GLIOMAS OF THE OPTIC PATHWAYS IN CHILDHOOD

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A small series of cases of optic pathway gliomas is being reported for two reasons: first, because their proper treatment is still a controversial subject and second, because of the importance of early recognition in permitting possible surgical cure instead of palliation. Gliomas of the optic pathways make up a relatively small portion of neoplasms of the brain. Martin and Cushing27 reported an incidence of 0.84 per cent in a series of 826 intracranial tumors. Taveras et al.33 found 34 cases in a series of 2000 gliomas (1.7 per cent). If the various reported series of optic pathway gliomas are inspected, it is found that approximately 75 per cent of these lesions occur in children under the age of 12.5,7,13,17,20,31,32 In our clinic 13 cases of primary tumor of the optic pathways have been encountered among a series of 256 intracranial tumors in young children during the past 10 years. This is an incidence of 5.1 per cent in the total series and 7.0 per cent if only the gliomas are considered.

Much emphasis has been placed on the fact that these tumors have only a slight malignant potentiality. Hudson17 first pointed out that even after incomplete removal, patients may survive for 20 years or more without evidence of progression of the tumor. This has been confirmed by the experience of others.25 McFarland and Eisenbeiss23 have even stated that if such a tumor is only partially removed it probably will not continue to grow. As recently as 1954, Marshall26 said, “On theoretical grounds complete excision might be desirable, but recurrence after excision of the major portion is very uncommon.” Many of these statements have been made by ophthalmologists on the basis of an anterior exploration of the orbit, an approach that makes it difficult to visualize the limits of the tumor. Also, since it has been well established that many of these gliomas grow very slowly, the occurrence of intracranial symptoms 10–15 years after the original operation might not come to the attention of the original surgeon. Posner and Horrax30 have pointed out that even after known intracranial extension, these patients may survive for a long time, their only symptom being loss of vision.

Analysis of the 13 patients seen at the Children’s Medical Center in the past 10 years with a verified diagnosis of optic pathway glioma reveals that on the basis of symptomatology and physical findings they fall into two groups, depending on whether the tumor is predominantly intraorbital or intracranial. This differentiation was first proposed by Dandy,8 but has not been used by many subsequent authors. The following case histories illustrate some of the important differences between these two groups.
CASE REPORTS

Intraorbital Glioma

Case 1. M.C., a 4½-year-old girl, was admitted to the Children's Medical Center because of increasing prominence of the left eye of 2 weeks' duration (Fig. 1). She had had no headaches and had noted no change in her visual acuity. Although there was some increased resistance to palpation of the globe, no tumor mass was palpable. The movement of the eye was unimpaired. Early papilledema was present in the left eye; the right fundus appeared normal. Visual acuity was diminished to 20/70 in the left eye and was normal in the right. Slight peripheral constriction was found in the visual field of the left eye, but the patient could not cooperate for detailed examination. There were no other abnormal findings and no evidence of von Recklinghausen's disease.

Roentgenograms showed the left orbit to be slightly larger than the right, but the optic foramen was normal. Films of the skull were otherwise negative. A left carotid arteriogram showed no evidence of displacement of the intracranial vessels and no abnormality of the orbital vascular pattern.

A left transfrontal craniotomy was performed. On exploring the orbit, a diffuse reddish swelling of the optic nerve was found. Further exploration demonstrated that this tumor lay entirely within the orbit. The nerve was first amputated from the globe. Intradural exploration of the chiasm was then performed and failed to show any abnormality of the intracranial portion of the optic nerve. The nerve was divided just in front of the chiasm, pulled through into the orbit, and removed. Since subsequent pathological examination showed that the tumor extended to the globe, the eye was enucleated 16 days later and the patient was fitted with a prosthesis.

Histologically, the resection extended 1 cm. behind the most proximal edge of the tumor and thus the neoplasm was considered to have been completely removed. The microscopic picture of this lesion was characteristic of an optic pathway glioma (Fig. 2). There was a matrix of fine neuroglial fibrils in interspaces of a delicate reticulated syncitium. The tumor cells were small with oval or elongated nuclei, some of which were darkly stained. Many of the cells showed vacuolization of the cytoplasm.

