GLIOMAS OF THE OPTIC NERVE AND CHIASM IN CHILDHOOD*

BY *Lois A. Lloyd,* MD

THE TREATMENT AND THE PROGNOSIS OF GLIOMAS OF THE OPTIC NERVE AND chiasm in children has always been unsatisfactory. All forms of therapy, including surgery, are not of proven value because of the unpredictable manner in which the tumor will spread in one patient but not in another. As a result, there have been advocates of surgical intervention, of radiological treatment, and therapeutic nihilists who feel that no form of treatment will do any good. In view of the lack of agreement on this subject, I have reviewed those cases available to me, to search for significant prognostic hallmarks and for a choice of therapy which would give the most favorable results.

Hoyt and Baghdassarian in 1969[1] reviewed the controversy over therapy of optic nerve and chiasmal gliomas. Their study of the natural history of this condition in 36 patients indicated that biopsy or surgical removal of the tumor did not affect the prognosis for vision or life. Indeed they advocated no treatment except measures to relieve unsightly proptosis or obstructive hydrocephalus. This startling advice will lessen the interest of ophthalmologists in making an early diagnosis of optic nerve glioma and militate against surgical removal of a purely localized orbital or prechiasmal glioma which heretofore has been totally excised. Hoyt's revised concept of treatment comes as a shock in spite of the fact that Martin and Cushing in 1923[2] stated that anyone who presumes to treat this condition by any therapy is overenthusiastic. However, the material in my study indicates that surgical removal still offers the best prognosis in this condition. This paper, therefore, re-emphasizes the advantages of surgical removal of optic nerve and of prechiasmal gliomas. It urges surgical inspection when a chiasmal glioma has radiological evidence indicative of a unilateral tumor. Chiasmal involvement and other surgically amenable conditions can only be excluded by direct inspection of the lesion.

*From The Hospital For Sick Children, Toronto, Canada.

TR. AM. OPHTH. SOC., vol. LXXI, 1973

HISTORICAL REVIEW OF THE LITERATURE

Gliomas of the optic nerve and chiasm although rarely diagnosed by an individual ophthalmologist have been reported frequently. There are many reviews of the subject. The first description in 1816 was by Scarpa.[3] The condition was again described by Wishart[4] in 1833 who first successfully removed an optic nerve tumor. His description is worthy of reproduction:

> Yorretta Douglas age 13. On looking downwards with the eye, a firm tumor can be distinctly felt near the situation of the lacrimal gland. For the first three months nothing was done for it, but after that there was such a rapid increase in size that the surgeon who was consulted pronounced it to be dropsy of the eye. He applied leeches over the eyebrow and blisters to the temple without producing any mitigation of the symptoms. At a consultation with Dr Gillespie and Professor Lizars it was agreed that nothing could be done to save the eye. I removed the eye, assisted by the gentleman and Mr Bert on the first of March.
>
> On examination of the eye after its removal, the disease was found to be seated in the substance of the optic nerve, the coat of the nerve being very much distended and evidently forming the outer cover of the tumor. The tumor was of a firm consistancy resembling cerebral substance, generally considered of a malignant nature. I have never met with any cases of the same description as this in the works of surgery or morbid anatomy which I have examined. The only one resembling it is related by Panizza[5] in his work "sul Fungo Midollare" in a little girl six years of age in which there was found on dissection not only a small tumor surrounding each optic nerve but a still larger cerebral mass at the base of the brain.

Von Graefe[6] in 1864, with the insight of his genius, accurately reported on two cases and laid down the criteria which are used today in the diagnosis of this condition.

In the first review of the literature, covering the 19th century, Byers[7] discussed 102 cases already published and added two of his own. In 1912 Hudson[8] reviewed 182 case reports in the literature. Lundberg[9] tabulated 123 cases from 1912 to 1934 for a total of 305 cases. In 1940 Davis'[10] superb review of the literature included a total of 380 cases; he added five more. Marshall[11] in 1953, at the Annual Meeting of the American Ophthalmological Society in Hot Springs, emphasized the association of optic nerve glioma and von Recklinghausen's disease. An excellent review in 1956 by Taveras[12] supported radiation therapy. Dodge[13] et al in 1958 agreed that transfrontal craniotomy was the best means of resecting optic nerve and chiasmal tumors. In 1959 Wagener[14] reviewed the

literature again and discussed various changes which may be seen ophthalmoscopically in this condition. Since then, some thirty[15-43] shorter reviews and case presentations have been reported in the English literature including papers on diagnosis, radiological examination, pathology, and treatment.

INCIDENCE

A discrepancy exists between the number of cases reportedly seen by ophthalmologists and the number treated by neurosurgeons. Collins and Marshall[44] (1910) of Moorfields Eye Hospital declared the incidence to be two in 388,000 patients with ocular complaints. In 1923 Martin and Cushing[2] stated that optic nerve gliomas made up 0.8% of all verified tumors and 2% of all gliomas. Yet later Cushing[45] (1932) quotes an incidence of 22 in 2,000 cases of brain tumor.

From the records of the Massachusetts Eye and Ear Infirmary[46] (1932) optic nerve glioma was found in four of 669,857 patients over a period of 36 years; at the Wills Eye Hospital, Philadelphia[47] (1958) in one of 230,742 patients over a period of 12 years. An American Federation of the Institute of Pathology study[48] reported 18 gliomata in 50,000 tumors. At the Walter Reed Army Hospital the incidence is six per 50,000 ophthalmic patients. Taveras[12] found 34 cases in a series of 2,000 gliomas, an incidence of 1.7%. Fowler et al[49] at the Children's Medical Centre, Harvard Medical School, found 13 cases of primary gliomatous tumors of the optic pathways in 256 intracranial tumors in young children over a ten year period, an incidence of 5.1% of intracranial tumors or 7% of gliomas.

Matson[50] in 1969, reported 27 cases of pathologically confirmed primary gliomas of the optic pathways in a series of 750 intracranial tumors. This is an incidence of 3.6% in the total series and 4.5% among the gliomas.

Approximately ten primary tumors of the optic nerve are reported annually and seven of these are gliomas, according to Bane.[24] Arkhangelsky[30] (1965) noted an incidence of one in every 100,000 patients but MacCarty[42] at the Mayo Clinic (1970) found optic nerve glioma to be the second most common orbital tumor. Four hundred and eleven case reports have been added to the 660 reviewed by Marshall in 1953, making a total of 1076.

TUMOR SITES

Wolff[86] suggested that the most likely origin of the tumor is ten mm behind the globe at the point of entrance of the central vessels. Hoyt[1]

found four out of seven gliomas of the nerve remained purely orbital. Boles[47] suggested the most likely point of origin is in the optic canal. The tumor extends from there forward into the orbit and may also grow intracranially toward the chiasm. Some authors are exponents of multicentric sites of origin[35] in one or both nerves, in the chiasm, in the retina, and at the optic disc.[27] The problem of multicentric gliomas has been discussed by Batzdorf and Malamud.[88] There is scant evidence for the presence of multipotential cells and there is little to account for the sometimes long delay between birth and manifestation of the tumor. The optic chiasm with one or both optic nerves and adjacent portions of the brain is more frequently involved at the time of diagnosis than optic nerve alone, as found by Martin and Cushing,[2] Jefferson,[57] Walsh,[89] Tym,[9] and others.

Only 11 cases of invasion of the optic disc have been reported prior to 1941. Bane[24] (1963), Hale[22] (1963), and Gartner[27] (1966) have added one such case each.

AGE

Fowler[49] found the average age of onset to be four and one half years. Levitt[91] stated that 75% of patients are less than ten years of age.

In Chutorian's series[41] of 56 gliomas, six tumors occurred at birth, 16 at over two years with a peak from two to six years and a range up to 15 years.

In the series from the Walter Reed Hospital[48] the average age of onset was ten to 12 years with a range from seven months to 47 years. The literature also includes a few other patients whose symptoms began after 40 years of age.

Otenasek[33] reported an optic glioma found in a 51-year-old black patient who also had a pituitary adenoma. Both tumors were excised at craniotomy. Bucy, Russell and Whitsell[62] reported a glioma in a 60-year-old patient. Hoyt[1] reported a glioma of chiasm and optic nerve found at autopsy in a 64-year-old woman.

Condon and Rose[32] described a 79-year-old woman who suddenly lost vision bilaterally over two weeks. At autopsy a right optic nerve glioma was found. This appears to be the oldest patient in the literature with this condition.

CLASSIFICATION

Leber[92] in 1874 divided gliomas into true (localized within the perineurium) and false (situated outside the dural sheath). Byers[7] labelled these intradural and extradural, most tumors being intradural.

Recent authors classify the tumor as intraorbital or intracranial. The intracranial tumors are more common than localized orbital gliomas.

FAMILIAL INHERITANCE

There have been three reports in the literature in which two members of one family have been affected with optic nerve glioma.

Holmstrom[93] described two sisters, Davis[10] and Manschot[70] each reported a brother and sister affected with optic nerve glioma.

Hoyt[1] found optic glioma in two generations of a family with von Recklinghausen's disease.

ASSOCIATION WITH VON RECKLINGHAUSEN'S DISEASE

The close and frequent association of optic nerve and chiasmal gliomas with von Recklinghausen's disease has been discussed by many authors, starting with Davis[10] and Marshall.[11]

Christensen[67] found this association in 50% of his series but simply mentioned the fact. Marshall[11] detailed the ocular as well as the general manifestations of von Recklinghausen's disease and thoroughly established the fact that glioma of the optic nerve occurs in the condition, as maintained by Davis.

Marshall's list of the ocular manifestations included: neurofibromatous tumors of the conjunctiva, corneal nodules and corneal nerve enlargement, neurofibromatous tumors in the uveal tissue, retinal and optic nerve and chiasmal gliomas, fibroma molluscum or plexiform neuromas causing thickening of the eyelids, asymmetry of the orbital walls with bony defects, optic canal enlargement, and neurofibromas in the orbit. Small neuromas on the iris most easily observed on slit lamp examination are diagnostic.

The clinical symptoms and signs in von Recklinghausen's disease include: ptosis, strabismus, proptosis (may be pulsating), rarely enophthalmos, visual failure with optic atrophy, buphthalmos, glaucoma, trichiasis, abnormal function of the nerves, visual field changes, papilledema, and hypermetropia.

The diagnosis of von Recklinghausen's disease can be made when, according to Crowe,[94] there are at least six café au lait spots on the skin and each is of at least 15 mm in diameter. Perhaps this form of von Recklinghausen's disease is more frequently associated with optic gliomas.

Thirty-seven percent of patients with optic nerve gliomas and 30% of patients with chiasmal gliomas have other manifestations of von Recklinghausen's disease. Neurofibromatosis is inherited as a dominant trait

so that one half of the offspring of the affected individual may be expected to have the disease. The offspring of an unaffected individual will remain normal. Abortive forms may show only café au lait spots. About one third of the patients may show the generalized neurofibromatosis of von Recklinghausen's disease.

ROENTGENOGRAPHIC FINDINGS

Van der Hoeve[95] introduced a roentgenographic method to demonstrate the optic foramina thus determining intracranial extension of intraorbital masses. The commonest finding roentgenographically in optic gliomas is a widened optic foramen without decalcification of its walls. Pfeiffer[96] considered an optic foramen of 6.5 to 7 mm, or 1 mm larger than the contralateral foramen, to be abnormal. Pfeiffer however noted enlargement of optic foramina in six patients with von Recklinghausen's disease who did not have optic tumors (quoted by Taveras[12] as a personal communication). Fowler and Matson[49] consider a normal optic foramen to vary between 4.1 and 4.65 mm in diameter.

