On a case with a tumour in each orbit : death, necropsy.

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MICROPHTHALMOS.

By E. Treacher Collins.

(With Plate IV.)

Conditions of the eye which differ considerably have been included under the term microphthalmos; roughly they may be divided into two classes. First, those in which the eyeball is simply abnormally small, *i. e.* very highly hypermetropic eyes, in which, beyond the defect in size there has been no arrest in development. Secondly, eyes which besides being small, have some other congenital abnormality, resulting from imperfect closure of the fœtal ocular fissure. This last class, of which I have specimens to bring before you this evening, may again be divided into, those where the defect is slight and where the eyeball retains nearly its normal shape, and those in which the accompanying abnormality is very gross, the eye being usually exceedingly small, while connected with it are one or more cysts. These cysts are often large, concealing the globe which is situated at the back of the orbit, so that its presence cannot be ascertained by clinical examination alone; hence these cases have been frequently spoken of as cases of anophthalmos, a term which is not of course, strictly speaking, applicable to them.

The following is a detailed account of my cases and the pathological examination of the eyes.

Case 1.—The two abnormally small eyes of an infant were kindly given to me for examination by Mr. Lang. The child had died when four days old from congenital heart disease; the aorta and pulmonary arteries formed one

common trunk, and there was a deficiency in the ventricular septum.

Pathological examination of the right eyeball.—It measures 19 mm. antero-posteriorly and laterally, and 18 mm. vertically. The cornea measures 9·5 mm. laterally and 8·5 mm. vertically. There is a small prominence in the sclerotic posteriorly, immediately below the optic nerve. The iris is well developed, several delicate fibres stretch across the pupil from its small circle on one side to a corresponding position on the other; these are evidently remnants of the pupillary membrane. The ciliary body presents its usual appearance. The lens is in its normal position. The vitreous appears healthy. The retina has numerous little rucks in it. At the seat of the prominence below the optic nerve, there is a gap in the sclerotic, through which a fold of retinal tissue projects.

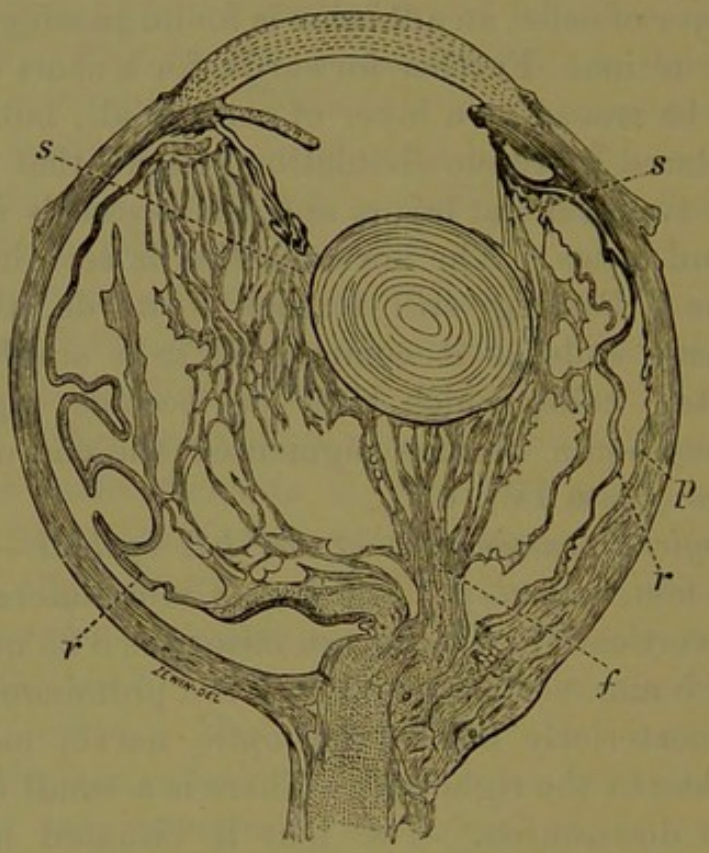
Microscopical appearances of the posterior half of the right eyeball.—No central blood-vessels can be seen in the optic nerve. The nerve-fibres after having passed through the lamina cribrosa all slope somewhat downwards; the upper ones afterwards curve backwards to the upper part of the retina. Below the optic nerve there is at first no retina, no uveal pigment layer, and no choroid, only a mass of nerve-fibres with fibrous tissue external to them. This fibrous tissue, representing the sclerotic, has a short distance from the lower margin of the optic nerve a break in its continuity. Into the gap thus formed the nerve-fibres pass, expanding somewhat after they have got through it, and becoming mixed with bodies like those found in the nuclear layers of the retina; external to this nerve tissue is a thin layer of fibrous tissue. On the side of the gap in the sclerotic furthest from the nerve, the retina commences with its usual layers, being continuous with the nerve-fibres emerging from the gap; round the edge of which also the uveal pigment layer turns. Tracing the tunics of the eye forwards from the break in the sclerotic, the retina is at first seen to possess its usual layers, the uveal pigment is present, also the choroid,