It is now 8 months since operation and the patient is asymptomatic (Fig. 3).

Intracranial Glioma

Case 2. A.P., a 7-year-old child, had a history of a squint of her left eye which
had first been noted 3½ years previously. Shortly after the onset of this symptom language difficulty developed and within a period of a few weeks speech became incomprehensible. She was examined by a doctor at that time who found that she could not see with her left eye. These findings did not progress and no specific therapy was instituted. Two weeks before admission to the Children’s Medical Center she began to have headaches for the first time which were associated with early morning vomiting. On physical examination she had weakness of her left lateral rectus muscle, but there was no proptosis of either eye. Papilledema was present in the right eye. The left fundus showed marked optic atrophy, and the eye was completely blind. Scattered over her body were café-au-lait spots and small subcutaneous masses characteristic of von Recklinghausen’s disease (Fig. 4).

Roentgenograms showed the left optic foramen to be twice as large as the right. There was some erosion of the apex of the petrous ridge on the left as well as some destruction of the inferior surface of the anterior clinoid process.

Operation disclosed a large tumor in the middle fossa arising from the left optic nerve. This was adherent to the left internal carotid artery and to the right optic nerve, but could be dissected free from these structures leaving them intact. The tumor extended into the orbit, but faded out posteriorly in the chiasm. The chiasm was amputated flush with the right optic nerve in order to spare the temporal retinal fibers on this side. The intracranial portion of the tumor was thus grossly removed.
Fourteen days later the left orbit was explored through the previously made frontal craniotomy and the tumor was found to extend into the globe itself. The intraorbital portion of the optic nerve and the tumor were then removed. Six months later the globe was enucleated.

Pathologically this tumor was designated as a glioma of the optic pathway. The lesion had been completely removed as far as could be determined by gross examination, but there is a possibility of some remaining microscopic involvement in the left optic tract posterior to the chiasm.

The child did well following surgery. The right nasal field of vision is still intact. One and a half years following her operation she began to show secondary sexual characteristics (age 9 years). It is now 3 years since the operation and 6½ years since her symptoms first developed—she has occasional headaches, but is otherwise asymptomatic.

SYMPTOMATOLOGY

The average age of our patients is 4½ years; there is an equal distribution of sex. The young average age is ascribable partially to the fact that these
patients came entirely from a pediatric population; however, this has also been the experience of other authors who have drawn their patients from a more widely scattered range of age.

The presenting symptoms depend on the portion of the optic pathway that is first involved, and although the same pathological process may be seen either intraorbitally or intracranially, the clinical picture varies depending on the origin of the tumor. Within the primarily intraorbital and primarily intracranial groups there is a certain uniformity of findings.

In the intraorbital group there are 4 children. None of these had evidence of von Recklinghausen's disease. The initial symptom in all patients was proptosis of the affected eye. This proptosis, as noted by other authors, is nonpulsatile and is usually an axial protrusion of the globe directly forward. If displacement does occur as the tumor enlarges it is most frequently inferior and lateral. Christensen and Andersen have said that there is usually no impairment of extraocular movements. Although this would seem to be a reasonable statement, 2 of our 4 patients had some limitation of ocular motility. This was not marked in relation to the degree of proptosis, however. In general, among orbital lesions, optic nerve gliomas are certainly much less apt to produce early alteration in eye movements than lesions of the bony orbit or of the extraocular muscles themselves.

These patients were seen early—the time after initial symptoms being 2, 4, and 5 weeks and 8 months. All had papilledema in the affected eye. Other writers have reported optic atrophy, but it may be that our patients were seen at such an early stage that this had not had sufficient time to develop. Two of these patients had decreased visual acuity on physical examination although they were unaware of it prior to admission to the hospital. Visual field examinations are unsatisfactory in this age group, but as far as could be determined none of the children had any obvious field defect. Although it is known that diffusely infiltrative tumors of this type often produce little interference with neurologic function, it may be that in older patients minor alterations in the visual fields can be found.

Palpation of the orbit is abnormal in the presence of an orbital glioma. Usually the tumor cannot be felt, but examination will reveal increased resistance of the globe to posterior displacement. Although papilledema was present in all, none of the patients in the intraorbital group showed other evidence of increased intracranial pressure. The papilledema under these circumstances is caused by intraorbital rather than intracranial obstruction of venous drainage from the retina.