Decalcification of the posterior wall of the orbit and lesser wing of the sphenoid has been recorded with gliomas as has calcification of the tumor itself.[29] If the tumor extends into the chiasm there may be:

1. flattening of the sella.
2. erosion of the anterior wall of the sella and undersurfaces of the anterior clinoid processes.
3. a "J" shaped, slipper, gourd, or shoe-sign; produced by pressure of the tumor on the lateral aspect of the chiasmal sulcus which becomes obviously hollowed out. Gourd-shaped sellae are also found in mongolism and Hurler's syndrome.

Schuster[29] found no changes in the sella in half his cases of gliomas of the optic nerve and chiasm and no cortical destruction in two thirds of his cases.

If the ventricular system is blocked there may be signs of raised intracranial pressure such as a beaten silver appearance of the skull and widened coronal sutures. After one month of raised intracranial pressure erosion of the clinoid processes can occur.

The normal distance from the chiasmatic point to the tuberculum sella varies from 10 to 23 mm as measured in the lateral view. This distance may be increased with gliomas.

Suprasellar calcification has been seen occasionally in gliomas. This was found in large tumors and the calcium varied from a single nodule to several granules spread over 3.5 cm, at the centre of the tumor.[29]

The diagnostic importance of the optic strut separating the optic canal from the superior orbital fissure was stressed by Cares and Bakay.[97] In neurofibromatosis with optic canal enlargement, the strut is not destroyed. In glioma of the optic chiasm the strut is deformed.

In chiasmal tumors, air in the chiasmatic cistern may outline the tumor of the nerve and chiasm. The remainder of the ventricular system is normal. There may be a deformity in the anterior part of the third ventricle and the chiasmatic cistern. The pneumoencephalogram has been shown to be falsely localizing in one patient.[98] In this patient the filling defect of the third ventricle with symmetrically dilated lateral ventricles was not due to pressure of a tumor, but was shown at necropsy to be due to a rare developmental anomaly; the coalescence of the dorsal thalamic parts.

In larger tumors the chiasmatic and infundibular recesses of the third ventricle may be pushed upwards and backwards. When the brain stem is pushed posteriorly by the mass there is obstruction of the aqueduct and dilatation of the ventricles. Still larger tumors block the foramen of Monroe as well as the aqueduct and produce hydrocephalus.

Pneumo-orbitography described by Bertelsen[99] may outline an orbital glioma. Ten cc of air injected into Tenon's space using a 5/8 inch needle following retrobulbar anaesthesia outlines the muscle cone and the globe. To demonstrate orbital tumors, Fogg[38] preferred injecting positive contrast media rather than air.

Holman,[15] like Hoyt,[1] believes that the diagnosis is mainly roentgenographic. Thus the diagnosis is based on changes in the routine skull films including enlarged optic foramen and sella turcica. Occasionally the tumor may be outlined by pneumoencephalography or ventriculography. Rarely an arteriogram helps to outline a particularly large tumor.

Since 1965[100] the visualization of the optic canal throughout its whole length by axial tomography has made possible the early diagnosis of intracanalicular optic nerve gliomas. The technique of Harwood-Nash[101] will be described in detail as the method of radiological examination in our series of patients.

PATHOLOGY

Byers[7] described variations of the fusiform expansion of optic nerve and noted that most tumors occurred in the posterior two thirds of the nerve. Variation in firmness, cyst-like masses and yellow to reddish gray color with occasional hemorrhagic spots were described. The early authors, (Byers[7] and Parsons[102]) felt that the tumor was of mesoblastic origin. Hudson[8] in 1912 disagreed and stressed the neuroglial origin of the

tumor. In 1923 Von Hippel noted the proliferation of neuroectodermal tissue in these tumors and the increased thickness of the nerve sheath around the optic nerve glioma. Verhoeff's[46, 104] magnificent descriptions of the microscopic appearance of sections of optic glioma have remained unchallenged. He noted three types of cells, any or all of which might appear in one specimen. There were finely reticulated cells suggesting exaggeration of neuroglia, coarsely reticulated cells with microcystic foci suggesting myxomatous changes, and cells of spindle shape forming coarsely fibrillated bundles, especially in areas where the sheath of the nerve was invaded. Some cells were oriented toward blood vessels to form pseudorosettes. The blood vessels were often hyalinized. Mitoses were not found. After adding 12 more cases to the literature, Verhoeff[104] concluded that all primary intraneural tumors of the optic nerve are gliomas and the spread of the tumor is by a progressive conversion of neuroglia into neoplastic cells.

In 1940 Davis[10] reviewed the literature and added five cases, including detailed microscopic studies. He felt that two thirds of optic nerve tumors were predominantly glial and one third endotheliomata. He also noted in many cases the thickening of the nerve sheaths surrounding the tumors. Some authors, including Christensen[67] and Liss,[105] have interpreted optic nerve gliomas as oligodendrogliomas. Rubenstein and Russell[51] used special stains to show that the optic nerve gliomas contained neuroglial fibrils of astrocytic lineage. Piloid astrocytes lying in nests of characteristically vacuolated cells within the trabeculated meshwork of astrocytes are sometime associated with mucinous areas, giving the microcystic appearance that Verhoeff interpreted as myxomatous. The piloid astrocytes form leashes of cells within the nerve substance and also infiltrate the expanded sheath. Rosenthal fibres may be present in the tumor cells.

Rosenthal fibres, once called "cytoid bodies" by Verhoeff,[46] have been shown by Herndon and Rubenstein[106] to be neurokeratin. They occur in certain cerebral and cerebellar astrocytomas, in optic nerve gliomas, and in various situations where a reactive gliosis has long been in progress. They result from degenerative metabolic changes in the cytoplasm and cytoplasmic processes of astrocytic glial cells. Electron microscopic studies indicate that they are found exclusively in the cell bodies and processes of astrocytes and never in oligodendrocytes or phagocytic cells. Zimmerman[107] states that optic nerve gliomas may contain acid mucopolysaccharide, in some cases sensitive to digestion by hyaluronidase.

Luse[17] and Anderson[35] have described the electron microscopic appearance of normal optic nerve and of glioma of the optic nerve. Light and electron microscopy show no evidence of degeneration, necrosis, or malignancy. Anderson noted that the extracellular space was often expanded. He thought that the mucoid substance was not due to astrocytic degenerative change, since no cellular necrosis was evident but that it was produced in the hypertrophied endoplasmic reticulum and Golgi appartus of the tumor cells.

The relative benign course of optic nerve gliomas has been repeatedly confirmed (Tym,[90] Matson,[50] MacCarty[42]). Malignant optic nerve tumors are rare. Saebo[60] and Mattson[118] have each contributed a case. Saebo's patient was a 43-year-old woman with unilateral proptosis, loss of vision of four month's duration, papilledema, and glaucoma. The optic foramen was enlarged. Treatment consisted of enucleation, incomplete removal of the tumor in the optic nerve, and radiotherapy. The patient died within a year with cerebral symptoms. Pathological diagnosis was glioblastoma multiforme.

TREATMENT OF OPTIC NERVE GLIOMAS

1. Surgical

Surgical removal was urged by Byers[7] who suggested that exenteration was not necessary. The Kronlein procedure,[108] introduced in 1888, was considered the operation of choice.

Alan Woods, in discussing Davis' paper[10] in 1940, protested against the frontal approach for removal of orbital tumors. He felt that the Kronlein route did not always permit total extirpation and that it might promote intracranial extension. He advocated a transfrontal approach, the bone flap being turned down from above and the roof of the orbit opened. He felt that in the hands of a competent neurosurgeon this was as safe as the Kronlein procedure.

Davis, like Hoyt in 1970, felt that the lesion in the optic nerve was part of a systemic disease. Other lesions presumably also existed in the chiasm, the brain and the fellow optic nerve. Therefore orbital decompression was only a palliative procedure to relieve exophthalmos and preserve the globe.

A lateral extracranial orbital approach with better exposure of the orbital contents than the Kronlein procedure may be preferred (Fogg).[38] A burrhole behind the zygomatic process of the frontal bone allows the orbit to be entered. The lateral wall is then removed down to the superior orbital fissure.

Berke[110] described a modified Kronlein approach in which the skin incision extended horizontally from the lateral canthus parallel to the zygoma. The enlarged external canthotomy results in a less unsightly scar. Adequate exposure is obtained by excising the lateral orbital wall with an oscillating Stryker saw.

A Killiam incision along the frontal and maxillary ridges gives good exposure of the orbit with little trauma, according to Spaulding.[48]

Walsh[89] has listed the indications which guide him in selecting the type of treatment used for tumors involving the anterior visual pathways. If the optic foramen is enlarged the neurosurgeon performs a craniotomy. The ophthalmic surgeon explores the orbit of the patient whose tumor clinically remains localized to the orbit. Walsh feels that a limited unroofing of the orbit gives an unsatisfactory approach to the orbital contents. A large unroofing requires an insertion of a tantalum plate to prevent herniation of the cerebrum into the orbit. Hence a modified Kronlein is the most satisfactory method of removing the orbital portion of the tumor.

Housepian[40] advocates the transcranial route for access to the apical structures of the orbit. It allows inspection of the chiasma and optic nerve at the same time. The lateral extracranial approach or a frontal craniotomy with modification is supported by many, including Dandy,[98,109] Love,[111] Matson,[50] Wadsworth,[34] and Fogg.[38] The optic canal may be unroofed if necessary. The majority of surgeons favor a two stage intracranial, followed by an orbital procedure. (Jefferson,[16] Bucy,[62] Macfarland,[63] Dodge,[13] Hanberry,[75] Fowler,[49] Holman,[15] Tym,[90] Chutorian,[41] MacCarty,[42] and many others).

2. Radiation Therapy

Taveras[12] found a dramatic restoration of vision in a significant number of his patients treated by radiation. This view has been supported by Chutorian.[41] Throuvalas[80] advocates radiotherapy before surgery in cases where the enlarged optic foramen indicates intracranial extension of the glioma.

Martin and Cushing[2] and Davis[10] thought that inoperable chiasmal gliomas should be treated by radiotherapy. Others who agree include Jefferson,[16] Dyke and Davidoff,[112] MacCarty,[42] and Fogg.[38] Hoyt and Glaser[43] on the other hand felt that radiotherapy was contraindicated in both chiasmal and optic nerve gliomas, since the natural course of the disease was usually protracted. This opinion is also expressed by Fowler,[49] Matson,[50] Wagener,[14] and Jain.[18]

PROGNOSIS

Byers[7] noted that a recurrence was rare following the surgical removal of an optic glioma but could usually be recognized by displacement of the globe. Hudson[8] was the first to mention that long survival was possible with only partial removal or biopsy of optic nerve gliomas. Posner and Horrax,[59] who reviewed the literature in 1948, suggested that the prognosis was not consistently as poor as estimated at that time. They published accounts of three patients who survived from four and one half to 12 years. The longest follow up reported in the literature is 41 years. This patient's chiasmal glioma was found at autopsy following a stroke, 41 years after her presumptive diagnosis had been made.[1]

Bane[24] reported a 24-year follow up with no recurrence following enucleation and removal of an orbital glioma in a child.

There are many reports of 20-year follow ups.[1, 8]

Hanberry[75] in 1956 concluded that the prognosis was better if the tumor could be completely excised. Dodge[13] agreed.

Recently (1969) Hoyt[1] has remarked on the long natural history of this condition and as a result urges conservative treatment for these patients.

CLINICAL SIGNS AND SYMPTOMS

Two distinct patterns of clinical signs occur; a pattern produced when the tumor is within the orbit, and one when the tumor is mainly intracranial. With both, the presenting symptom is usually a visual loss which precedes the proptosis by several months, depending on the site of the tumor. Loss of vision begins earlier if the glioma is intracranial than if it is only orbital. Fortunately the orbital tumor reveals its presence early by producing proptosis.

