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COMMUNICATIONS

AN UNPIGMENTED PRIMARY TUMOUR OF THE OPTIC DISC*

(A contribution to the knowledge of the
Phakomata of the Eye)

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PRAGUE AND GLASGOW

PRIMARY tumours of the optic disc are generally rare. They provide the clinician with difficulties, and the diagnosis is not an easy one. It is necessary to distinguish the growth from an inflammatory manifestation and from a congenital anomaly. Then the question arises as to whether the growing tissue is a benign or a malignant growth. The answer to this question is often so impossible that our uncertainty leads us to the decision to excise the affected eye, even when its function is still preserved. Even then, when we are in a position to study the growth histologically, our ignorance of the cellular structure of these blastomata is still overwhelming.

The tumours of the optic disc are especially interesting from the general pathological point of view. The blastomic character of this growing tissue is mostly unrecognisable in the cases of phakomata.

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We find tumours of the disc in Bourneville's tuberous sclerosis and in von Recklinghausen's neuro-fibromatosis. It is possible that primitive cells of the eye vesicle, which did not take part in the co-ordinated development, perhaps under the influence of an endocrine evolutionary period, start a new growth. The equilibrium of the germinal layers is disturbed at some time during the growth. Mesodermal tissues appear in neuro-ectodermal tumours. It is difficult sometimes to decide which part of the tumour is the primary growth and what is secondary tissue reaction. The growth itself may develop in a pathological way, mostly with a tendency to disintegration as in Bourneville's disease, where the retinal buds of primitive retinal cells are disintegrated and discharged as vitreous clouds. That is an instance of *regressive metamorphosis*. On the other hand, it is well known that tumours in Bourneville's disease, the neurinoma of von Recklinghausen's disease, the angioma in von Hippel-Lindau's disease, or the angioma in Sturge-Weber's, may be linked with a true blastoma (glioma). Here the growing tendency of undifferentiated embryonic cells is pathologically increased.

There are two questions of a general character which are of special interest.

(1) Is the number of ocular phakomata exhausted with the four known diseases, Bourneville's, von Recklinghausen's, von Hippel-Lindau's and Sturge-Weber's?

(2) Is a phakoma always a multiple anomaly or is a phakomatous growth possible in one tissue only, *i.e.*, in a certain tissue of the eye, without provoking the variety of repeatedly-described tissue changes in skin, brain, spleen, kidney, etc.?

We describe here the clinical and histological data of a case which may throw some light upon these two, and perhaps some other related questions.

History of case

Family History:—The boy's parents, grandparents and other relations were all healthy, and none exhibited any signs of mental deficiency, epilepsy, blindness, glaucoma, mollusca or neuro-fibromata. He has four brothers and they are healthy and intelligent. The eldest brother aged eight and a half has a small ventral hernia in the xiphisternum area. He has one sister four and a half years. Her skin is rough, hard, dry and cracked on forearm and legs.

Patient:—He was first examined in a School Clinic in September, 1942, aged seven and a half years. He was referred to the clinic on account of defective vision in the left eye, and a convergent strabismus. He was an intelligent boy, well built and well nourished. Previous illnesses included measles, whooping

cough and two attacks of pneumonia in early childhood. The visual acuity of the right eye was 6/6, and that of the left with a correction of +1.0 D.Sph. 6/36. There was no exophthalmos and no local thickening of the eyelids. Externally both eyes had a normal appearance. At the first investigation the upper two thirds of the left disc were covered by a whitish smooth mass of two disc diameters. Two and a half years later the growth had increased to about four disc diameters. Fig. 1 shows the condition of the growth at that time. The disc is covered by a greyish white mass of an oval shape with a smooth surface. The margins of the tumour are tuberosus and rise steeply from the fundus (+1 D.) to a height of eight dioptres. Most of the tumour mass is not vascularised except for a small part in the lower temporal area. The nasal part of the mass is covered with haemorrhages, some fresh, some old. The tumour extends equally on the nasal and temporal sides of the disc. There is scattered pigment in the lower half of the fundus, with depigmented spots and superficial haemorrhages which may be sub-hyaloid. The pigment is predominantly in the deeper retinal layers. There is no engorgement of the vessels. There are small yellowish white patches of exudate in the fundus near the tumour. The field was full.