Among the 9 patients in the intracranial group the symptoms and signs were quite different. In general, the history was somewhat longer than in the purely intraorbital group, averaging 20 months. Six patients had decreased visual acuity as a presenting complaint. Again the determination of visual field defects was extremely difficult because of the young age of the patients. The finding of irregular bitemporal field defects as evidence of involvement of the intracranial portion of the nerve and chiasm has been
well described by Cushing and it is probable that if reliable examination could have been done this would have been evident. Only 2 patients presented with proptosis, and both of these had intraorbital as well as intracranial tumor. Five of them had optic atrophy in the affected eye or bilaterally, 1 had bilateral papilledema, and 2 had atrophy in one eye and papilledema in the other.

Increased intracranial pressure was a frequent sign if the tumor was located intracranially. In addition to the eye signs, 3 of these children had a positive Macewen's sign and 3 had an unsteady gait which was probably related to increased pressure. Further evidence of intracranial tumor are signs of hypothalamic dysfunction and occasionally other symptoms caused by involvement of structures in the neighborhood of the optic chiasm. In 3 of our patients sexual precocity developed—at ages 7, 8 and 9.

Four of the children in this group have von Recklinghausen's disease. This corresponds well with the findings of other authors who have reported that about one-third of patients with optic pathway gliomas showed stigmata of generalized neurofibromatosis. One of these patients had a sibling with von Recklinghausen's disease and an optic nerve glioma.

RADIOGRAPHIC FINDINGS

It should be emphasized at the outset that gliomas of the optic pathways may be present either intracranially or intraorbitally without any alteration in the appearance of the plain roentgenogram. It should likewise be stated that the radiographic signs produced by these tumors are not pathognomonic: they may be duplicated by other lesions in this area.

Plain orbital roentgenograms in patients with intraorbital gliomas may show evidence of enlargement of the optic foramina. The average normal foramen is bean-shaped with dimensions of 4.1 by 4.65 mm. It is always necessary to compare both sides in order to discover minor variations. It must be remembered, however, that the foramina are absolutely symmetrical in only 45 per cent of the normal population, in 40 per cent they may differ as much as 10 per cent in size, and in the remainder variations up to 20 per cent may be noted. The contour is normally smooth; therefore, any irregularity, hyperostosis, or erosion is apt to be pathological. The commonest abnormal finding in patients with gliomas of the optic nerve is a smooth, circular expansion of the optic foramen (Fig. 5). It is, of course, necessary to have films of good technical quality in order that the contour and dimensions of the two foramina can be compared. Enlargement of the optic foramen also is found occasionally with other lesions, and therefore, although it is most frequently seen with optic nerve tumors, it is not always pathognomonic.

Various ancillary aids to roentgenographic diagnosis have been suggested. Orbital tomography has been said to give additional information about small intraorbital masses. This has been modified by injecting air into the orbit prior to tomography. Such a technique may delineate small areas of
enlargement of the optic nerve which will allow differentiation between gliomas and other intraorbital tumors. In the use of tomographic techniques in this region the possible hazards of excessive roentgen exposure should be evaluated carefully, especially in young people. In our clinic we have had no experience with this procedure and we doubt the wisdom of its use as a routine diagnostic maneuver. It has been suggested that carotid angiography may be of assistance in the diagnosis of orbital tumors. This is primarily of value in differentiating optic nerve tumors from the more vascular orbital lesions, particularly angiomata and metastatic neoplasms.

In 2 patients in our intraorbital group there was enlargement of the optic foramen. The tumor in these cases did not extend all the way through the optic canal (Fig. 6). If this radiographic sign had been used as a contraindication to surgery, as has been suggested, the opportunity for curing these children would have been lost. Another of the intraorbital tumors caused slight enlargement of the entire orbit, the foramen being normal. In 1 patient the plain roentgenograms were entirely normal. Angiography was performed in 2 of the patients with intraorbital tumors and in both it was normal.
In the intracranial group the plain roentgenograms of the skull proved to be abnormal in all cases. In 4 of these patients the optic foramen was enlarged and in 2 the sella turcica was eroded. The characteristic deformity of the sella turcica associated with glioma of the optic pathway was first described by Martin and Cushing in 1923.