In orbital gliomas the initial symptom may be proptosis. Visual acuity, usually reduced, is often not noticed by the patient. The history is usually short, a few months, and shorter than in patients with intracranial involvement. Von Recklinghausen's disease may or may not be present.

The globe protrudes forward at first and later moves inferiorly and laterally. No pulsation of the orbital contents occurs. There is seldom any alteration in ocular movements, or involvement of the extraocular muscles. The tumor is nonpalpable but orbital resistance to posterior displacement of the globe seems increased.

Optic nerve gliomas, particularly in the orbit, produce disc edema.

More posteriorly placed tumors, especially in the intracranial portion of the nerve cause optic atrophy. Evidence of tumor at the optic disc, or occasionally normal discs may be seen ophthalmoscopically. Increasing hypermetropia may occur, due to the pressure of the tumor on the posterior surface of the globe. If the optic disc appears normal, and there is ridging of the retina in the posterior pole there is usually a mass present, pressing on that aspect of the globe. If the disc is swollen the ridging is usually due to traction.

In intracranial glioma decreased vision in one or both eyes is the presenting sympton. Visual field defects (bitemporal or homonymous hemianopias) can be plotted in older children. Proptosis occurs occasionally and suggests intraorbital as well as intracranial tumor. Optic atrophy is commoner than papilledema, although either or both may be present. Increased intracranial pressure produces bilateral papilledema. A positive Macewen's sign (increased resonance on combined percussion and auscultation of the skull due to distended lateral ventricles), unsteady gait, hypothalamic dysfunction (obesity, sleepiness and lethargy), and sexual precocity are frequent signs. When the tumor spreads to involve the third ventricle and hypothalamus, death results from mechanical pressure on vital structures.

CLINICAL MATERIAL AND METHODS

In the past 27 years (1945-1972) 41 patients (31 verified pathologically and 10 not) with childhood gliomas of the optic nerve and chiasm were treated or observed. For this study, all the charts were reviewed; the history, age at onset, association with von Recklinghausen's disease, intelligence quotient, symptoms and physical signs were noted.

Proptosis was measured by a Hertel exophthalmometer. Visual acuity was estimated by the patient's ability to see or follow a light or to count fingers. Refraction and the Sheridan-Gardiner test were performed in children under three years and the Snellen test, using the E game, numbers, or letters was performed in those over three years. Visual fields were plotted on a Ferree-Rand perimeter and tangent screen where age and cooperation made this test possible. Routine skull roentgenograms (anteroposterior and lateral) were made in all patients. After 1969 axial tomograms were made in patients in whom the history and physical examination suggested optic glioma or roentgenograms indicated optic canal abnormality. Pneumoencephalograms, ventriculograms, and arteriograms were performed when indicated.

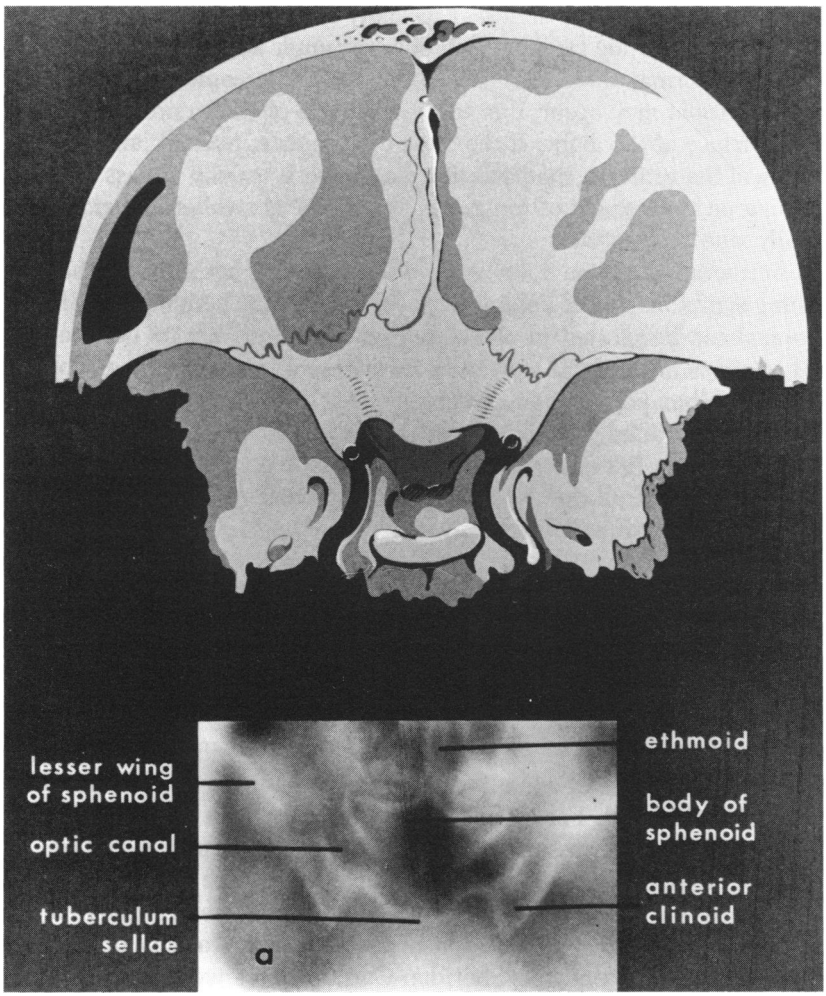

FIGURE 1

Diagram showing coronal section of normal skull through the optic chiasm. a) Axial tomogram showing normal optic canals.

FIGURE 2

Hyperextended head position of patient having axial tomography of the optic canals. A. Outer canthus of the eye. B. The upper junction of the ear and scalp. C. Mid-point of A-B. D. Junction of the saggital plane and line extrapolated upwards from C.

METHOD OF AXIAL TOMOGRAPHY OF THE OPTIC CANALS

The entire length of the optic canal is examined roentgenographically to detect the site and the extent of the enlargement. An accurate demonstration of the anteromedial posterolateral longitudinal margins of the canals, together with the intracranial and orbital meati, is important to the early diagnosis and long term evaluation of optic nerve gliomas. Precise localization of the lesion is necessary in planning surgical or radiotherapeutic treatment or both. Tomography of the optic canals, along their longitudinal axes provides simultaneous visualization of the horizontal section of both canals in one roentgenograph. It also allows the anterior clinoids, limbus sphenoidale, tuberculum sella, posterior clinoids and the lesser wings of the sphenoid to be measured. (Figure 1) Tomography thus provides comprehensive knowledge of the basic anatomical and developmental anatomy of these structures. The method has been reported by Harwood-Nash[101] in 1970.

METHOD

a Hypocycloidal polytomography is performed with the polytome table horizontal. The child is placed in a supine position on a padded box, 6 inches high, with the neck hyperextended over the edge, so that the vertex touches the table top. Sedation is rarely needed. (Figure 2)

b A line joining the outer canthus of the eye (A) and the upper junction of the ear and scalp (B) parallels the table top. (Figure 2). In this position the interorbital plane is horizontal. The tube is then aligned with a point (D) marked on the child's neck at the junction of the saggital plane, and the line extrapolated upwards from the mid-point of the line joining A and B.

c Three trial exposures are performed, the middle exposure at the level of A-B, and the other two 0.5 cm above and below this line respectively. The optimum tomographic level is measured from the vertex on the table top. Six exposures, 1 mm apart, are performed on one film around this optimum level.

d The average technique for the children is MA-50 timed for 6 seconds, and KVP-60. The skin dosage is approximately 0.85 rad, positioning of the cones avoids exposure of the corneas.

e True anatomical measurement is obtained by multiplying the measurements made on the roentgenograph by a factor of 0.77.

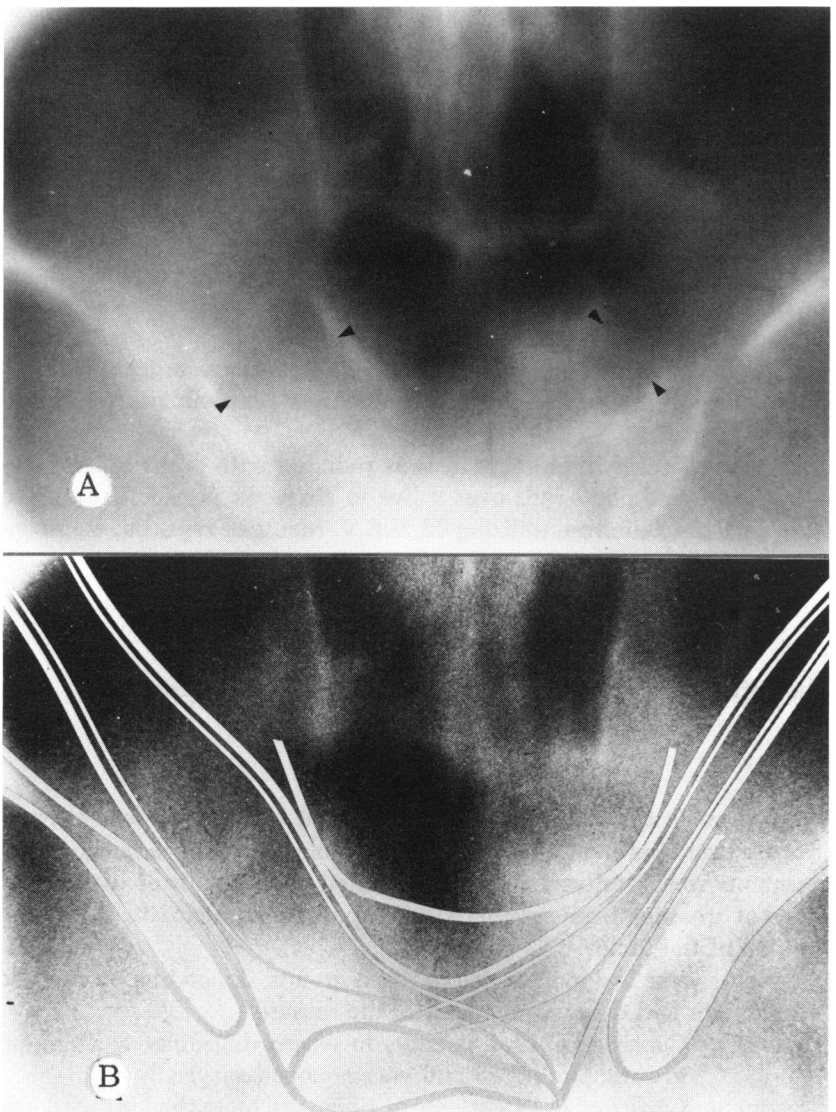

FIGURE 3

A: Axial tomogram showing unilateral dilation of the right optic canal and B: artist's drawing to demonstrate right optic nerve glioma.

During the past two years, 300 children have undergone this procedure for conditions as varied as anophthalmus, optic atrophy, fractures of the anterior clinoids, parasellar tumors, and optic gliomas. A tomogram of the optic canals of a child with an optic nerve glioma is shown in Figure 3.

TREATMENT

The type of treatment whether surgical removal of the tumor, craniotomy with or without biopsy, surgical shunting procedures, radiation, or combinations of these were noted.

The neurosurgical operation varied with the neurosurgeon.[50, 120] To expose the orbit we have used the modified Kronlein procedure described by Berke.[110]

In selected cases the tumor site was radiated with doses ranging between 5000 and 5500 rads over a five to six week period. Usually we have used our Betatron, utilizing 22 N.E.V. roentgen rays, but occasionally the Cobalt unit was used.

