PRIMARY TUMOURS OF THE OPTIC NERVE AND OF THE CHIASMA; WITH A REPORT OF A CASE.*

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INTRODUCTION.

THE subject of tumours of the optic nerve is one of peculiar interest both from a clinical and from a histological point of view. In those instances in which swelling of the intraorbital portion of the nerve occurs such symptoms as protrusion of the eyeball, impairment of vision, and of the ocular movements naturally invite the attention of the ophthalmologist. On the other hand, cases in which the tumour affects chiefly the intracranial portion of the nerve and the chiasma constitute a difficult problem for the neurologist. This is on account of the difficulties arising in the differential diagnosis of such tumours from other growths, which may originate in the same locality but in entirely different structures. The symptoms are regional, and are exemplified by those produced by a tumour of the hypophysis. The question, however, of a correct diagnosis cannot only be one of personal satisfaction, as in the interests of cranial surgery it is desirable to be able to recognize what structures are primarily affected. Operative interference may be beneficial in the one case, whereas it may not be justified in the other, as will be pointed out later.

Under the heading of primary tumours it is intended to include only those of subdural origin. It is true that tumours of this class are of uncommon occurrence, but we are fortunate in possessing such careful compilations of the recorded cases as those of Byers and of Hudson. Byers,¹ in 1901, collected from the literature 102 cases of primary tumour of the optic nerve. In 1912, Hudson² reached a total of 182. His work is of special importance, because of the fact that he made a classification of the tumours according to the histological details recorded. The first cases to be described were those of Wishart,³ in 1833, Middlemore,⁴ in 1838, and Heymann,⁵ in 1842.

It has long been recognized that tumours of the optic nerve are possessed of an extremely low degree of malignancy. In the first place, they grow very slowly. What is more striking, however, as has been

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shown in the case of intraorbital tumours, is that after their removal recurrence of the growth is almost unknown. Even after an obviously incomplete removal the duration of life may vary from months to many years.

From the large number of recorded cases which have been successfully operated on by the ophthalmic surgeon the impression is gained that the majority of the tumours are confined to the intraorbital part of the nerve. This, however, is far from being correct. Numerous instances are on record where, after removal of the tumour in the orbit, followed by death from accidental causes, such as meningitis, autopsy has revealed the growth to extend as far as, or to include, the chiasma. For example, in a case of Fischer's,⁶ a left intraorbital tumour was removed, probably a glioma. At autopsy the intracranial part of the left nerve, the chiasma and the right optic tract were found also to be involved. Axenfeld and Busch⁷ report a case of a walnut-shaped tumour which filled the right optic cavity. Removal of the whole of the swollen portion of the nerve was not possible, as, although the nerve anteriorly was of normal thickness for a distance of 6 mm. behind the globe, posteriorly it was twice its normal thickness and immovable in the foramen opticum.

Up to a fairly recent date great diversity of opinion existed as to the nature of these tumours. In most of the early reported cases they were thought to be of mesodermal origin. From their appearance they were variously described as myxomas, fibromas, fibromyxomas, fibrosarcomas and myxosarcomas. Hudson, however, having paid special attention to their histological features, came to the conclusion that the majority are glial in origin, and therefore ectodermal. More recently Fleischer and Scheerer,⁸ among others, have supported this view, and it is now generally acknowledged that the type of growth which affects the optic nerve most commonly is a glioma.

Almost the only other type of tumour with which we are concerned is of mesoblastic origin, viz., endothelioma. In his classification of 182 tumours, Hudson considered that 118 were of glial structure, and that only 29 were endotheliomas. A small group he placed under the heading of fibromatosis. The remainder could not be classified with certainty. Sarcomas and other tumours of dural and extradural origin with secondary involvement of the optic nerve do not enter into the scope of the present article.

Some facts in regard to the age of onset are worth mentioning. Gliomas of the optic nerve usually occur in young people, a large number of the cases being in children below the age of five. Endotheliomas have a more evenly distributed age-incidence, but on the whole are more common after than before the age of thirty.

Certain differences between the gliomas and the endotheliomas in their mode of growth may be indicated. Gliomas originating in the

intraorbital portion of the nerve appear to have a greater tendency to spread in a central than in a peripheral direction along the nerve. It is a curious fact that in a large number of the recorded cases of intraorbital glioma a small portion of the nerve immediately behind the eyeball has been found to be unaffected except by secondary changes. Endothelial tumours, on the other hand, show no such predilection, and not infrequently are found in close apposition to the back of the eye. Centrally, however, tumours of this type do not extend beyond the nerve. I can find no case recorded in which the chiasma was affected by extension of the growth. Multiple endothelial tumours of the optic nerves have been found. Apparently glioma of both nerves does not occur without the chiasma being involved in the growth. Willemer⁹ records an unusual case of glioma in which, in addition to involvement of the whole of the left optic nerve and chiasma, there were two small swellings of the right optic nerve within the orbit.