which, however, is more cellular than normal, and devoid of pigment. A short distance further on the choroid ceases and the uveal pigment layer becomes an unpigmented layer of cells; an adhesion is found passing between it and the retina. Further forwards, for a short distance, it cannot be traced as a layer of cells at all, but is apparently replaced by tissue simulating retina—that is, tissue which has two granular layers and blood-vessels in it, but no rods and cones. The normal retina is seen internal to this tissue. Passing still further forwards, the outer retinal tissue ends as it commenced in a single row of unpigmented cells, which later on become pigmented. Where they again become pigmented the choroid again commences (Plate IV).

Pathological examination of the left eyeball.—It measures 17 mm. antero-posteriorly, 18 mm. laterally, and 16·5 mm. vertically. The cornea measures 8·25 mm. laterally and 7·5 mm. vertically. There is a prominence in the sclerotic posteriorly below the optic nerve, more pronounced than in the right eye. There is a small coloboma of the iris downwards. The lens is situated nearly in the centre of the globe, a considerable space being left between it and the posterior surface of the iris; it is almost round in shape, measuring 5 mm. antero-posteriorly and 5·5 mm. laterally. The ciliary processes, thin and much elongated, pass almost directly backwards towards the sides of the lens. In the centre of the vitreous is a band of fibrous tissue, which passes forwards from the back of the globe below the optic nerve to the posterior pole of the lens; this band is broad posteriorly, and gradually tapers off as it passes forwards. Around this central band the vitreous appears normal. The retina has some small rucks in it. Below the optic nerve, in the situation of the prominence seen externally, a fold of retina seems to be included in a gap in the sclerotic.

Microscopical appearances of the left eyeball.—The structure of the cornea appears normal. In the position of the coloboma of the iris, the uveal pigment ends about

on a level with the point of termination of Descemet's membrane in the fibres of the ligamentum pectinatum.



Semi-diagrammatic section of left eye of Case 1. *s*. Suspensory ligament of lens stretched and attached to elongated ciliary processes. *r*. Retina much folded. *f*. Fibrous tissue in centre of vitreous holding lens back. *p* points to pigment epithelial layer at the position where it ceased to be pigmented and where the choroid ended.

The fibres of the ligamentum pectinatum below are numerous and widely separated; many of them pass into what may be considered the anterior surface of the rudimentary iris. The fibres of the suspensory ligament, passing from the much elongated ciliary processes, slope backwards and a little inwards to the sides of the displaced lens. The cells lining the capsule of the lens cease above in the usual position, and the nucleated zone presents there its normal appearances. Below, the nucleated fibres, instead of running concentric with the capsule, pass directly inwards at right angles to it. In the lower and posterior part of the lens substance, there