PATHOLOGY

The pathological findings at biopsy or necropsy were recorded.

FOLLOW UP

When possible the children were examined at frequent periods approximately every six months and ocular, neurological, and radiological assessments were performed where indicated. The results of the various types of treatment are compared with particular regard to the initial position of the tumor.

Patients were assigned to one of three groups, depending on the site of the tumor and the clinical course of the disease.

GROUP I Consisted of nine patients in whom the tumor was limited to one optic nerve and was removed surgically.

GROUP II Consisted of 12 patients in whom the tumor had invaded one or both optic nerves and the chiasm. In none of these has the vision or general condition worsened during the follow up period.

GROUP III Consisted of 20 patients in whom the site of the tumor was the same as that in Group II, but whose vision and general condition worsened. Five are dead and one is presumed

dead. Necropsy in the five revealed widespread extension of the glioma which apparently began in the optic chiasm. Patients with astrocytomas, secondarily invading the optic chiasm were excluded from this study.

TUMOR SITES

I found no evidence that the tumor began at more than one site. Either it began in the chiasm and involved one or both optic nerves, or it involved the optic nerve and the chiasm on one side, or it began in one optic nerve alone. The optic tract was involved with the chiasm in two patients (Case #29 and Case #38).

Clinically the chiasm was involved in 32 patients out of the total 41, 16 had bilateral symptoms. In six, the chiasm and left optic nerve only were affected and in ten the chiasm and right optic nerve only. Chiasmatic gliomata were verified pathologically in 22 patients. Four had chiasm and left nerve involved, four had chiasm and right nerve, and 14 had chiasm with both optic nerves included in the tumor at time of diagnosis.

RESULTS

RESULTS OF GROUP I CASES

Group I consists of nine patients in whom the tumor was limited to one optic nerve and was removed surgically. Two patients were males and seven were females. The age of onset ranged from three to eight years; four patients being four years of age. Von Recklinghausen's disease was present in five of the nine, two of whom also had a family history of von Recklinghausen's disease. The intelligence quotient was normal in all patients.

The presenting symptom was proptosis in seven of the nine patients and had been present for from three weeks to two years. Frontal headaches had been a feature in one patient and ocular pain of rather short duration in another. Papilledema found incidentally by a physician-father in one instance (Case #6) led to further investigation. Only one patient had a history of strabismus, and surgical correction had been undertaken one year before the diagnosis of optic nerve glioma was made.

All patients had proptosis varying from 1 to 7 mm on the affected side (Figure 4). The visual acuity in the affected eye was reduced in all patients. Two patients had no light perception at the time of diagnosis. One had inaccurate light projection and the remainder had vision of

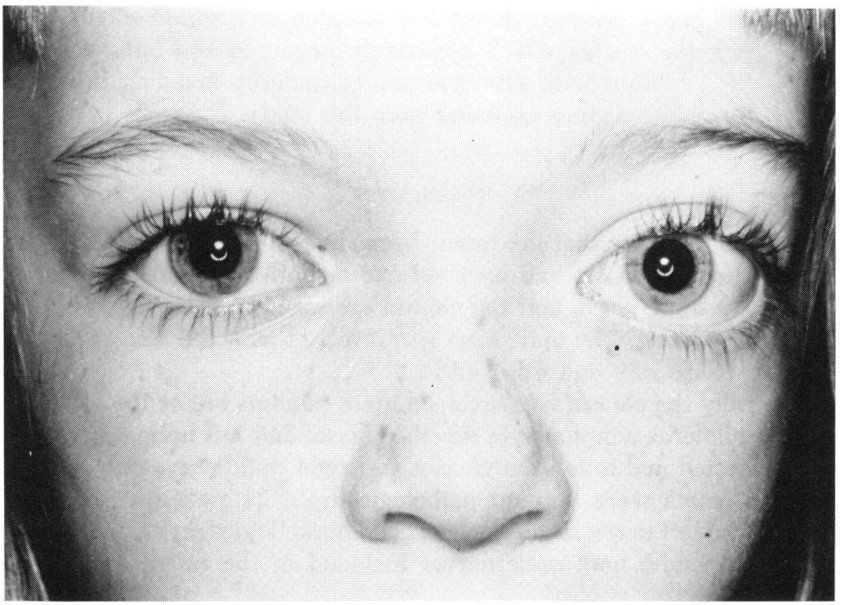

FIGURE 4
Unilateral proptosis of left eye in child with optic nerve glioma.

20/100 or less. except for one child whose vision was 20/50 on the affected side. One temporal and one constricted field defect in the affected eye was plotted. The visual field was normal in all unaffected eyes except in one patient where poor cooperation prevented visual field assessment. Papilledema was found on the affected side in all but two patients, varying from a slight blurring of the disc margins to gross swelling with hemorrhages and exudates. Optic atrophy occurred in only two patients. In all nine patients the disc was normal on the unaffected side. No other retinal abnormalities were noted and no tumor could be identified in the swollen discs. A sixth nerve palsy, present in two children resulted in esotropia in one. Exotropia was present in two other children, one of whom had had corrective surgery. None had nystagmus.

RADIOLOGICAL FINDINGS IN GROUP I

The characteristic finding was a dilated optic foramen on the affected side in the routine skull roentgenogram (Figure 5). Only one child had a normal skull roentgenogram showing normal optic foramina. No child

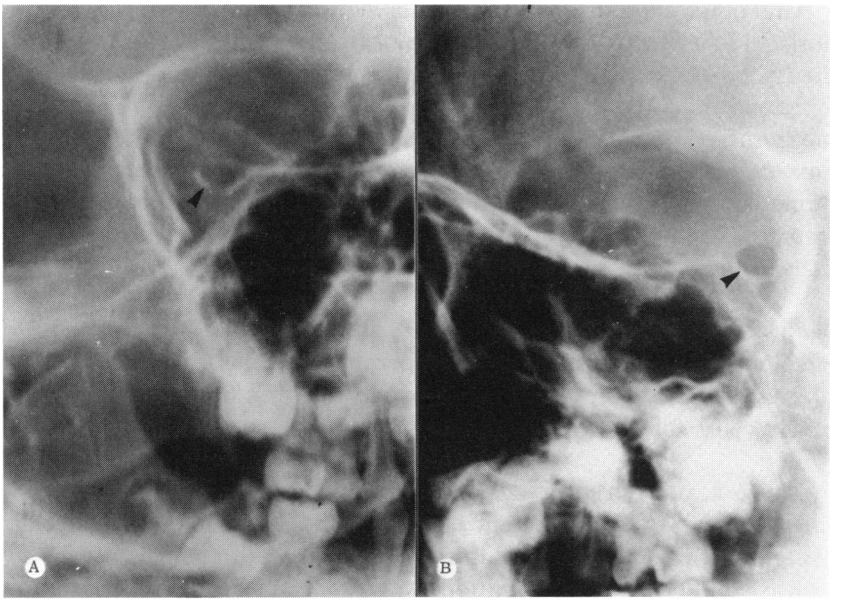

FIGURE 5

Roentgenogram to show the optic foramen (indicated by arrow). A. Note the normal oval right optic foramen. B. Diffuse swelling of the left optic foramen due to optic nerve glioma.

had separation of the coronal sutures or other signs of increased intracranial pressure. The right clinoid appeared thinned in one child, a finding confirmed by tomography. An encephalogram in this patient showed asymmetrical filling of the lateral ventricles, the left being larger than the right. Axial tomograms in four of these patients showed enlargement of the optic canal on the affected side.

SURGICAL TREATMENT IN GROUP I

Only one patient was treated solely by a modified Kronlein procedure (Case #1). Eight patients had craniotomy with biopsy and in one of these the craniotomy was repeated (Case #2). Two years after craniotomy a second craniotomy was performed and the proptosed eye was enucleated. At the second craniotomy no evidence was found that the tumor had crossed the incision between the nerve and the chiasm. The tumor was growing forward from the mass in the optic canal toward the orbit.

One other child in this group underwent enucleation to relieve proptosis. In four others, removing the tumor from within the orbit by a modified Kronlein procedure was sufficient treatment for the proptosis.

In one child, in whom the tonogram showed a dilated optic canal, the neurosurgeon unroofed the canal, and removed the intracanalicular and intracranial portion of the optic nerve to within 3 mm of the chiasm. No tumor was found in the specimen. However tumor was found microscopically in the orbital part of the optic nerve which was subsequently removed by a modfied Kronlein procedure.

RADIATION IN GROUP I

One child (Case #2) received postoperative radiation therapy following the second craniotomy. No further extension of his tumor has been seen in six years follow up.

PATHOLOGICAL VERIFICATION IN GROUP I

In all patients of Group I, optic nerve glioma was verified pathologically. The tumor was contained within the nerve sheath and microscopically consisted of closely packed fibrous strands, arranged in a whorl pattern. The number and size of nuclei varied. No mitotic figures were seen in any specimen.

FOLLOW UP IN GROUP I

The length of follow up studies of patients in this group ranged from nine months to 15 years. In all the visual acuity and visual fields in the remaining eye were normal. Skull roentgenograms showed no change in the optic canals after nine years. The tomogram repeated in one child, a year after diagnosis also showed no change in the size of the optic canals. In another child the tomogram, five years after diagnosis, showed the size of the canal to have decreased on the affected side (Case #8). One child (Case #1) had a postoperative right sixth nerve palsy with esotropia, which was corrected surgically. Three others had a temporary postoperative sixth nerve palsy which required no treatment. All children appeared to lead normal lives with, of course, normal vision remaining in one eye only.

RESULTS OF GROUP II CASES

Group II consisted of those 12 patients in whom the tumor had invaded one or both optic nerves and the chiasm and in whom the disease did not progress during the follow up period.

CLINICAL FINDINGS IN GROUP II

The eight females and four males in this group, ranged in age from four months to nine years. Seven of the 12 children were five years of age or younger. Von Recklinghausen's disease was present in six and two of these also had a family history of von Recklinghausen's disease. One child with no evidence of von Recklinghausen's disease had a sister with café au lait spots. The intelligence quotient was low normal (70 to 80) in three patients, two of whom also had von Recklinghausen's disease. Two children had been admitted to the neurological service, one (Case #12) because of a weak left arm and leg with bilateral hyperreflexia and Babinsky sign, the other (Case #20) because of headaches, nausea, vomiting and listlessness. Both of these children required surgical shunting procedures to relieve the obstructive hydrocephalus.

In this group, visual loss, commoner as a presenting symptom than proptosis, occurred in six patients and had been present for from five days to three years prior to diagnosis.

Proptosis (3-4 mm) was the primary problem in two patients and was noted in two others. In all patients the proptosis was of recent onset. Two patients complained of ocular pain and five presented with strabismus of from one to two years duration. One patient had undergone previous strabismus surgery. An incidental finding of papilledema on routine examination brought one patient into the hospital for further investigation (Case #10).

Visual loss was bilateral in three patients. One had no light perception in either eye; another, light perception only in both eyes. The third could count fingers when using one eye and had no light perception in the other. In the other nine patients visual loss was unilateral, varying from no light perception only to 20/200 vision. The visual fields could not be tested in three patients in this group, because two were too young and the other had no light perception. One patient had a bitemporal visual field defect and in the remaining eight patients the visual fields appeared normal. Optic atrophy occurred bilaterally in three patients and unilaterally in four. Papilledema occurred unilaterally in six patients, one of whom had optic atrophy in one eye and papilledema in the other. One patient had esotropia with a sixth nerve palsy and another had esotropia without nerve palsy; another had exotropia. One patient in this group had a searching nystagmus associated with blindness (Case #12).

