 3 examined cases, and a normal curve.)

The fields of vision show characteristic changes in accordance with the changes demonstrated in the fundus oculi. The defects of the visual fields are mainly symmetrical in the two eyes (see Plates I and II). The peripheral parts are normal, but all cases show

FIG. 2.

Atrophia gyrata. Curves for dark-adaptation. Biophotometer. Adaptation to dark for 20 min., followed by 10 min. exposure to light before examination.

almost absolute annular scotomas. These widen with the advance of age, partly through peripheral spreading, but essentially through contraction of the central parts. In S.H., aged 44 years, they remain only an area inside of 10° .

The condition is familial, being demonstrated in 4 brothers of a family of 9 children. It has neither been traced to their ascendants nor descendants. Consanguinity of the parents has not been demonstrated here. The condition is probably due to a recessive gene, a possibility that will be more closely discussed in the following.

Discussion

The picture presented by the 4 patients is unquestionably that of a clinically uniform and progressive chorio-retinal condition, answering the diagnosis of *atrophia gyrata choroideae et retinae*. Discussion of the differential-diagnosis with regard to the various

types of retinitis pigmentosa, retinitis albescens, coloboma retinae, etc., has been considered superfluous.

As already mentioned, the finding by several authors (Jacobsohn 1888, Beckershaus, Böhm, Smith and Usher 1916, and Zorn 1919), of retinitis pigmentosa within families where chorioideremia and gyrate atrophy have been demonstrated, has caused much confusion around these conditions. If so, it may be questioned whether the latter conditions and retinitis pigmentosa occur independently, or whether there exists a more intimate connection between them. This question is difficult to answer on account of the often unsatisfactory information given in descriptions of the cases. Jacobsohn has thus named his case "retinitis pigmentosa atypica," Leber (1877) has characterised Mauthner's case as an extreme retinitis pigmentosa, whereas Nettleship (1908) considered a connection between these conditions and retinitis pigmentosa improbable.

Chorioideremia is the condition most commonly described in connection with retinitis pigmentosa. Somewhat strange, however, seems Beckershaus' finding of a yellowish-white optic disc and "fadendünn" retinal vessels in this 33 years old patient in a family where retinitis pigmentosa had been demonstrated. This also applies to Böhm's case, in which the optic disc was pale and the retinal vessels contracted.

It will be emphasised in this connection that no case of retinitis pigmentosa has been found in this examined family, where the clinical picture is unmistakable.

Beginning of the disease. Determination of when and how the disease has commenced, has not been possible on basis of the present material. The appearance of night-blindness proves that it begins in early youth. Usher (1935) states the age of his youngest chorioideremia patient to be 14 years. Average age of the patients at the time of the diagnosis was 27.45 years for chorioideremia, and 17.36 years for gyrate atrophy. Werkle has shown gyrate atrophy in a patient aged 10 years. When and how the condition has begun has therefore never been stated. Thus these factors offer no certain clue to the recognition of various types of the disease.

In the present cases the condition has been followed from the age of 27 to 46 years, and a steady progression has been observed. Even in the 27 years old patient (Case 1, I.H.) considerable changes were demonstrated in the fundus, in spite of the relatively inconsiderable subjective symptoms. Judging by this development, the first beginning must have taken place very early in life.

The changes in the fundus oculi are mainly symmetrical in the

two eyes, and similar in the 4 patients. The demonstrated variations must be attributed to progress of the condition. Comparing the changes in the fundus in the present material to earlier descriptions is rather difficult, because of the often unsatisfactory information given. Bedell's statement, quoted in the introduction, may seem justified. A number of reports show accordance with findings in the present cases, but others show great variations.

It must be kept clearly in mind, however, that the question is of a homochronous condition with a progressive course, and that other factors, *e.g.*, excessive myopia and the patient's complexion may influence the phenotype of the disease. Also other ocular conditions and eventual diseases may partly be traced in the picture.

The atrophic changes in the present cases are localised to a certain part of the fundus. This cannot be expected to be alike for all cases, and evidence of variations on this point is found in the literature. Thus McGuire (1932) in an 11 years old patient with atrophía gyrata, has found atrophy of the extreme part of fundus. Cutler (1895) found an atrophic zone around the optic disc, then a normal annular zone and more peripherally another atrophic zone. (Cutler's patients are the same ones that have been described by E. Fuchs.) In such cases the total clinical picture will be decisive for the diagnosis.