is a group of nucleated cells resembling squamous epithelial cells. The ciliary body, choroid, uveal pigment, and retina in the upper part of the eye appear healthy. In the lower part the ciliary muscle is much elongated, and the choroid can only be traced backwards as far as the equator of the globe, its posterior part being absent. The uveal pigment layer just previous to the termination of the choroid is thrown into several folds; from this position it is continued backwards, first as a layer of unpigmented cells and afterwards as tissue which looks like degenerate retina. The band of tissue passing through the centre of the vitreous is composed of bundles of nucleated fibres, with small blood-vessels coursing amongst them; it is adherent posteriorly to the sclerotic, and anteriorly, where it is very thin and reduced to but a few fibres, it joins the posterior capsule of the lens; the vitreous is continuous with it at the sides. There are no central blood-vessels in the optic nerve; all its fibres after passing through the lamina cribrosa bend directly downwards, the upper ones curve round again to the retina above, which begins in a fold. The lower ones seem to end abruptly at the band of fibrous tissue which passes forwards through the vitreous. Below this band of fibrous tissue some very degenerate-looking retina, consisting mostly of nuclear bodies, is seen embedded in a gap in the sclerotic. The retina in the lower part of the eye has its inner granular layer separated into two, some fibres separated by spaces running transversely between them.

Case 2.—Frank A—, æt. 18, was admitted to the Moorfields Hospital under Mr. Silcock on April 19th, 1891. He stated that his right eye had been in its present condition since he was born. He does not think the swelling has increased in size so long as he can remember, nor has he at any time had any pain in it. Soon after he was born he was taken to Mr. Critchett, who said that there was an eye present in the orbit. No family history of any congenital abnormality could be obtained, and the

patient himself was free from any except that of the eye. On raising the right upper lid, which drooped, a prominence about the size of a normal eyeball was seen, which consisted of a lobulated cyst with thin, partly translucent walls. No eyeball was visible. He had lateral nystagmus of his left eye; the fundus of it appeared healthy, but vision was equal to $\frac{6}{12}$ only. T. n. The patient wished to wear a glass eye on the right side; to enable him to do this, the cyst and a rudimentary eye, to which it was found to be attached, were removed: during the operation the contents of the cyst escaped. The orbit seemed well formed; there was no depression of its roof.

Pathological examination.—Dissection of the mass removed from the orbit shows it to consist of a small eyeball, measuring 9 mm. antero-posteriorly, with a complete cyst attached to its lower part, and a portion of a second cyst, the neck of which is situated a little to either the outer or inner side of the other, it is impossible to say which.

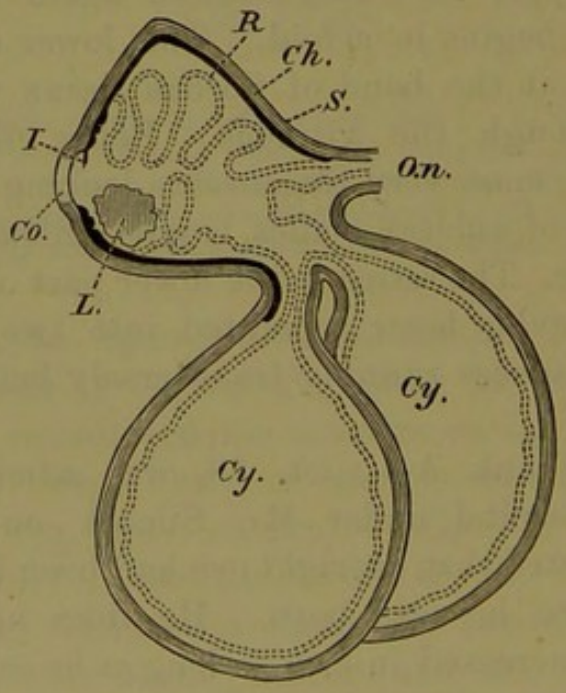


Diagram showing the relation of cysts to the eyeball in Case 2.

The complete cyst is multilocular; in places its walls are thin and transparent, in others there are thick fibrous

bands. A small rudimentary opaque cornea can be distinguished by the fringe of conjunctiva left attached to its margin ; it measures 2·5 mm. laterally. At the posterior part of the globe is a grey circular band, the sheath of the optic nerve.