RADIOLOGICAL FINDINGS IN GROUP II

The skull roentgenograms in one patient originally showed a normal optic foramen, one month later the foramen had enlarged to 8 mm (Case

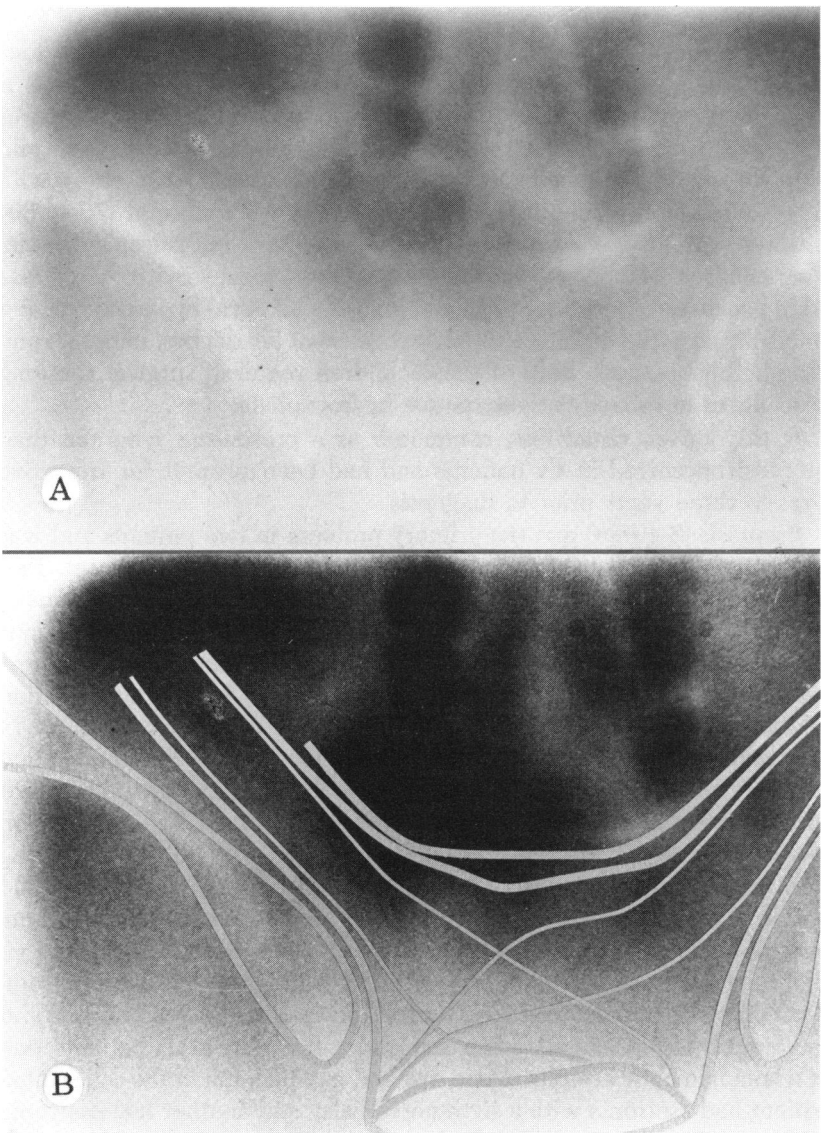

FIGURE 6

A. Bilateral dilation of the optic canals in tomogram of glioma of the optic chiasm involving both nerves. B. Artist's conception superimposed on tomogram of same as A.

#11). In two other patients the optic foramina appeared normal, but in one of these, subsequent tomograms showed enlargement of the optic canal (Case #17). Enlargement of the optic foramen was unilateral in eight patients and bilateral in two (Case #10 and Case #16).

Other abnormalities noted in the routine skull roentgenograms were splitting of the coronal sutures in two patients (both of whom had hydrocephalus with raised intracranial pressure) and erosions of the anterior clinoid processes or abnormalities of the sella in six patients.

Tomography of the optic canals in the six patients in whom it was performed, revealed bilateral enlargement in one patient (Figure 6) and unilateral enlargement in three others. The canals appeared normal in two patients (Case #11 and Case #12). The chiasmal lesion was demonstrated by air encephalography in six patients, by ventriculography in two, and by arteriography in four.

SURGICAL INVESTIGATION IN GROUP II

Surgical resection of the tumor was impossible in this group. Ten patients underwent craniotomy for biopsy. Unfortunately in one patient the biopsy specimen was lost. In another patient, craniotomy revealed a normal appearing optic chiasm so no biopsy was taken. One patient (Case #16) had a modified Kronlein procedure to remove the orbital tumor, although the proptosis was slight (2 mm). Shunting procedures to relieve hydrocephalus were performed in two patients (Case #12 and Case #20).

No treatment was given to one patient in this group. Surgery was not performed because the child had hypertension and was ill (Case #21).

RADIATION IN GROUP II

Radiotherapy was given to eight patients.

PATHOLOGY IN GROUP II

Pathological verification was made in nine patients. Microscopically the tumors resembled those of Group I. No evidence of malignancy was found.

FOLLOW UP IN GROUP II

The length of follow up for patients in Group II has been from six months to 11 years. Visual acuity has become no worse except for the visual loss from the surgical biopsy on the side of already poor vision.

Visual acuity improved from what it was at time of diagnosis in two of the 13 patients in this group. In one (Case #11), the vision improved

from light perception only to counting fingers following craniotomy, biopsy, and radiation therapy. The improvement may be attributed to the radiation therapy. The other (Case #19) improved spontaneously from 20/300 to 20/20 after craniotomy failed to show any tumor; biopsy was not done. He has been re-examined over a period of four years and vision has remained normal. In ten other patients the vision remained unchanged. Four patients had temporal visual field defects on re-examination. In only one patient had the defect been recognized at the time of diagnosis, four years previously. The other visual field defects were not felt to be due to a surgical complication but rather lack of cooperation at earlier examinations.

A postoperative sixth nerve palsy occurred in two patients, one was cosmetically straight and one had esotropia. Two other patients developed strabismus in amblyopic eyes and in one other patient strabismus persisted in a blind eye.

RESULTS OF GROUP III CASES

These 20 patients in whom the tumor invaded one or both optic nerves and chiasm and in whom the disease progressed constituted the final group of this series.

There were ten males and ten females whose ages varied from nine months to 12 years with an average age of six years. Eight of the 20 patients had von Recklinghausen's disease and three of these also had a positive family history of that condition. One other patient with no evidence of the disease herself had a family history of café au lait spots. The intelligence quotient was low normal (70 to 80) in nine of these patients, four of whom also had von Recklinghausen's disease.

CLINICAL FINDINGS IN GROUP III

The presenting symptom in nine patients was visual loss of from six weeks to five years' duration. Only one patient presented with precocious puberty which had been noticed for one year. Symptoms and signs of increased intracranial pressure such as headaches, falling, drowsiness, hydrocephalus, clumsiness, and increasing somnolence were noted in nine patients. One had had hemiplegia for six months and another for three months. One patient's complaint of bulging eyes (Case #41) had led to ophthalmic investigation. No proptosis was measureable, however. Optic atrophy found on routine ocular examination caused another patient to be hospitalized for further studies (Case #40).

Visual acuity was reduced in both eyes to no light perception in three patients. In 14 the vision ranged from 20/100 to light perception. Unilateral loss of vision was present in three patients only. Vision was normal in one patient at the time the presumptive diagnosis was made and was reduced to only 20/30 in two patients, in whom the diagnosis was not verified pathologically.

A bitemporal visual field defect was recorded in five patients and a homonymous hemianopic field defect in one patient. In five patients in this group there was no record of the visual field at the time of diagnosis, because they were too young to record accurate fields, even by confrontation.

Optic atrophy was noted in 15 patients and was much commoner than papilledema which was noted in three. The discs were thought to be normal in one patient only, and in one child (Case #33) they were not seen. A sixth nerve palsy was also noted in one patient in this group at the time of diagnosis. Another had esotropia and four others showed exotropia. There was one patient with marked hypertropia. Nystagmus, searching in type, was seen in three patients and a jerk type of nystagmus, indicating brain stem damage was seen in seven other patients.

RADIOLOGICAL FINDINGS IN GROUP III

Skull roentgengrams showed abnormalities in the optic foramina in 15 patients, bilaterally in 11 and unilaterally in four. The optic foramina were normal on both sides in five patients. Coronal sutures were separated, indicating increased intracranial pressure, in 12 of these patients. Ten of them had abnormalities in the region of the sella, a finding seen in three other patients without separation of sutures. Tomography of the optic canals was done in five patients and was helpful in making the diagnosis. The air encephalogram contributed to the diagnosis in 13 of the 14 in whom it was performed. Ventriculograms were confirmative in seven patients and arteriograms in four of the five patients having arteriography.

SURGICAL INVESTIGATION IN GROUP III

Ten patients underwent craniotomy with biopsy, confirming the diagnosis of glioma. Enucleation or modified Kronlein procedures were unnecessary because no patient had significant proptosis. Seven patients had shunting procedures to relieve hydrocephalus. Two patients had craniotomy without biopsy, because at the time the optic nerve and chiasm appeared normal and a diagnosis of arachnoiditis was considered

more appropriate. However in one of these patients the visual acuity decreased from 20/20 in both eyes to 20/100 and 20/50 in right and left eyes respectively, and the visual fields showed a bitemporal defect; in the second, a tomogram three years later showed that the optic canal had increased in size.

RADIATION IN GROUP III

Fourteen patients in this group received radiation; four in addition to shunting procedures, seven following craniotomy with biopsy, and three without surgical treatment. Those not radiated had craniotomy with biopsy (three patients), craniotomy without biopsy (two patients), and a shunting procedure (one patient). The three patients who only received radiation therapy had progressive visual loss. Three others who had radiation therapy combined with shunting procedures died.

Pathologic verification of the tumor was made in 13 of the 20 in this group. There was no evidence of malignancy and nothing to differentiate the cell type or the pleomorphism from those of Groups I or II. Extension of the tumor into the surrounding tissues was the only pathological difference from Groups I and II.

FOLLOW UP IN GROUP III

The follow up period varied from two to 13 years. One other patient, impossible to find six months after treatment, is presumed to be dead (Case #24). Among the survivors re-examined, the visual acuity has decreased to 20/100 in all but one. One patient has been sent to a home for mentally retarded children. Two have hemiparesis and epilepsy, and one although blind is working and supporting himself fairly adequately. Two patients have sixth nerve palsies and one has an exophoria. Skull roentgenograms have shown no change in the size of the optic canal in seven patients, an increase in size in the canal in three patients, three to five years after diagnosis.

Necropsy has been performed in five patients all of whom died as the result of the tumor extending from the chiasm into the third ventricle and hypothalmic regions. Death occurred two weeks, one month, six months, and two years after diagnosis, in patients who had had shunting procedures to relieve their hydrocephalus. Four of the patients who died had received radiation treatment.