This is a pear-shaped configuration of the bony contour produced by erosion of the tuberculum sellae and the anterior clinoid process (Fig. 7). In 3 patients both the sella turcica and the optic foramen were altered. Therefore, in this group, all patients showed some abnormality in the plain films.

A further aid in defining the extent of these tumors is pneumographic examination of the basilar cisterns. Such a technique may outline even a small mass lying in the region of the optic chiasm. Angiography also may be of some help, although deformities of the anterior portion of the circle of Willis would not be noted unless a rather large mass were present. If the patient has signs and symptoms of increased intracranial pressure it is likely that there is a mass obstructing the ventricular system; in these circumstances, ventriculography is the safest and most instructive manner in which to visualize the extent of the tumor.

PATHOLOGY

The optic nerve is not a cranial nerve in the usual sense, but, rather, an
extension of a tract of the brain and, therefore, it contains the same glial elements that are to be found elsewhere in the central nervous system. It might thus be expected that tumors arising in this region could derive from any of the glial cells of the brain, and this is probably the case. There have been convincing reports of glioblastoma multiforme originating within the optic nerve,\textsuperscript{24} but as a rule gliomas of the optic pathways are more benign. Occasionally verified gliomas have been reported to involve the retina itself.\textsuperscript{24,25}

Some authorities have considered that the majority of these tumors are derived from cells of the astrocytic series.\textsuperscript{2,15} A great deal of evidence has been accumulated on the other hand through the use of special stains to show that the predominant cell is an oligodendrocyte rather than a spongioblast or astrocyte.\textsuperscript{5,18} The possible oligodendrocytic origin of these lesions is of particular interest in view of the association of these tumors with von Recklinghausen’s disease, as oligodendrocytes are probably the counterpart in the central nervous system of the Schwann cells in the peripheral nerve. Regardless of what the primary cell may be in this neoplastic process, the tumors seem to have a consistent histologic pattern and therefore they have been designated only as gliomas of the optic pathways rather than by a more specific histologic classification.

The usual pathologic picture seen in these lesions is generalized swelling of the nerve with hypertrophy of the pial septa. There is scant vascularization of the tumor and the walls of the vessels are usually normal. Within these tumors Christensen and Andersen\textsuperscript{5} described four distinct cell types. There are small cells with round nuclei and delicate fibrils which seem to be identical with the normal oligodendroglia of the brain. As transition from these there are coarsely reticulated cells that are polygonal in shape with large dark nuclei and fewer fibrils. These cells are oligodendrocytes and are found typically in this type of neoplasm. There are also sickle-shaped cells of astrocytic origin and occasional large cells resembling neurones which sometimes have more than one nucleus. There are frequently some degenerative changes such as vacuolization of the cytoplasm.\textsuperscript{34} In general, the histologic picture is one of a mature and benign glioma. This is verified clinically by their slow rate of growth and by the fact that they have shown no tendency to metastasize by way of either the blood stream or subarachnoid pathways.

All the tumors in this series conform reasonably well to the above description. There was no apparent difference between the intraorbital and intracranial tumors histologically. Likewise, the tumors in patients with von Recklinghausen’s disease did not vary to any significant extent from the others.

As has been mentioned, in addition to this characteristic type of lesion there may occur typical tumors of the astrocytic series; more malignant neoplasms, such as glioblastomas, have also been reported. There were no such lesions found in our patients.
TREATMENT

These tumors were originally treated usually by ophthalmologic surgeons who exposed them anteriorly through the orbit. This was considered to be the safest method, which it probably was, 40–50 years ago, despite the fact that it was associated with a 10 per cent incidence of meningitis.17 Although the danger of infection is less of a problem at present, there are certain major disadvantages of the anterior approach which pertain even today. By this route is not possible to expose the region of the optic foramen adequately, and extension of a tumor through the foramen cannot be seen—much less treated properly. The use of roentgen examination to exclude intracranial extension of a predominantly intraorbital lesion is not justified.4 Therefore, it is not possible to be sure prior to operation whether the neoplasm is completely intraorbital. It does not seem reasonable to be satisfied with incomplete removal on the assumption that the remainder of the tumor can be expected to stop growing or regress spontaneously.