The lower part of the right fundus showed changes similar to those seen in the corresponding part of the left fundus. On the left side of the scalp a small lump the size of a bean, easily movable and rounded and of a hard consistency, was noted. This was regarded as a sebaceous cyst. He had a birth mark on his back (dorsal region) in the form of a small mole.

X-ray of Skull showed that the foramen opticum was slightly enlarged, but there was no calcification of pia or cortex, and no calcified angiomas. There was no difference in the size of the orbital cavities.

Slit-lamp examination of the right eye showed no abnormality of the corneal nerves and no nodules in the iris. Clinically the anterior half of the left eye showed no abnormality. As tubercular and syphilitic causes were eliminated a diagnosis of blastoma was considered. The change in size observed over a period of two and a half years was too obvious for the assumption of a congenital anomaly. Therefore the possibility of a phakoma or true blastoma was considered. Phakomata being sometimes linked with a true blastoma (glioma) it was decided after so long a period of observation to excise the eyeball. This was done in March, 1945, under a general anaesthetic, along with a piece of the optic nerve 9 mm. in length. The eyeball was fixed in ten per cent. formalin and then divided horizontally. Stereo-photo (Fig. 2) shows the extent of the tumour. It measures in its greatest horizontal diameter 10 mm. and is 4 mm. in thickness. One half of the globe was

embedded in celloidin, while the other half was kept in gelatine for frozen sections.

The cornea and angle of the anterior chamber are perfectly normal and the ligamentum pectinatum well developed. The iris tissue shows a denser pigmented area at its surface towards the pupillary margin. There is an eversion of the pigmented layer of the iris.

The great mass of the tumour consists of a spongy tissue with large cells, the plasma of which is clear and swollen. The nerve fibres in front of the cribriform plate show a system of spaces of different sizes (Fig. 3). Many of the larger ones are divided by fine fibres. Some of these spaces are empty, others display a very delicate honeycomb pattern resembling Coats' ghost cells (Fig. 4, A and B). It is a foamy structure in celloidin sections. The main mass of the tumour is built up of the same cells, some in a fairly good state of preservation (Fig. 5).

Many of these cells have no nucleus. In others the nucleus is pressed against the wall, and appears flattened. In some the nuclei are well stained and of a round shape, varying in size and with a similar appearance to xanthomatous cells. The retina is not pushed aside as in papilloedema, but is infiltrated by the growth, and has lost its characteristic structure. The nuclei of the outer nuclear layer are only recognisable at the temporal and nasal margins, but even here the nuclei are scattered in an irregular manner and their arrangement is interrupted by huge foamy cells. There is no trace of rods or cones in the area corresponding to the growth. About 1.5 mm. from the margins of the disc the retinal structure becomes recognisable. The foamy cell mass invades all the retinal layers equally. On the temporal side a regular foam cell tissue infiltrates into Henle's fibre layer, and here the neuro-epithelium is well preserved. Within the peri-macular ganglion cell masses there are many ganglion cells, three to four times their normal size, outstanding on account of their larger and lighter coloured nucleus and the paler cytoplasm. These ganglion cells are absent on the temporal side of the macular area. The infiltration of the retina occurs similarly towards the nasal side. Here the retina shows eosin-red exudates in the inner nuclear and the outer granular layers as in hypertensive retinopathy.

A remarkable cavernous structure restricted to the nasal half of the optic nerve begins about 4 mm. behind the lamina cribrosa and occupies an area of about 3 mm. (Fig. 6). It does not reach the end of the optic nerve in the specimen. This appears normal. The cavernous changes have no relation to the vessels, which are normal. The arachnoidal sheath is thicker than normal and the endothelial cells are increased in number.

The choroid is somewhat thickened, the thin-walled vessels being

FIG. 1.

FIG. 2.

FIG. 3.

Survival of the infiltrated disc. Low power view of the tumour.