After the specimen had been hardened in Müller's fluid it was divided into two by a section passing anteroposteriorly through the globe.

A rudimentary iris and ciliary body can be made out. The choroid lines the sclerotic in the normal way ; folded retinal tissue fills the interior of the globe. The interior of the cyst is much wrinkled, a grey membrane lining it. An equatorial section through the lateral half from which the second cyst projects shows that the cavities of both of them communicate with the interior of the globe through the sclerotic, and that some greyish tissue, probably retinal, fills up their necks.

Microscopical appearances.—The anterior epithelium of the cornea extends down in the form of processes into its substance ; Bowman's membrane is indistinguishable ; the anterior layers of fibrous tissue of the cornea are less regular, more wavy, and have a larger number of cells between them than usual ; blood-vessels also course amongst them. The posterior layers of fibrous tissue and Descemet's membrane present more their ordinary appearances. The iris shows considerable irregularity of the uveal pigment on its posterior surface ; it is smaller on one side than the other, its tissue is more condensed than normal ; on the side on which it is largest a rudimentary sphincter muscle can be distinguished. The ciliary muscle is imperfectly developed ; at the lower part of the eye the ciliary processes are not present in their usual position, but there are several small folds in what corresponds to the non-plicated part of the ciliary body. In sections which pass through the outer part of the globe, beyond the pupil, a very shrunken lens is seen; its fibres are degenerate, and in places have calcareous deposit in them ; its capsule is very wrinkled. The choroid is

well formed; on the inner surface of its elastic lamina, surrounded by uveal pigment, are some masses, hyaline in structure, which present all the appearances and reactions of the so-called colloid nodules. The retina is much folded; its commencement at the ora serrata is clearly defined: nowhere can any rods or cones be seen, its external limit being the membrana limitans externa. The two granular, two molecular, and ganglion-cell layers are in parts well formed. The nerve-fibre layer has tracks in it here and there which stain a purplish colour; possibly this is due to persistence of some of the medullary sheaths. There are several scattered patches of uveal pigment in the substance of the retina.

On tracing the sclerotic round in the region in which the cysts commence, a break is met with in its continuity; it is here found to be continuous with the irregular fibrous tissue forming their outer walls. The choroid cannot be traced beyond the margin of the gap in the sclerotic. The uveal pigment layer, however, turns round the edge of the gap into the neck of one cyst, and is continued on for a short distance in the wall of the cyst itself as a convoluted layer of unpigmented cells. Retinal tissue fills up the necks of the cysts; it is mixed up with what appear in the sections to be isolated bundles of fibrous tissue. The optic nerve is very small; its central artery is present.

The walls of the cysts consist externally of fibrous tissue, very similar to that forming the dural sheath of the optic nerve. In it are numerous small blood-vessels, and a few oval patches of closely packed small round-cells. Inside the fibrous tissue coat is a layer composed of delicate branching cells with large nuclei; this is thicker in some parts than in others: it is probably altered retina. This tissue is met with throughout the inner surface of the cyst, which has been removed entire, even at its lowest parts. Amongst the branching cells are numerous variously sized hyaline bodies; they resemble the colloid nodules frequently found on the inner surface of the elastic lamina, and like them are unaffected by acids;

they have, however, taken the logwood stain rather more deeply than these structures usually do.

Deutschmann (1) in 1881, from his investigation of a case of bilateral coloboma of the iris and choroid in a rabbit, advanced the theory, which has been widely accepted and quoted, that so-called arrests of development were only changed developments of the eye the result of intra-uterine inflammation.

It seemed strange that inflammation should thus limit itself to the fœtal fissure. Höltzke (2) who examined microscopically a microphthalmic eye with coloboma from a rabbit, while accepting Deutschmann's explanation of the changes he found, remarks, " Why this inflammation was just at the fissure which is so important for the development of the eye cannot be decided, unless it was favoured by the great vascularity of this neighbourhood."