The statement has been made by Marshall26 that operations in the region of the chiasm are not only dangerous, but often fatal because of damage to vital centers. The recent paper by Love and Benedict21 in which they reported only 1 death in 35 patients who had removal of intraorbital tumors by the transcranial route would seem to refute this argument. The use of cortisone and adrenocorticotrophic hormone as an adjunct to the surgery of parasellar lesions has improved the morbidity and mortality of such procedures.19 Certainly intracranial exploration of the chiasm for evaluation of extent of the tumor and the possibility of radical resection should nowadays carry a negligible risk.

With the exception of 2 patients who had had surgical treatment prior to coming under our care, a uniform operative approach has been used. With a presumptive diagnosis of glioma of the optic pathways a transfrontal exposure of the roof of the orbit and the region of the chiasm is performed. If there are definite clinical signs of intraorbital involvement, the roof of the orbit is removed extradurally. The orbit can thus be decompressed and explored adequately. If tumor is found in the nerve a resection up to the globe is done. Whether or not there is clinical evidence of intracranial extension it is wise to open the dura mater and visualize the nerve and chiasm. In most instances it is best to resect the optic nerve back to the chiasm. This does not give the patient any additional disability to that already sustained in the intraorbital procedure and does provide further assurance that the tumor has been completely removed. Indeed, on occasion, it may be possible to remove an involved portion of the chiasm itself if it is felt that this will insure complete excision of the neoplasm. Such a procedure may further impair the patient’s vision in the opposite eye, but a hemianopic field of vision is not an intolerable neurologic defect, and is justified if complete removal can be accomplished. If, however, there is gross involvement of the entire chiasm or the optic tract so that complete removal is precluded, it is better to be more conservative and remove only sufficient tissue for biopsy. If, in
such a case, there is any remaining vision in the affected eye it is our feeling that careful decompression of the orbit and optic canal may give the best chance for improvement, or at least for delay in further visual loss. It is likely in this circumstance that the patient will have a reasonably long period of survival with slow progression of symptoms. There is certainly no justification for increasing disability by an operation that will not be curative.

It is only by this type of exploration that the tumor can be evaluated properly and those patients selected in whom complete surgical extirpation is warranted. Certainly at the present time surgery is the only definitive method of curing these patients. When complete removal of the intraorbital and intracranial portions of the tumor has been accomplished and it is found that the tumor has extended into the globe, enucleation followed by insertion of a prosthesis may be done by the ophthalmologist at a later date. It is possible to leave the eye in place if there is no neoplasm in the distal end of the nerve; however, in all of our patients enucleation proved necessary in order to achieve complete excision of the tumor.

In the 4 patients with purely intraorbital tumors the above method of therapy was used, and in all it was found histologically that the tumor had been completely resected. These patients are now living and well 1 month, 8 months, 5 years, and 8 years following operation. All of these patients have normal vision in the remaining eye.

Of the 9 patients in the intracranial group 2 died postoperatively. These were the 2 earliest cases in our series. In both there was found to be a large intracranial mass from which a biopsy was taken, no attempt being made to remove the entire tumor. Both of these children died within 3 days of their initial operation in status epilepticus. There was no evidence of operative complication found at postmortem examination and no adequate anatomical explanation was found for their death other than the large tumor extending posteriorly in the middle fossa together with a minimal degree of cerebral edema. These patients were both operated upon prior to the availability of cortisone.

The other 7 patients of the intracranial group are living, 6 of them with useful vision. The patient who is blind had already lost all vision prior to operation. One of these patients is 7 years from the time of his initial operation, 3 are 4 years, 1 is 2 years, 1 is 6 months, and 1 is 1 month. Unfortunately, most of these patients are too young to allow accurate objective measurement of visual acuity, but at least they are all carrying on without special visual or sight-saving aids. Three patients have subsequently shown sexual precocity, that is, adolescent secondary sexual characteristics developed before the age of 8 or 9. The others are either still too young or have shown no evidence of premature sexual maturation. No objective analyses of endocrine function have been carried out on the whole group.