In the present cases there has been found a more or less normal looking chorio-retinal rim. This finding varies in the literature and it can therefore not be considered characteristic for those cases considered as atrophía gyrata. This rim, or parts of it, has also been mentioned in cases described as choroideremia or total atrophy. (Alexander 1910, Connor 1919, Zorn, Wolf (1930), Parker and Fralick 1931, Smith and Usher 1916, and Bedell). Neither does this point seem to make a difference between the two described types, which is also in accordance with the findings in the present material. Continued atrophy in the oldest patient is here believed capable of causing complete disappearance of the rim, thus at this stage justifying the diagnosis of choroideremia. In this patient the peripheral rim was already at forty-six hardly detectable even in good mydriasis.

Choroideremia having been described as a defect or malformation, progress of the condition might *a priori* be thought particularly prominent in gyrate atrophy. Not even this factor makes a distinction between the two types possible. Alexander has thus observed progressiveness in "congenital absence of the choroid." Usher and Smith (1916) have described choroideremia in a 24 years old patient. On re-examination 19 years later there was found

striking progress of the condition. Usher (1935) himself says that gyrate atrophy would probably have been found on examination at an earlier stage. Also the finding on first examination of "dark red areas at the extreme periphery of the fundus" is worthy of notice.

Wernicke has observed definite progressive changes in a case of atrophía gyrata. He further found a picture resembling that of atrophía gyrata in the right eye and of choroideremia in left eye. Werkle has studied the condition in two brothers, aged 10 and 20 years, and in another patient aged 50 years, and does not disregard the possibility of the two types representing different stages of an identical disease. Neither has the study of earlier descriptions nor of the present material revealed peculiarities in the changes of the fundus capable of characterising the two types.

Normal retinal vessels and optic discs have been demonstrated in most descriptions of both types, whereas changes have been mentioned in some cases. Reference is here made to what previously has been written (*v.s.*), and only the finding in the present cases of normal discs and retinal vessels recalled. The latter have possibly been somewhat thinner than normal in the oldest patient. In patients where retinitis pigmentosa and choroideremia with papillary and vascular changes have been found in the same family, reliability of the diagnosis may possibly be questioned.

Refraction. Myopia. Beckershaus believes myopia to form part of the picture of atrophía gyrata, using this factor as differential-diagnosis with regard to choroideremia.

Excessive myopia was present in the cases first described (E. Fuchs). Usher has in his studies of the earlier publications often found mention of myopia, also in choroideremia. In this condition myopia was found in 35 of 39 eyes, in 23 thereof not exceeding 3 D. Maximal myopia was -16 and -13 D. In atrophía gyrata 23 of 35 eyes were myopic, and in 17 of these the myopia exceeded 3 D. Maximal myopia was -18 and -20 D.

Myopia has been demonstrated in one case only of the present material (Case 2, O.H.), and here to a moderate degree. Accordingly the symptom of myopia can hardly be used for differentiation between the two types. On the other hand myopia may, *qua* such, with the consequent atrophic changes partly influence the clinical picture.

Fields of Vision. Few publications are supplied with charts. As a rule there is merely a mention of concentric contractions. From the literature Usher has found the following for choroideremia.: Fields of vision are concentrically contracted in 19 cases of 22, are full in 1 case, and in 2 there are no records; ring

scotoma in 3 cases. For atrophía gyrata he found: Fields of vision were full in 5 cases of 26, concentrically contracted in 16 cases, no note in 5, ring scotoma in 1.

The finding of more cases of ring scotoma in choroideremia than in atrophía gyrata is somewhat surprising. The opposite result might be expected.

Typical annular scotoma is found in all our cases, corresponding to the changes in fundus. The fact that annular scotoma in certain cases is easily overlooked, may be a possible explanation of this disagreement.

Also in Alexander's case of choroideremia annular scotoma has been shown, but this diagnosis was, as mentioned, possibly not quite reliable.

Obviously the fields of vision will change with development of the condition. Annular scotomata will be present in some cases, but are hardly capable of characterising various types of these conditions.