Primary tumours of the optic nerve very rarely extend into the head of the nerve in the eye. Gliomas and endotheliomas, however, originating in the nerve head tend to spread backwards along the nerve. Endotheliomas, according to Sidler-Huguenin,¹⁰ develop more often in the nerve than at its head. Gliomas of the retina and papilla, on the other hand, are probably more common than those of the nerve itself. Secondary invasion of the nerve occurs either by way of the lamina cribosa, or along the path of the posterior ciliary vessels, the growth infiltrating the fibres of the sclera and spreading into the dura and subdural spaces around the nerve (Snydacker¹¹, Neame¹²). In the case of primary gliomas of the optic nerve infiltration of the dura does not occur.

Not infrequently growth may be present in other parts of the brain or its meninges, of a type similar to the tumour of the optic nerve according as it is glioma or endothelioma. The cerebral gliomas in such cases may develop independently of the nerve growth or as extensions of a chiasmal tumour into the neighbouring substance of the brain. As examples of the latter, in a case of v. Graefe's¹³ there was a large mass of tumour in front of the left corpus striatum which was in immediate connection with a glioma of the left optic nerve and chiasma. Schott-Mauthner¹⁴ reported a case in which the parts involved by the growth included the whole of the right optic nerve, the chiasma and the under surface of both frontal lobes.

HISTOLOGY.

Glioma of the optic nerve usually involves the pial and arachnoid sheaths as well as the nerve itself, in which it originates. Cases such as Pollack's,¹⁵ in which the growth does not extend through the pia, are unusual. Invasion of the dura by the tumour substance does not occur, and I can find no case recorded in which this membrane has been pene-

trated. On entering the swelling the nerve fibres become widely separated, and in sections at the thickest part of the tumour it is often impossible to detect the presence of axis cylinders at all. The interseptal spaces of the nerve are widened and irregular in shape, and the fibrous tissue composing the septa is often swollen owing to the presence of tumour cells between its component fibres. A similar swelling and irregularity of arrangement of the pial and arachnoid membranes are also commonly observed. Very frequently interruptions in the continuity of the pia or arachnoid are present, and tumour tissue may distend the subdural space. Here and there the arachnoid may have a thick laminated appearance as if stimulated to hypertrophy by the growth within.

The essential substance of the tumour consists of glial cells and fibres. Cell bodies are difficult to distinguish under ordinary magnifications owing to the scanty protoplasm most of these cells possess. Various types of nuclei are met with, some oval or nearly round, staining moderately well, and others more elongated in shape, which stain more darkly. In the former type dark chromatin granules can be seen at the periphery, apparently just under the nuclear membrane. No direct continuity can be made out between the nuclei and the glial fibres among which they lie. On the other hand, long fibres sometimes appear to proceed from the ends of the elongated nuclei. Much larger irregularly-shaped cells with eccentric pale-staining nuclei are occasionally seen.

The consistency of these tumours varies greatly. The majority are hard and dense, being composed chiefly of closely set glial fibres, the cellular element being relatively small. Areas of degeneration having a myxomatous appearance are sometimes present. For the most part the glial fibres run in the long axis of the nerve except in the meningeal spaces, where their course may be most irregular. The vascular supply of the tumours is generally meagre.

Endothelial tumours originate in the sheath of the nerve, and, having surrounded it, bring about a gradual atrophy of the visual fibres by compression. Some hypertrophy of the neuroglial tissue may take place. Penetration of the pia with invasion of the nerve itself seldom occurs. The masses of endothelial cells are found chiefly in the subdural space, in the dura, and occasionally extend into the structures outside this membrane.

The composition of this type of tumour is in every way similar to the endotheliomas of the membranes of the brain. There is the same grouping of the cells in whorl-formation. It is nowadays generally accepted that the majority of endotheliomas develop from the cells which cover the arachnoid membrane. Histologically the cellular tissue of the tumour bears a strong resemblance to those clusters of endothelial cells which are often present on the arachnoid in the normal state, especially in relation to the Pacchionian bodies. These cell clusters in

growing, may become attached to and enter the dura mater, sometimes losing all connection with their point of origin. In this manner it can be understood how endothelial tumours may come to involve the dura alone. This method of development has been specially referred to by Cushing¹⁶ in discussing the origin of the cerebral meningiomas (endothelioma).

DESCRIPTION OF CASE.

The case to be described is one in which a glioma affected the intracranial portions of both optic nerves and the chiasma, and in which an

FIG. 1.—Drawing of tumour *in situ*.

entirely separate tumour of the same nature was present in the brain. I wish here to express my gratitude to Dr. Poynton for permission to give the following report.