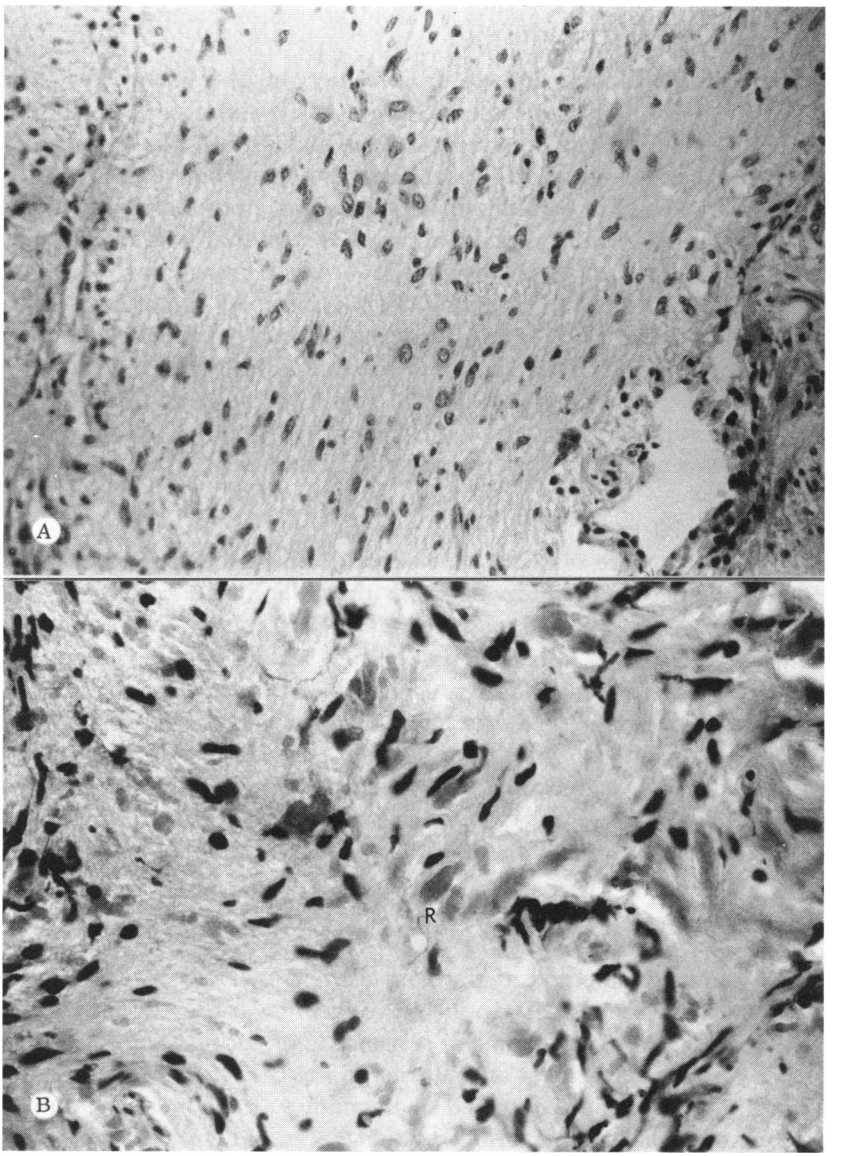

FIGURE 7

A: Tumor astrocytes within nerve. Hematoxylin & eosin × 80 enlarged. B: Rosenthal fibres (R) Tumor astrocytes within nerve. Hematoxylin & eosin × 128 enlarged.

To determine whether the type of pathology might influence the prognosis of these tumors, microscopic slides were reviewed in the 30 cases in this institution; 26 from surgical biopsies and four from necropsies. One autopsy was performed elsewhere. No significant pathologic differences existed. The appearance did not differ from those already described. All tumors were astrocytomas. The material was divided into four groups by pathologic appearance but not graded for degree of malignancy. This grouping cannot be regarded as definitive. Where material was abundant, the appearance might vary considerably within a single tumor. In some instances the amount of material received measured only 1-2 mm, an amount inadequate to permit a statement about the whole tumor.

The following groups do not correspond to the clinical grouping I - III.

GROUP A1 - 10 CASES

These tumors were of slight to moderate cellularity and had a background stoma of fine, interweaving eosinophilic fibrils (Figure 7). The nuclei were regular, small, and elongated. Two tumors showed mild to moderate thickening of fibrous tissue septa within the optic nerve. One contained many Rosenthal fibers. One showed considerable nuclear variations with moderate sized, vesicular, lobulated nuclei, and also contained astrocytes with abundant eosinophilic cytoplasm. One other tumor contained a few large bodied astrocytes situated at the border between persisting optic nerve and tumor. These may have been reactive astrocytes, but it is difficult to differentiate tumor proper from reactive astrocytes.

GROUP A2 - 4 CASES

These tumors, composed of fibrillary astrocyres, were very similar to the tumors of Group A1. The optic nerve sheath was present and showed considerabe fibrous thickening in response to tumor invasion (Figure 8). In one case the diameter of the optic nerve was 0.4 cm and the thickened sheath was 0.3 cm and contained small nodules of tumor cells. Frequently a whorled pattern was formed by the glial tumor and reacting fibrous tissue. Masson, van Gieson, and reticulin stains showed small compact nodules of tumor cells surrounded by bands of collagenous fibrous tissue of varying thickness and density. In two the number of Rosenthal fibers in the tumor was much greater where the tumor had involved the nerve sheath than where it had not. Similarly areas of mucinous degeneration

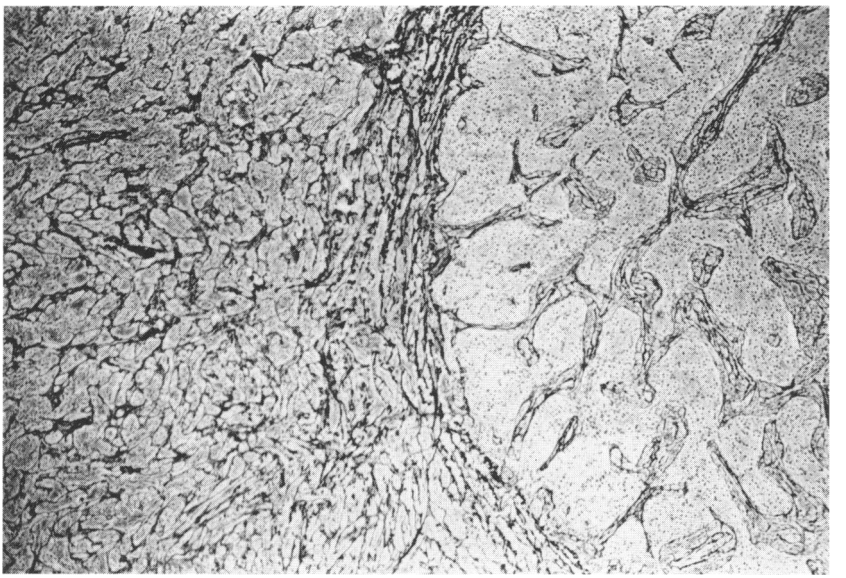

FIGURE 8

Optic nerve on right, note thickened septa. Sheath on left, reticulin surrounds nest of tumor cells. Reticulin × 128 enlarged.

of tumor were more frequent in the nerve sheath if it was involved. These areas were characterized by wisps and bands of tumor cells surrounding spaces in which there was a small amount of eosinophilic proteinaceous material.

GROUP B - 9 CASES

These tumors were more cellular than those of Group A (Figure 9). Nuclei were more densely packed and varied from round and ovoid to elongated. There was an eosinophilic fibrillar background but nuclei and fibrils were arranged in interweaving ribbons and bundles of cells. The bands of tumor cells were occasionally divided by rather slender bands of fibrous tissue. A few small foci of cystic degeneration were present. One of these tumors penetrated the nerve sheath to produce a reaction similar to that seen in Group A2.

GROUP C - 4 CASES

These tumors had a lacy appearance (Figure 10). Regular nuclei were distributed on thin eosinophilic bands which surrounded small regular

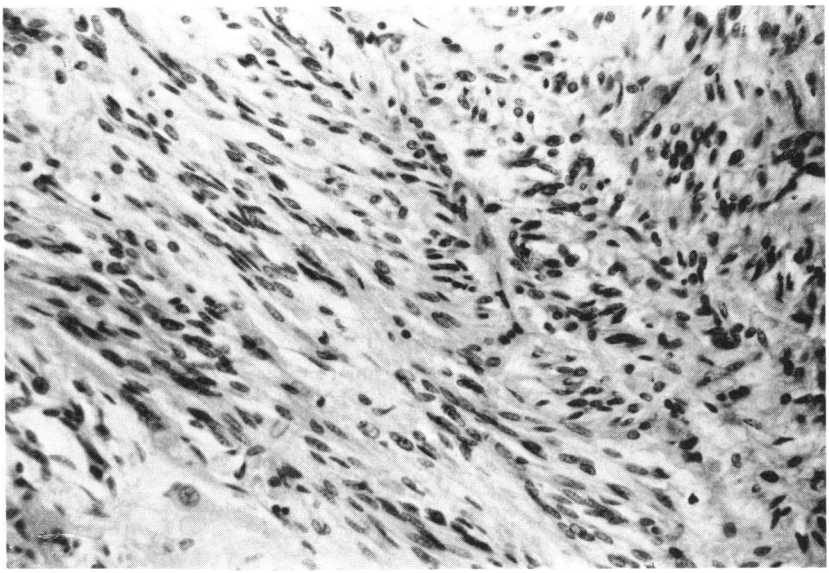

FIGURE 9
Interweaving bundles of tumor cells. Hematoxylin & eosin × 80 enlarged.

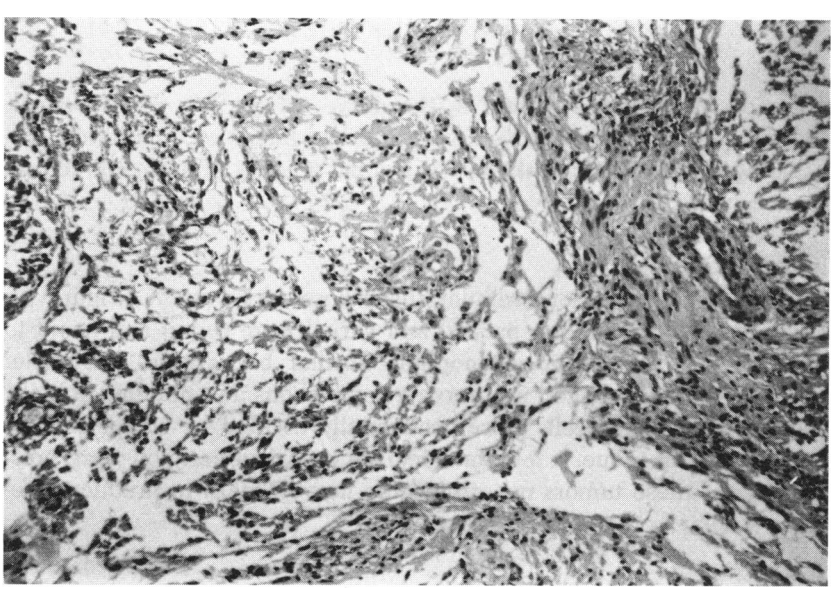

FIGURE 10
To show lacy appearance. Hematoxylin & eosin × 32 enlarged.

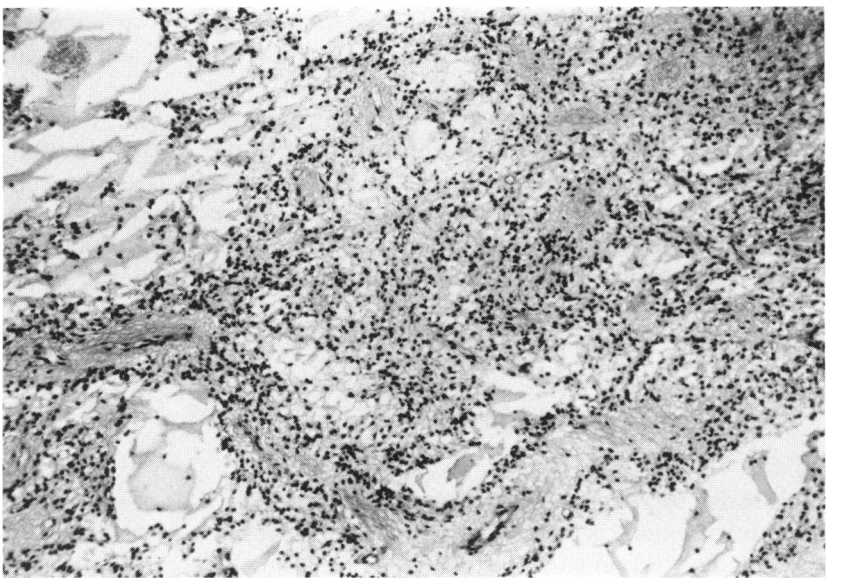

FIGURE 11
Microcystic area. Hematoxylin & eosin × 32 enlarged.

spaces. A complete cross section of one nerve was available and showed markedly thickened fibrous septae surrounding small areas of tumor with its lacy, finely cystic appearance. This nerve measured 1.3 cm in diameter. There was a little thickening of the nerve sheath in this case, as compared to those in Group A2. Only one case showed nuclear atypia.