More recently Hess in three papers (3, 4, and 5) has given the details of the microscopical examination of a series of microphthalmic eyes with colobomata; in these he found no sign whatever of past or present inflammation, from which he concludes that it has very much less to do with the production of congenital malformations than has generally been assumed.

Coming now to the cases recorded in this paper, I may say that in neither of the eyes of the first case is there anything which would lead me to suppose that the changes shown were inflammatory in origin. In the second the nodules of round cells found in the cyst-wall may be inflammatory; if so they are of recent production, and as the eye was not removed until the patient was eighteen years old they cannot be considered as having had anything to do with the causation of the congenital defect.

The left eye of my first case resembles closely Case 1 in the first (3) and Case 1 in the third (5) of Hess's papers, in that in all of them, passing through the centre of the vitreous from the posterior pole of the eye to the back of the lens was a band of fibrous tissue containing an artery or arteries. Hess, I think rightly, considers this fibrous

tissue to be the result of atypical embryonic development of the intruded mesodermic layer which goes to form the vitreous.

In my case it seems impossible to regard it as organised inflammatory exudation because of its position, the regularity of its structure, and the way in which it merges into the normal vitreous at the sides.

In the 'Ophthalmic Hospital Reports' (6) I have described four eyes in which, immediately behind the lens in the anterior part of the vitreous, a mass of elongated cells were found similar in appearance to those seen in the centre of the vitreous in the left eye of Case 1; in three of these eyes the central hyaloid artery of the vitreous remained persistent and patent. I have described these masses of elongated cells as thickenings of the fœtal posterior fibro-vascular sheath of the lens. I now think that it is very probable that they also were mesoblastic tissue which should have formed vitreous, but which had developed in an abnormal way, because it remained vascular. There is a point in Hess's cases upon which he lays some stress, which is absent in mine. He found that the fibrous tissue reaching the back of the lens passed round its lower border and became united to the ciliary body; to this band of tissue he is inclined to attribute the iris coloboma present in both his cases. My case also had a coloboma of the iris, but the fibrous tissue ended at the posterior pole of the lens; there was no prolongation round its margin.

One of the most striking features in the left eye of Case 1 was the abnormal position of the lens; it was situated nearly in the centre of the globe. Becker (7), in his well-known work on the lens, says, "In many cases of microphthalmos the lens or its rudiment remains in contact with the retina or optic nerve entrance; in others it is somewhat more advanced, and is embraced by the hyaloid artery behind and the pupillary membrane in front, but still lies abnormally deep in the eye. Persistence of the hyaloid artery and of at least a portion of

the vascular capsule of the lens is the rule in these congenital abnormalities."

In several of the microphthalmic eyes examined by Hess the lens was situated abnormally far back.

It would appear that the formation of fibrous tissue in the centre of the vitreous holds the lens back, keeping it moored to the posterior pole of the eye while the anterior parts grow forward. Hence the marked stretching and elongation of the fibres of the suspensory ligament and of the ciliary processes.

In both eyes of Case 1 there was a prominence at the lower and posterior part, which was formed by the inclusion of a fold of retinal tissue passing through a distinct gap in the sclerotic. Projecting from a similar part of the globe in Case 2 were two cysts.

A large number of microphthalmic eyes have now been examined microscopically, in which there were protuberances in the region of the fœtal ocular cleft. From the descriptions which have been given, it would seem that they are not all formed in the same way. Arlt (8) considers them to be due to stretching of the lower wall of the globe, weakened by the absence of choroid and partial defect of retina and sclerotic, the result of intra-ocular pressure. Hess accepts this explanation for the series of cases in his second paper. Kundrat (10) describes the cystic formations connected with the lower wall of the eye as due to a projection of retinal tissue through the fœtal fissure into the mesoblastic tissue beneath the globe, this following on some defect in the development of the middle cerebral vesicle. Rindfleisch (9), who examined a microphthalmic eye with cyst attached from a six to seven month fœtus, which had hydrocephalus and the orbital roof pressed down so that it was convex below, thought that the alteration in the orbital roof compressed the globe, so bringing about a widening or reopening of the choroidal cleft and an intrusion of the retinal tissue into the surrounding mesoderm.