Central vision. The above Table I (p. 836) shows the reduction of vision to be considerable, and capable of causing blindness at forty. Long before this, however, the patients are greatly inconvenienced by the accompanying night-blindness and the reduced fields of vision. From the literature the reduction of vision is seen to be considerable in most of the reported cases. For choroideremia Usher thus finds: Of 34 eyes, vision below 6/60 in 9: for atrophía gyrata, of 35 eyes, vision was below 6/60 in 9. For both types the reports were: Vision ranged from 60/60 to p.l.

Sense of colour is normal in all the examined individuals, in accordance with reports from literature.

Night-blindness. The 4 affected persons have complained of night-blindness. This symptom is also constantly found in the earlier descriptions. Objective examination with biophotometer (see Text-fig. 2, p. 838) shows dark-adaptation to be greatly reduced in all patients.

Lenticular opacities. As already mentioned, all lenses were clear in the present cases of atrophía gyrata. Waardenburg (1939) claims posterior cataract to be a usual occurrence in atrophía gyrata, but rare in choroideremia. Usher reports opacities in the lenses in 29.41 per cent. of his choroideremia cases and in 58.6 per cent. of atrophía gyrata cases. Also this factor is of little use for the diagnosis of the different types.

Aetiology and pathogenesis. The condition is now known to be hereditary and thus connected with the genes. The description of the one type as a congenital defect or malformation and

the other one as an acquired atrophy is therefore incorrect. Both are congenital, but their presentation may vary. This is common in the so-called homochronous conditions.

As for the pathogenesis of the conditions it is only known that a gradual atrophy of choroid and retina takes place in the central part of the fundus. The choroidal vessels diminish and vanish, the pigment disappears essentially from the atrophic parts, being deposited along the borders as the process progresses. The starting point for the atrophy is unknown, but a glistening, white annular zone will gradually develop around the macular region and the optic disc. The process extends somewhat peripherally, but essentially it spreads through concentric contraction of the macular area. The appearance of the macular region remaining normal for so long a time, is explainable by an independent blood-supply of this region. The pigment-projections with their lagoon-like formations indicate a progressive process. In the eldest of the affected brothers (see Fig. 4, Plate I) distinct traces are seen of former choroidal vessels.

No pathologic-anatomical examination of this condition has been made.

Family investigations. Heredity. It has already been mentioned (p. 834), that family examinations including 6 generations, indicate a recessive mode of heredity.

Usher has collected the earlier results in this field, presented below in Table 2.

TABLE II

Demonstrating manifestations of choroideremia and atrophia gyrata within the families. (Usher, 1935).

Type	Number of cases	Number		Number of families	Consang. in No. of families	Appearance of the affected families in No. of generations
		M.	F.			
Choroideremia	22	21	1	19	0	All in one generation
Atroph. gyrata	26	15	11	14	5	{ 4 in 1 gen., 1 in 3 gen. 1 in 2 generations

Of 22 patients with choroideremia only 1 was female. They were all from one generation. 26 atrophia gyrata patients, distributed among 14 families, showed a female contribution of 11. In 4 families the patients were all from one generation, in 1 they are found in 3 generations (Werkle), and in 1 family in 2 generations (Jacobsohn).

In no case of choroideremia has consanguinity been demonstrated, whereas such relationship has been found in 5 of 14 families with atrophía gyrata (Cutler, Mori, Komoto, 1914; Böhm and Arganaraz, 1917).

The finding of consanguinity in 5 of 14 families with atrophía gyrata strongly indicates a recessive mode of heredity.

Where the condition has been traced through 2 and 3 generations, the information obtained is too scarce for further estimation. Werkle's work includes 13 night-blind individuals in 3 generations. Only 3 of these patients have been more closely described, and only 6 of 13 examined. The same uncertainty attaches to Jacobsohn's case. Manifestation of the condition in several generations is therefore not considered definitely proved.

The present material consists of 4 male patients. The above table shows choroideremia to be found mostly in males, while atrophía gyrata is more evenly distributed among the sexes. The possibility of gonosomal heredity suggests itself. However, the available information concerning the affected women's families is too vague for solution of this problem.

Benzini (v.s.) noticed an atrophic halo around the optic disc in the mother of one of his patients with choroidal atrophy, and therefore suggested that the condition might be dominant. As already mentioned similar findings have been made in the present material, but the atrophic halo has been considered a senile phenomenon.