FIG. 4A.

Nasal part of the tumour infiltrating all retinal layers.

FIG. 4B.

Temporal part of the tumour.

FIG. 5.

Cell groups of the temporal part of the tumour.

FIG. 6

Cavernous degeneration of the optic nerve.

wide, and many entirely empty and not collapsed. There is no nerve fibre growth.

Mallory staining shows that all the holes are situated in the nerve fibre and retinal tissue exclusively, and not in the mesodermal part. Silver staining for reticulum does not show up any reticulin in the holes. The reticulum content between the tumour cells is moderate. There is a sub-hyaloid haemorrhage in front of the nasal part of the tumour. There is very little tumour tissue at the disc in the part of the eye embedded in gelatine. The few tumour cells found do not show any fat staining. The holes in the cavernous part of the optic nerve are fat free. Muco-carmin staining does not reveal the presence of mucin.

Studies of the retina in bulk unstained showed that a film of blood and fibrin was closely adherent to the retina even in the periphery. The choroid in bulk showed circle-shaped defects in the pigmented epithelium. These punched out defects were present in considerable numbers. We cannot rule out the possibility of an artefact.

Discussion

This tumour cannot be considered as a blastoma in spite of the fact that its growth was observed clinically. We consider the case as a phakoma (van der Hoeve, 1921), a malformation resembling a new growth developing from undifferentiated embryonic neuroectodermal cells which normally would grow into glial and ganglion cells, and have become misplaced or abnormal in quantity.

Clinically the case here described showed great similarity with Stallard's case (1938), in which a greyish hemispherical nodular mass covered the disc with flecks of exudate in the retina adjacent to the disc. This (Stallard's) tumour infiltrates the disc and the retina and shows small cysts and areas of hyaline degeneration. A wedge is driven between the nuclear layers. The rods and cones are degenerated beyond the tumour limits. There are exudates in the outer molecular layer. Swollen cells arranged in clumps have a slightly granular plasma and eccentric nucleus. There were mental disturbances, ataxia, and disturbance of the auditory nerve.

This case of Stallard's belonged to a family affected with von Recklinghausen's disease in two generations, and showed signs of phakoma in other parts.

The diagnosis of a Recklinghausen intra-ocular tumour is easier when plexiform neuro-fibromatosis of the lid is visible as in Davie's case (1939), which was associated with glioma. In this case degenerated nerve fibres were found somewhat jellified, and parts of the nerve were in a state of almost complete liquefaction.

Our case shows a high degree of disintegration of the tumour

cells. Regressive processes seem to be the feature in these misplaced cells, as in Bourneville's disease, where cystic arrangement of the primitive retinal cells and their cloudy dissolution are essential features. (Loewenstein and Steel, 1941). Van der Hoeve (1936) regarded syringo-myelia as a form of phakoma. The regressive process here is an important feature of the phakoma.

Robson, Blackwood and Cookson (1941) described a case of neuro-fibromatosis of the choroid, which showed a growth of predominantly myelinated nerve fibres and bi-polar cells with ovoid bodies consisting of neurofibrils. In this case the blastoma character is apparent.

The variety of cellular changes in neuro fibromatosis is very marked according to Percival Bailey (1932). He found even pseudo-xanthomatous cells. The cavernous structure may result from their presence.

We do not doubt the phakomatous nature of our case, but it does not correspond to any of the forms so far described. It resembles most the Recklinghausen tumour described by Stallard. The cells, however, forming our tumour are different and do not suggest an origin from nerve fibres. Loewenstein (1945) has described a growing melanotic tumour of the disc which infiltrated optic nerve, retina and choroid. The depigmented slide revealed a naevus cell character. There were aberrant nerve fibre bundles running behind the retina. Neuro-epithelium was not developed in the area of the nerve fibre malformation.