D. F., a girl of five and a half years, was brought to hospital with a history of severe headaches, vomiting and constipation of one month's duration. Two years previously she had been under treatment for a 'cold' abscess on the postero-external surface of the right iliac bone. Nine months before her admission to the Sick Children's Hospital, Great Ormond Street, a small hard tumour was removed from the subcutaneous tissues covering the right great trochanter. It is not possible to indicate definitely the nature of this tumour,

but from examination of a small part it appeared to be chiefly composed of fibrous tissue. There was no history of trauma in this case, and the family history was unimportant.

On admission to hospital the child was found to be rather below the average height for her age, but was decidedly obese. Her weight was 51 lb., the normal weight for her age being, roughly, 41 lb. Her hands were rather broad and thick, with short stumpy fingers. She was not troubled by abnormal thirst, or by polyuria. A large patch of brown pigmentation of the skin was present on the left side of the abdomen. Beyond this no other pigmented areas or other peculiarities of the skin and subcutaneous tissues were observed.

The patient was usually very drowsy and difficult to examine, and any attempts to test the visual fields were defeated. Visual acuity appeared to be good, as she could see and recognise people moving about the ward.

FIG. 2.—Tumified parts excised, showing swelling of optic tracts and tuber cinereum.

On ophthalmoscopic examination the edges of the discs were seen to be a little blurred, and about + 2 D. of swelling was present in each eye. The discs appeared to be undergoing secondary atrophy. Both pupils were large and inactive to light, and there was paresis of the left external rectus muscle. A left hemiparesis, including the face, was present, and progressed rapidly in severity. Spasticity of the left extremities was absent; they were, on the contrary, rather hypotonic. Sensation was unaffected. Both knee jerks were very sluggish, and the left plantar reflex was extensor in type. The Wassermann reaction of the blood was negative, and the spinal fluid showed no abnormalities. No definite diagnosis was made in this case beyond the probability of a tumour being situated at the base of the brain. A decompressive operation was performed, but the child succumbed a short time afterwards.

At autopsy the intracranial portion of both optic nerves, the chiasma, tuber cinereum and corpora mamillaria were found to be greatly swollen. Part of each optic tract in apposition to these structures was likewise enlarged. Very little alteration in the shape of the third ventricle could be detected. The degree of swelling and general appearances of the affected parts can best be judged from the accompanying illustrations. The swollen optic nerves tapered distally, becoming of normal size at a point 2 mm. anterior to the optic foramina. Both these apertures were enlarged.

In the brain an enormous partially cystic tumour occupied almost the whole of the frontoparietal area of the right hemisphere. In shape the sella turcica was very shallow and wide in all directions. The pituitary body was

flattened, and the pars anterior and infundibular stalk were of a semitransparent and gelatinous consistency.

HISTOLOGY OF THE TUMOURS.

Stained by Bielschowsky's method, sections of the optic nerve and chiasma show a great reduction in the number of nerve fibres. They are widely separated and are more numerous in the optic nerves than in the chiasma, where they are practically absent in the central area. With Weigert-Pal's stain the myelin sheaths are seen to be very scanty, and in several patches in the chiasma they are entirely absent. Neuroglial tissue, stained with Victoria blue, is seen to be enormously increased in quantity. This overgrowth consists chiefly of neuroglial fibres. These form a dense meshwork, of which the fibres for the

FIG. 3.—Dense overgrowth of neuroglial fibres in central area of chiasma.

most part run transversely in the central areas of the chiasma, and longitudinally in the optic nerves. In the nerves, however, the glial fibres at many points take a course perpendicular to the fibrous tissue septa. Relatively to the fibres the cells are few in number. The nuclei consist chiefly of two kinds, small round or oval nuclei, and a more elongated form. An occasional larger neuroglial cell of irregular shape with an eccentric pale-staining nucleus can be distinguished.

Sections stained by van Gieson's method show great distortion of the connective tissue septa, but no evidence that they have been infiltrated by the new growth. The sheaths do not appear to be affected. The vascular supply of the affected parts is poor.

Histologically the appearances of the tumour in the right hemisphere are those of a soft, very cellular glioma.

SYMPTOMATOLOGY.

The symptoms produced by glioma and by endothelioma of the intraorbital portion of the optic nerve are essentially similar, but commonly show slight modifications according to the type of tumour present. Exophthalmos is the most obvious feature of these cases, and, secondly, impaired vision or blindness upon the side affected. Where the tumour is a glioma vision is apt to be interfered with before the occurrence of exophthalmos, which is only natural considering the origin of the growth is in the nervous structures. Conversely, endothelial growths commonly give rise to exophthalmos prior to any impairment of vision, the destruction of the visual fibres being more slowly brought

FIG. 4.—To show wide separation and scarcity of visual fibres in swollen optic nerve.

about by the swelling of the nerve sheaths. The occurrence of temporal hemianopia progressing to blindness, with changes at the disc in the eye opposite to the one primarily affected, indicates in the case of a glioma that the growth has extended back to and involved the chiasma. Strabismus may occur in either case, but is apparently not a common event. Restriction of the ocular movements is more frequently caused by endothelial tumours, which can be explained by the fact that they more often involve the portion of the nerve immediately behind the eyeball than do the tumours of glial origin. Pain is not usually complained of. The changes at the disc in both cases consist either of slight swelling with evidence of secondary atrophy, or of atrophy alone.