Four of the 7 remaining patients had partial removal of the intracranial mass; 1 had a grossly complete removal of the intracranial mass as well as
removal of the intraorbital portion of the optic nerve and globe. Two patients had only exploration of the chiasm with no attempt to excise the lesion because it was found that there was extensive involvement of both optic nerves and chiasm. In those patients who have an inoperable intracranial mass causing increased intracranial pressure by blocking the anterior portion of the third ventricle, a cerebrospinal fluid shunting procedure may give symptomatic relief. This was done in 1 of our patients by performing a bilateral ventriculocisternostomy.

The use of roentgen therapy in these lesions is a subject of some debate. Evaluation of any such therapy is difficult because many of these tumors grow very slowly even without any definitive treatment. Thus, length of survival cannot in itself be used as a criterion of the efficacy of roentgen therapy. Many of the recorded statements must be regarded as clinical impressions, since many of the data on which they are based do not bear statistical scrutiny.

Duke-Elder is of the opinion that roentgen therapy is of little value. Cohen recognizes the fact that these tumors are very slowly growing, but in some cases he feels that radiation treatment seems to be of limited value. More recently Taveras et al. reported that roentgen therapy is effective in the treatment of these lesions. However, of 17 patients with verified gliomas with adequate follow-up in their series only 4 were objectively improved (using the criterion of visual acuity). In the other 13 patients there was either no change or they continued to have slow progressive visual loss, as is usually expected. The most significant results were noted in a group of 9 patients in whom the diagnosis was made only on clinical and radiographic evidence. Of these, 6 patients were definitely improved clinically, and sometimes to a remarkable degree. It is felt, however, that such observations must be considered with reservation because of the occurrence of other lesions simulating these gliomas both clinically and radiologically, and thus possibly giving rise to misleading conclusions. Although this report indicates that roentgen treatment has been of value in certain cases, there is no proof of an appreciable effect on the majority of these lesions.

None of our patients with purely intraorbital lesions was given postoperative roentgen therapy since it was felt that total surgical excision had been accomplished. Among the intracranial group 1 was given a depth dose of 4850 roentgens to the region of the chiasm and involved orbit and 1 was given 2830 roentgens to the intracranial portion of the optic nerves and chiasm. There was no evidence of improvement of vision in either of these 2 patients; however, their signs have not progressed significantly 6 months and 4 years after treatment. In the 5 patients who had no therapy other than partial surgical excision the results are comparable. It would seem reasonable in our opinion, therefore, that if a glioma of the optic pathways cannot be completely excised it would be well to give roentgen therapy to the areas involved in the hope that it might be of some value in delaying further growth. Based on our own limited experience it cannot be assured that any improvement in neurologic status will take place after such treatment.
GLIOMAS OF OPTIC PATHWAYS IN CHILDHOOD

SUMMARY

Gliomas of the optic pathways are slow-growing, non-metastasizing brain tumors occurring predominantly in childhood. The presenting signs depend on whether the neoplasm originates from the intraorbital or intracranial portion of the optic pathway.

Progressive unilateral proptosis combined with decreasing visual acuity is the common presenting clinical picture in the primarily intraorbital gliomas. Increased intracranial pressure combined with decreasing visual acuity is the characteristic feature of primarily intracranial optic pathway gliomas.

Enlargement of the optic foramen and deformity of the sella turcica as seen by roentgenograms are suggestive but not diagnostic of this tumor and do not reliably indicate the extent of the lesion.

On the basis of our recent experience with 13 tumors in children under 12 years of age and information gained from review of the reported experience of others, it is felt that transfrontal craniotomy and orbital unroofing offers the best opportunity for satisfactory evaluation of the extent of these lesions, and the only opportunity for complete removal when this is surgically feasible. Total excision in 5 of our 13 cases is felt to have been accomplished.

When complete excision is inadvisable, histologic verification by biopsy is recommended, followed by roentgen therapy in the hope of slowing down further growth of the tumor. If an inoperable chiasmal tumor extends into the orbit and there is remaining vision, orbital decompression as well as irradiation is recommended.

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