GROUP D - 2 CASES

Considerable variation existed within these tumors (Figure 11). In one place tumors consisted of round to ovoid astrocytes on a fine fibrillar background with moderate sized cysts, and resembled microcystic cerebellar astrocytoma. In other places the nuclei were aggregated into little groups surrounded by bundles of eosinophilic fibrils.

In all cases in this series the tumor replaced and destroyed the normal axons and myelin of the optic nerve. Where sufficient material was available it was possible to see the tumor cells infiltrating between myelin sheaths, which may persist for some distance into the tumor, but ultimately degenerate and disappear.

Two of the necropsy cases showed considerable necrosis. The necropsy cases were distributed one in Group A1, two in Group B and one in Group D.

Rosenthal fibers were much more frequent in tumors where they invaded nerve sheaths. This relationship supports the suggestion that these fibers are produced as the result of interference with the cell metabolism, for it is reasonable to suppose that where tumor astrocytes are surrounded by fibrous tissue they are at a disadvantage in receiving a normal blood supply compared to tumor astrocytes within the optic nerve itself.

DISCUSSION OF THE RESULTS

SITE

In this series there is no evidence to suggest multiple sites of origin. Bilateral involvement of both optic nerves and chiasm is as frequent as unilateral involvement of one nerve and chiasm. Involvement of the optic tract is present in only two patients out of 41 (Case #29 and Case #38). This agrees with the findings in other series that tumors localized to the optic nerve are less frequent than those involving the chiasm. When only one optic nerve is involved there is a slight preference for the left side. This was noted by Byers.[7] All but one of the nine orbital tumors in this series extends to the intracranial portion of the nerve. Hoyt[1] noted that three out of seven orbital gliomas extended intracranially.

SEX

Though there are more females than males, the difference was not significant. Byers[7] and Hudson[8] also found the prevalence among females to be greater than among males.

FAMILIAL INHERITANCE

In this series there is a brother and a sister (Case #41 and Case #8); the tumor in only one has been verified pathologically (Case #8). Holmstrom,[69] Davis,[10] Manschot,[70] and Hoyt[1] have described the disease in siblings.

INCIDENCE

How common is optic nerve glioma? In the past 27 years there were 41 cases in 601,000 hospital admissions, of which 148 were orbital tumors. During the same period there are 810 brain tumors, 315 of which proved

to be astrocytomas. Therefore the incidence of optic nerve and chiasmal gliomas is 5% of all intracranial tumors, 13% of all astrocytomas, 0.0067% of total hospital admissions and 28% of all orbital tumors.

Russell[51] in 1940, indicated an incidence of 1% of intracranial tumors and 6% of orbital tumors. The difference between her figures and my figures is probably due to the fact that she is reporting on admissions to an ophthalmic hospital and I am reporting on admissions to a general childrens' hospital. Matson's[50] reported incidence was 3.6% of 750 brain tumors, in the Children's Hospital Medical Centre of Peter Bent Brigham Hospital.

AGE

Age at the time of diagnosis averaged five years; the oldest patient being 12 years and the youngest being four months. Cases have been seen at adult hospitals in older age groups but are not included here. Chiasmal gliomas are usually diagnosed earlier than are those confined to the optic nerve, because of the frequency of clinical signs and symptoms suggesting intracranial tumor or obstructive hydrocephalus. When the tumor affected only the nerve, reducing visual acuity with or without producing proptosis, the lesion was not suspected as early; perhaps because children do not complain of visual loss or the development of proptosis.

The present study indicated that the proven cases are diagnosed at an earlier age than are the unproven cases. Although some tumors are undoubtedly present at the time of birth, the signs and symptoms appear more commonly at four to five years of age and within the first decade of life. Hoyt[1] stated that 80% are diagnosed in infants and preschool children and can be considered congenital. The fact that these tumors occur in young children does not make them necessarily congenital in origin. There is also lack of pathological evidence in our series that these tumors represent congenital cell rests.

ASSOCIATION WITH VON RECKLINGHAUSEN'S DISEASE

Von Recklinghausen's disease has been a feature in 40% of the current patients. A family history of this condition was elicited in another nine patients including two patients in whom no café au lait spots were present. Most of our children with von Recklinghausen's disease were diagnosed because they had café au lait spots (Figure 12). Other stigmata, such as small pigmented or nonpigmented iris tumors and skin nodules, were infrequent. We found normal intelligence in two thirds of the whole series.

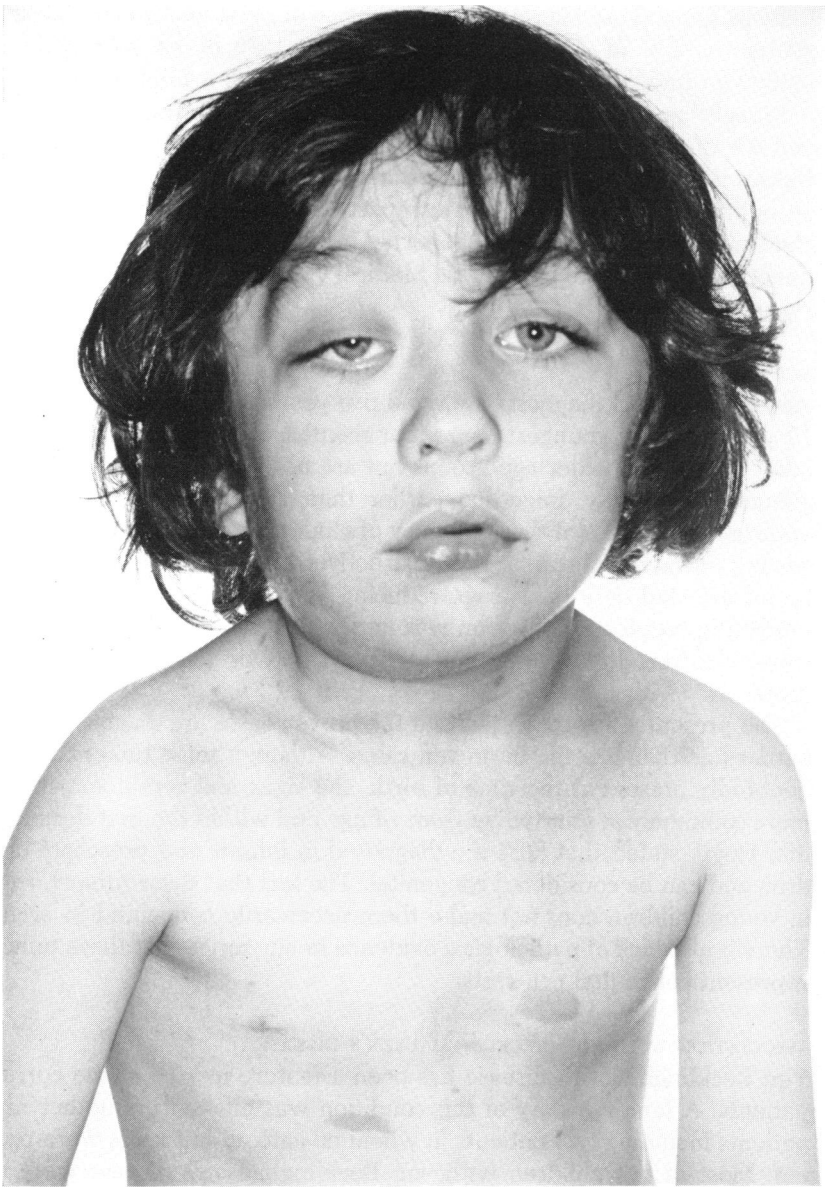

FIGURE 12

Unilateral proptosis and ptosis of right eye in child with right optic nerve glioma associated with von Recklinghausen's disease. Note café au lait spots on trunk.

DIFFERENTIAL DIAGNOSIS

Rucker[68] states that tumors of the chiasmal region constitute 15% of all brain tumors. Firstly there are four commoner lesions involving the pituitary. Pituitary adenoma (chromophile or chromophobe) and chiasmal glioma are often difficult to differentiate. However pituitary tumor usually occurs in adults, optic atrophy is almost always bilateral,[89] and pituitary dysfunction may be present. A craniopharyngioma often shows suprasellar calcification. An optic nerve meningioma is commoner in the second decade of life than in the first. Intracavernous carotid aneurysm is usually demonstrated by arteriography and is accompanied by third nerve palsy including pupillary involvement.

Then there are a group of lesions that are less frequent. If a primary lesion is found, particularly in the chest, metastatic tumor should be suspected. Epidermoid tumor or intracranial dermoid should be suspected if roentgenograms show a bony defect of the sinus with reduplication of its walls and calcification in the tumor. Multiple unilateral cranial nerve palsies, occurring in the third to the fifth decade in males may point to a diagnosis of chordoma. To differentiate between arachnoiditis and chiasmal glioma, direct surgical inspection is necessary. Hydrocephalus of the third ventricle will be demonstrated by air studies. Other rarer conditions affecting the chiasm such as a colloid cyst can be demonstrated by air study, or fibrous dysplasia of bone, by skull roentgenography.

Finally there are rare causes of disease in the pituitary region. Lipodystroendothelioma, hemangioendothelioma, and ganglioneuroma can be differentiated by pathological examination of the mass; granulomas (tuberculous, sarcoid, or syphilitic), are suggested by the chest roentgenograms, blood and skin tests. Post traumatic callus formation can be seen on skull roentgenograms and disseminated sclerosis is diagnosed by history and neurological findings of topographically scattered lesions, and perhaps sclerosis of the internal carotid arteries impinging on the lateral border of the chiasm can be demonstrated in some patients by arteriography.

Combinations of these conditions may occur. Otenasek[11] described a pituitary tumor and optic nerve glioma occurring in a 51-year-old patient. There was visual loss and optic atrophy but no pituitary dysfunction or changes on roentgenography. Both tumors were removed.

The differential diagnosis of expanding lesions of the orbit is also a broad problem and I will mention only four points. Zimmerman[113] reviewed 214 primary tumors of the orbit in children and noted that rhabdomyosarcoma was the most commonly found malignant tumor and

glioma of the optic nerve was second in frequency. An orbital neurofibroma producing a slowly progressive proptosis with muscle palsy may be the only sign of neurofibromatosis. Sinus infection or orbital mucocele is usually excluded by otolaryngological examination. Vascular tumors may produce intermittent proptosis.

In view of this differential diagnosis certain recommendations for investigation of patients suspected of having optic nerve or chiasmal glioma can be made. To exclude neoplastic, inflammatory, or vascular causes, consultations with an internist, neurosurgeon or otolaryngologist may be necessary after the ophthalmologist has completed his examination. The roentgenographic study often supplies the key diagnostic point.