Arlt's view is, I think, inapplicable to the cases recorded in this paper; certainly in Case 1, for in both the eyes from it there was a distinct gap in the sclerotic wholly filled by a fold of retina which broadened out on its outer surface.

In neither Case 1 or 2 was there any hydrocephalus: in Case 1 the roof of the orbit was not specially examined, but in Case 2 it possessed its normal curve.

Kundrat's theory best explains, I think, the changes in these eyes. Unfortunately there is no note of any examination of the brain in Case 1.

The retina in both eyes of Case 1 was found to be rucked, and in Case 2 it was thrown into numerous folds. Such foldings and detachments of the retina are commonly met with in microphthalmic eyes. Von Ammon (12) pointed out that in the human fœtal eye the retina is, between the fourth and eighth or ninth month, normally in a folded condition. This point, which I have had abundant opportunities of confirming, is not usually mentioned in text-books on embryology.

In eyes which do not attain their normal size these folds fail to get flattened out. It is easy to conceive, that should there be delay in the closure of the fœtal cleft of an eye one of these folds of the retina might protrude through it, and become nipped by the mesoblast tissue around the outer layer of the secondary optic vesicle (which afterwards becomes differentiated into choroid and sclerotic) as it closes round.

Such a condition of things is analogous to the sequestration of a portion of the cuticular epiblast in one of the branchial or other fœtal clefts which leads to the formation of dermoid cysts. Kundrat suggests that a portion of retinal tissue that has become shut in by mesoblastic tissue may go on to cystic formation; if this be so, Case 2 is probably only an extreme condition of the same processes as have occurred in Case 1, and in which cystic formation has occurred.

Considerable interest attaches to the composition of the

walls of cysts which are found connected with microphthalmic eyes. All of them seem to have two coats—an outer one of fibrous tissue continuous with the sclerotic, and an inner of more or less highly developed retina. In a case reported by Mr. Lang (11), of which I made a pathological examination of the specimen, the inner coat consisted only of bodies like those met with in the granular layers of the retina, arranged in separate patches. Gallemaerts (13) has recently described a case in which the lining membrane of the cyst resembled closely that in Case 2 in this paper. It consisted of a continuous layer of branching cells and granular bodies.

Rindfleisch, in the case previously referred to, found the inner wall of the cyst composed of retina, with its layers well developed, pigment epithelium, and an elastic lamina. The inner surface of the retina was directed towards the interior of the cyst. De Lapersome (14) and Czermak (15) also found fairly well developed retina lining the interior of cysts connected with microphthalmic eyes, but in their specimens the outer surface of the retina (that with rudimentary rods and cones on it) was directed towards the interior of the cyst. The former of these two authors, to account for this position of the retina, suggests that it had become secondarily detached and convoluted, that one of these folds facing the ocular cleft had become pushed into it, perhaps by a fluid analogous to that contained in retinal cysts, and yielding to this pressure was invaginated like a glove finger and forced outwards into the cellular tissue of the orbit. As I have pointed out above, the retina in the human fœtal eye is normally in a folded condition, and it is only necessary to imagine some delay in the closure of the ocular cleft and in the development of the viteous, and the mere continued growth of the retina would tend to make it protrude through the cleft.

In the inner wall of the cyst in Case 2, were numerous bodies similar in appearance and reactions to those often met with on the inner surface of the choroid, and described

DESCRIPTION OF PLATE IV,

Illustrating Mr. Treacher Collins's paper on Microphthalmos.

Microscopical appearances of posterior half of the right eye of Case 1. It shows the break in the continuity of the sclerotic, through which a mass of nerve-tissue (1) is protruding.

(2) Points to the position at which the choroid ceases, and where there is an adhesion between the retina and the uveal pigment layers.

(3) Shows where the uveal pigment layer is apparently replaced by tissue simulating retina.

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