Waardenburg (1939) reported a case of atrophía gyrata choroideae et retinae and stated:

1. Consanguinity in the families is found in 40 per cent. of atrophía gyrata and never in choroideremia.
2. Cataracta posterior is common in atrophía gyrata, but is very seldom in choroideremia.
3. In atrophía gyrata females are often affected, but in choroideremia only in 1 of 22 cases.

It seems evident from what is said in the above discussion and from the statements in the present material that these signs are not reliable in differentiating between distinct types of this disease.

Therapy. No effective method for dealing with the condition itself is known. But the patients' families should be told of the eugenic measures for preventing further distribution of the condition. They should then be informed of the laws of heredity for recessive conditions. Preferably, neither the patients themselves, nor their brothers and sisters should have any children. If any of them should wish to marry, he or she should be told of the danger of intermarriage.

In the present cases the patients themselves have seen the responsibility conveyed by the heredity of this serious disease, and have accepted its consequences. Case 2, O.H., was married and had a child already at the time of examination. This latter (aged 17 years) was normal on the last examination. The other patients have remained unmarried.

Conclusion

Homogeneity of the clinical picture and progress of the disease in the 4 affected brothers have been shown. The progress of the process in these patients is so marked that on further development it must be presumed to result in total atrophy of choroid and retina. The condition has been established at an age of 27, but considering its appearance at this age, compared to the development observable in the patient of 46 years, its beginning at a very early age seems probable. This also agrees with the hereditary nature of the condition.

The clinical picture presented has been found corresponding to the term *atrophia gyrata choroideae et retinae*, the annular atrophy in the central part of fundus being its most conspicuous symptom.

One has compared this clinical picture with those described in the literature as far as this has been possible on account of inadequacy of earlier descriptions. Comparison of the symptoms, one by one, has revealed no certain evidence of these conditions representing two different types: choroideremia or *atrophia gyrata*.

Here the clinical picture of the disease *atrophia gyrata* is given, and until a distinct clinical picture of choroideremia, different from this is stated, it can not be justified to continue regarding them as different diseases.

Summary

The present work gives the clinical description of *atrophia gyrata choroideae et retinae* in 4 brothers.

First a review is given of earlier problems in connection with this condition. Earlier literature has specially discussed whether *atrophia gyrata* and a condition described as choroideremia should be regarded as two different diseases, or whether they merely represent two developmental stages of an identical disease. Reference is here particularly made to statements by Duke-Elder and Bedell, clearly showing the clinical picture of the two conditions to be far from clarified.

A number of reports, possibly responsible for this uncertainty, are pointed out.

Next follows a clinical description of 4 male patients belonging to the same generation (27, 38, 44 and 46 years old), the clinical

picture of whom is seen to answer to the description atrophía gyrata choroideae et retinae. There are further coloured illustrations of the changes in fundus oculi, charts showing the fields of vision, a diagram showing the results of biophotometrical examinations of dark-adaptation and there are family investigations with a pedigree.

The examinations show a uniform clinical picture in the 4 brothers, the only demonstrable variations being attributable to progress of the condition with the advance of age. Considering the development of the condition in these patients from an age of 27 to 46 years, its first beginning at an early age seems probable. It seems reasonable to presume that continued development of the condition would result in total atrophy of choroid and retina causing the picture to resemble that of choroideremia. On basis of the present cases, however, the annular atrophy in the central part of fundus has been found to be the most prominent symptom, and the clinical picture answering the term of atrophía gyrata choroideae et retinae.

In an attempt to establish symptoms capable of characterising different types of these conditions, the clinical descriptions of the 4 patients and their symptoms have been compared, one by one, to those found in the literature. The comparison has been complicated by the often somewhat unsatisfactory descriptions. However, nothing has been found to justify the continued classification of the two conditions: atrophía gyrata and choroideremia, into two different types. This does away with the earlier conception, mentioned in the introduction, of the former being an acquired, progressive degeneration (atrophy) and the latter a chorio-retinal defect or malformation.

This is also in accordance with the fact that a division into different types has not been possible on basis of heredity, both types apparently being due to recessive genes.

Finally the eugenic measures have been mentioned, that ought to be taken to prevent further distribution of the condition.

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INTRA-OCULAR PHAKOMATA—A REPORT OF THREE CASES*

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IN 1932 van der Hoeve grouped the syndromes of Bourneville, of von Hippel and Lindau, and of von Recklinghausen under the title of the "phakomatoses." Later the syndrome of Sturge-Weber was added, making a fourth.

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