We think that Loewenstein's case and our new one may be explained in a parallel manner. The optic stalk as far as invagination extends consists of the two layers of the secondary cup. The outer one corresponds to the later hexagonal layer. The outer layer of the optic stalk shows no sign of pigmentation in man, and disappears according to Juler and Ida Mann (1922) entirely; taking part possibly in the formation of neuroglia or blending with and becoming lost in the sheath of the nerve. There are a few exceptions only in which the outer layer of the stalk is pigmented, that is in the embryo of the bat, the sheep and the chicken, but this pigment disappears again in the course of further development. It is not known whether this pigment exists for a restricted period in the optic nerve. Clinical experience tells us that the disc of the new-born is of a greyish colour due seemingly to a pigmentation which vanishes later. George Coats (1909) found that the hexagonal cells stop sharply at the optic nerve, and that there is no transitional stage between pigmented epithelium and neuroglial frame work of the nerve. He described a pathological case which exhibited a deep pocket at the edge of the nerve entrance lined partly with pigmented and partly with unpigmented epithelium. Further up the nerve little patches of retina and

pigmented epithelium were discovered, these being completely isolated and surrounded by tissue of the optic nerve. These pigmented patches were present in both optic nerves of an anencephalic child.

Another finding, that of Juler and Mann (1922), proved that pigmented epithelium ran round the edges of the scleral foramen continuously from the bulb along the optic nerve. This pigmented epithelium was normal at many places lining the optic nerve. At others it penetrated the adjacent tissue towards the interior of the optic nerve.

These two cases show a high degree of misplacement of cells of the outer layer of the secondary cup in the area of the optic nerve. George Coats had already stressed in 1909 this frequent metaplastic development in congenitally abnormal eyes.

The majority of these misplaced embryonic tissues disappear during development. Some cells may escape conversion into neuroglial structures. They may act as an obstacle for the outgoing nerve fibres which ought to find their way from the retina into the optic stalk, and so cause the aberration of some bundles as in Loewenstein's case. On the other hand these misplaced and preserved embryonic cells may be the focus of the later phakomatous formation. The phakoma caused by the implantation of the embryonic cells from the outer layer of the cup may produce a pigmented phakoma (Loewenstein's case), that from the inner layer an unpigmented growth (our case).

Summary

A case of unpigmented tumour of the disc is described in a nine year old boy, its growth having been observed over a period of two and a half years. Histological investigation showed a tissue consisting of large foamy cells, the contents of which were neither fatty nor mucinous. The nature of the regressive process was not determined.

The tumour tissue infiltrated the surrounding retina, the posterior layers of which were missing and were perhaps undeveloped. There was a cavernous degeneration in a large part of the optic nerve. The caverns were empty or filled with a fine foamy substance. A film of sub-hyaloid blood covered wide areas of the retina. The growth is explained as a phakoma arising from the neuro-ectodermal cells of the optic stalk, into which the fibres of the retinal ganglion cells grow. As the two layers of the optic stalk consist of potentially pigment producing cells (the outer layer) and non-pigmented ones (the inner layer), misplacement of either of them may be responsible for the growth of a pigmented or non-pigmented phakoma of the disc. The existence of both malformations can be proved.

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CONJUNCTIVAL HAEMORRHAGE DUE TO AN INFECTION OF NEWCASTLE VIRUS OF FOWLS IN MAN*

(Laboratory and Contact Infection)

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HAIFA, PALESTINE

In the ophthalmic literature, no case of haemorrhagic conjunctivitis due to the Newcastle virus of fowls, has been mentioned up to the present date as occurring in man.

As is known, this Newcastle virus disease causes a 90-100 per cent. mortality in fowls. The disease got its name from the City of Newcastle-on-Tyne, England, where it first appeared in 1926, and was described in detail by Doyle in 1927. He proved that this epidemic was caused by a filter-passing virus which, as proved also by others, was fatal to fowls even in the dilution of 10^6 .

This disease of fowls is widely spread in the East, but has been observed in the West, *viz.*, in England, only twice, in 1926 and 1933.

In Palestine, the disease first appeared in 1937, and was described by A. Komarov, D.V.M., Government of Palestine Poultry Diseases Officer, Northern District; it re-appeared in 1945.

A case of laboratory infection in man caused by Newcastle virus

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