Gliomas affecting the chiasma and the intracranial portions of the optic nerves may attain a considerable size. Owing to the pressure effected upon surrounding structures the symptoms they produce are almost identical with those caused by tumour of the hypophysis. Besides the disturbance of vision, the symptoms consist of drowsiness, obesity, defective growth, and frequently some degree of polyuria and polydipsia. It is, therefore, unusual even to suspect clinically that the chiasma and optic nerves are the seat of growth. Martin and Cushing,¹⁷ in a period of eight years, met with seven cases of glioma of the chiasma and optic nerves, in two of which the growth did not extend through the optic foramina. There are certain points with special reference to which they consider it might be possible to distinguish tumours of the chiasma and optic nerves from those of the hypophysis. In three of the seven cases where perimetry was possible, although one eye was blind, the hemianopic defect in the visual field of the other was not so complete and clear cut as it is so often found to be in cases of pituitary tumour. The loss of vision in both eyes due to a chiasmal tumour tends to be more rapidly progressive, whereas with a pituitary tumour partial vision in one eye at least is usually retained over a considerable period. An important feature observed with the aid of stereoscopic plates of the skull taken laterally was that the pituitary fossa appeared to be lengthened owing to the distension of the optic foramina. Minor distinctions such as these are of importance from the surgical point of view. While advocating the benefits of operation in the case of a pituitary neoplasm, one would not hesitate to condemn the removal of a chiasmal growth as long as any sight remained. When blindness is complete operation is useless, as by then the tumour will probably have invaded neighbouring structures.

RELATIONSHIP OF GLIOMA NERVI OPTICI TO NEUROFIBROMATOSIS.

Whether any relationship exists between glioma of the optic nerve and von Recklinghausen's disease, neurofibromatosis, is a point of great interest. The actual number of cases in which tumours of the optic as well as of the other nerves have been present is extremely small. When compared by their histological features, it does not appear that the two types of tumour are in any way allied. Differences in development between the optic and other nerves must, however, be taken into account. The optic nerves form part of the central nervous system, and have a composition unlike that of the peripheral nerves. It is conceivable that the tumours in either case are the result of a similar disturbance of embryonal development. Both conditions are probably of congenital origin. The early onset in the majority of cases of glioma of the optic nerve supports this view. With regard to neurofibromatosis, Thomson¹⁸ considered that it is a developmental disease of the peripheral nervous

system commencing in intrauterine life. Another feature which tends to form a link between the two conditions is the frequency in either case with which a glioma of the central nervous system is present. With regard to the occurrence of gliomas of the brain or spinal cord in cases of neurofibromatosis, Verocay¹⁹ considers that they form no accidental combination, but are in close histogenetic relationship with the nerve tumours.

The view that gliomas of the optic nerve and multiple tumours of the peripheral nerves are in the nature of homologous formations of congenital origin was first advanced by Goldmann.²⁰ In connection with neurofibromatosis, Bruns²¹ accepts the possible occurrence of blindness due to 'neuromas' of the optic nerve.

Of the cases of optic nerve tumour in association with neurofibromatosis the most important is Cushing's (Case No. VII.). A tumour involving the chiasma and both optic nerves up to the optic foramina was seen at operation, and from histological examination of a small piece removed subsequently proved to be a glioma. In Prudden's,²² Serres',²³ and Westphalen's²⁴ cases, one or other optic nerve presented a slight enlargement just before piercing the sclerotic in two of the cases, and before entering the optic foramen in the third. The histological nature of the swellings in these cases is unfortunately not stated. It is possible that in Westphalen's case the growth was of endothelial origin, as a small tumour of the dura showing concentric arrangement of cells was present over the right frontal lobe. Michel²⁵ recorded the case of a sixteen-year-old girl, who developed elephantiasis neuromatosa of one leg at the age of six months. At autopsy a glioma was found involving the chiasma and right optic nerve. In a case reported by Emanuel,²⁶ that of a child of three with a tumour, probably a glioma, of the optic nerves, the child's father presented the typical features of fibroma molluscum, and the grandfather was said to have been similarly affected. It is suggested that heredity, which is a common feature in neurofibromatosis, may have been a factor in the production of the child's condition.

In conclusion, while agreeing that a definite relationship between the two conditions is hard to prove, I believe there is nevertheless some justification in assuming that it does exist.

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