Skull roentgenograms including Waters and Caldwell projections of both optic foramina and lateral stereoscopic views of the skull and views of the base of the skull, and most important, tomograms of the optic canals are readily available and are essential. Pfeiffer[96] has indicated that the diagnosis is roentgenographic in 40% of patients. While roentgenograms are helpful, a normal sized optic foramen does not prove that the tumor is limited to the orbit. Orbital venography through the frontal vein or air injected behind the globe will help outline an orbital tumor.[99] Pneumoencephalography may demonstrate the chiasmal sulcus when an intracranial lesion is suspected. Ventriculography and arteriography are of less help unless the intracranial lesion is large.

CLINICAL

These patients are brought to the ophthalmologist and the neurologist for different reasons. The ophthalmologist is consulted because of visual loss, unexplained field loss, optic atrophy, proptosis, and strabismus. On the other hand, the neurologist and neurosurgeon are consulted when a chiasmal lesion produces symptoms and signs of increase intracranial pressure such as bilateral visual loss, associated with headaches, nystagmus, vomiting, hemiparesis, and convulsions.

Symptoms from Pressure

There is nothing characteristic about the headaches associated with chiasmal lesions although some of them seem to be accompanied by restlessness, occasional vomiting, and convulsions, indicating increased intracranial pressure. Symptoms resulting from pressure on the third ventricle and hypothalamus include hydrocephalus, diabetes insipidus, lethargy, sleepiness, obesity, and faulty sexual development.

Proptosis

Crawford,[114] in reviewing 257 cases of proptosis in the Hospital for Sick Children, Toronto, found only 41 due to tumor of which four were gliomas. More common were inflammatory, vascular, metabolic, and other neoplastic causes. Spaulding[48] on the other hand, on surveying the material at the Armed Forces Institute of Pathology found that all the patients with gliomas had proptosis.

Vision

Proptosis is not necessarily the first reason for seeking medical help. Visual loss is commoner.

Visual acuity was not impaired in only three patients in my series. The probable explanation is that tumor surrounded by nerve often leaves a few compressed but unaffected fibres at its periphery. Only later does the mass compress the nerve and destroy vision by pressure, or by obstructing the blood supply to the nerve. The visual acuity at the time of diagnosis ranged from no light perception to 20/100.

Optic Disc

When the tumor was close to the globe, edema of the disc was a more common finding than was optic atrophy. Since there was no associated increased intracranial pressure, the disc swelling on the affected side was probably due to obstruction of the venous return from that optic disc by tumor. Martin and Cushing[2] felt some swollen discs might be due to tumor at the disc. When the tumor was distal to the globe or intracranial, optic atrophy was more frequent.

Papilledema and optic atrophy had an equal incidence in Group II where tumors of the chiasm and optic nerve did not progress clinically. Ten out of 12 patients in this group also showed no signs of generalized raised intracranial pressure.

In Group III where prognosis for both life and vision was poor, 75% of the patients showed optic atrophy in spite of roentgenographic evidence of raised intracranial pressure in 60% of this group. Perhaps this reflects the very slow growth of the tumor.

The presence of unilateral papilledema therefore, may suggest a slightly more favorable prognosis. Papilledema in one eye and optic atrophy in the other worsens the outlook, and bilateral optic atrophy is the least favorable.

Arkhangelsky[30] described retinal hemorrhages similar to those seen in retinal vein occlusion. Secondary rubeosis iridis with hemorrhagic

glaucoma following retinal vessel occlusion was described in one case of optic nerve glioma by Hovland.[28]

No optic disc or retinal tumors were seen in our series, and apart from pigmentary retinal changes in one patient (Case #18), no retinal lesions were found.

In three patients, all of whom had neurofibromatosis, the ophthalmoscopic examination showed myelinated fibres in two (Case #19 and Case #21) and glial tissue extending from the disc in the third (Case #40). These findings were not noticed until the swelling of the discs had subsided. They persisted. The myelin fibres of von Recklinghausen's disease have been considered incidental by Moore[116] and Copeland.[119] Shapland[117] postulated some metabolic agent derived from the tumor cells stimulating a glial reaction.

Visual Fields

Visual fields cannot be counted as an aid to diagnosis in very young children because they cooperate poorly. After the age of six most children will respond to confrontation testing. Careful visual fields of the opposite eye are helpful although chiasmatic involvement is not always reflected by demonstrable visual field defects. This may have the same explanation as the sparing of the vision in some patients. That is, enough chiasmal nerve fibres are unaffected by tumor and the fields are normal by the usual testing.

Strabismus

Strabismus surgery was performed on two patients before the diagnosis of glioma was made. In the presence of von Recklinghausen's disease, strabismus in amblyopic eyes (even without definite optic atrophy) should always make the surgeon suspicious of a compressive lesion of the optic nerve such as glioma. The four instances of sixth nerve palsies we noted probably resulted from pressure of the tumor on the nerve. Tym[90] stated that no case has been recorded where the tumor has invaded or enveloped the ocular muscles or their nerves to produce ocular muscle palsies.

Nystagmus

Vertical and horizontal gaze evoked jerk-type nystagmus, seen most frequently in patients of Group III, makes one suspect brain stem compression. Searching pendular nystagmus was characteristic of those children who were blind.

RADIOLOGICAL FINDINGS

Standard roentgenography of the optic canals and sella demonstrate only the orbital orifice of the optic canal and the lateral appearance of the clinoids and optic sulcus respectively. The intracanalicular portion of the optic canal and intracranial orifice cannot be visualized by these techniques. Evans and others[115] state, or quote other authors, that in optic nerve gliomas of the orbit 70% were confined to the anterior portion of the optic canal; 22% of children with optic gliomas had normal standard roentgenographs of the anterior canal orifice and, furthermore, four children with normal roentgenographic orbital foramen had a widened cranial orifice seen at operation. Transcanalicular extension of an optic glioma without evidence of canal enlargement is very rare.

Our own experience concerning the value of standard roentgenographic techniques confirms these findings.

However, the routine roentgenographic findings are not alway characteristic of glioma of the optic nerve, even when it is suspected. Skull roentgenograms repeated on different occasions showed normal optic foramina in four of our proven cases. It is not enough to make a skull film when this diagnosis is suspected, even though enlargement of the optic foramen is the commonest single roentgenographic abnormality in optic nerve glioma. If split coronal sutures are found, chiasmal invasion with hydrocephalus and increased intracranial pressure is likely. Abnormalities of the sella might make one suspicious of a craniopharyngioma.

The best single radiological technique to confirm the diagnosis is axial tomography. It is unnecessary when optic foramina are enlarged by standard techniques, but if there is only a slight suspicion of enlargement of the optic canal, tomograms will demonstrate funnelling and enlargement of the intracranial portion in contrast to the orbital part of the canal.

The pneumoencephalogram has been helpful in outlining the chiasmal groove, the chiasm, and the nerves in some patients, even where it appears abnormal. However, intracranial exploration has sometimes revealed this to be untrue. In the last 15 children in whom we have diagnosed glioma of the optic nerve or chiasm, the standard pneumoencephalogram without tomography has often failed to identify intracranial involvement or to reveal the true size of this involvement once identified. In one instance, where roentgenograms of the chiasmal groove suggested that the chiasm was involved, craniotomy showed it to be normal (Case #19). Arteriograms have been of little help in making the diagnosis. Because of these shortcomings, both axial tomography of the optic canals

and anteroposterior tomography as part of a pneumoencephalogram in children with gliomas of the optic nerve should be performed.

TREATMENT

No Treatment

In only one patient have we followed Hoyt's[1] advice and undertaken no treatment. Our reasons were medical (Case #21). Visual acuity has not changed but the optic canal is enlarging, indicating that the tumor is growing.

In one patient, because the optic nerve appeared normal on intracranial surgical inspection, no biopsy was taken. After operation the vision return to normal and has remained so (Case #19). It is possible the decreased visual acuity was due to a reactive gliosis. However, the radiologic evidence indicates that this must be a slowly growing astrocytoma leaving enough unaffected nerve fibres to maintain normal visual acuity. Further visual loss should eventually occur in this child.

Two other patients (Case #40 and Case #41) in whom no tumor was found on craniotomy have been followed for three and five years. In one the vision had decreased and in the other enlargement of the optic canal by tomography has indicated further growth of tumor.

Indication for Surgery

1 If radiographic evidence indicates that the tumor is contained wholly within the orbit, it should be removed through a modified Kronlein approach.[110]
2 If the roentgenograms show enlargement of the optic foramen or canal or if sections of the tumor removed at a Kronlein procedure show that the tumor has not been totally removed, then intracranial operation to remove the remainder of the tumor should be done.[97]
3 If the tumor is unilateral and both intracranial and intraorbital, the first approach should be transcranial. After that procedure, if proptosis is still present, the tumor should be removed from the orbit.

Surgical Treatment

Case #2 is of interest. At operation the tumor was left in the optic canal, but removed both orbitally and intracranially. Afterwards the tumor grew within the optic canal extending forward into the orbit and producing further proptosis. It did not cross the cut end intracranially. It would appear that if the nerve is cut between tumor and chiasm it will not cross the gap and invade the chiasm.

In this series there has been no significant neurosurgical complications, such as hemiparesis from craniotomy or from biopsy. Surgical adjuncts such as lumbar puncture, hyperventilation, urea or mannitol to shrink the brain, and cortisone to protect the patient during operation, together with increased surgical experience, have contributed to making intracranial exposure of the orbit and chiasm a procedure with small risk.[50] The optic nerve is sacrificed on the side of the tumor, resulting in no light perception, but this has not been a great loss, since in most of the patients the vision was already reduced to either light perception or less than 20/100. The postoperative ptosis and strabismus usually improve without surgical correction and occur rarely.

RADIATION

Vision decreased slowly in three patients who had radiation as the only form of treatment (Case #37, Case #38 and Case #39). Radiation probably slowed the progression of visual loss and general deterioration. Any brain tumor requiring radiation should receive the maximum dose. In earlier years, here and elsewhere, lower doses of radiation may have stimulated growth of tumor. If there is already visual loss radiation does not help, however, it may slow the extension of the tumor and prevent further loss of vision. Radiation therapy is indicated when the lesion cannot be excised and symptoms progress or when the lesion is bilateral with chiasmal involvement and surgery is impractical.

PROGNOSIS

My study has revealed no indication, from age, sex, signs and symptoms, radiological, or pathological findings, which patient will have a slow course with little change in vision and a good prognosis for life, or which patient will lose vision, develop hydrocephalus and compression of vital midbrain structures.

Radiological evidence does not always indicate chiasmal involvement or freedom from it. Only intracranial exploration will show in which cases of unilateral glioma with optic foramen enlargement the tumor can be excised without affecting the chiasm.

Prognosis is best for patients of Group I, that is when the tumor is limited to one optic nerve, the optic foramen on that side is not enlarged, and the tumor can be completely resected. In one patient (Case #1), an Indian girl with many café au lait spots, these conditions were met; histologically the entire tumor appeared to be included in the portion

of the nerve removed. Repeated examinations over the past 15 years revealed no recurrence of tumor at the site of removal or elsewhere.

Prognosis is second best for patients of Group I, in whom the tumor is limited to one optic nerve and is totally removed surgically. The optic foramen and optic canal are enlarged, but craniotomy reveals a normal chiasm and the nerve anterior to the knee of Willbrand's crossing fibres is free of tumor. Eight patients were in this group. None have shown evidence of extension of the tumor over periods ranging from one to 13 years.

The Group III patients in this series were the ones with the downward course. In these patients the vision and general condition went downhill during the follow up period. These were the patients who showed bilateral enlargement of optic foramina, roentgenographic evidence of chiasmal involvement, and bilateral neurologic signs. However, when these patients are first seen there is no way to predict the ones in whom the tumor will continue to extend and in whom the tumor will remain localized.

SUMMARY AND CONCLUSION

Hoyt[1] from a review of his material, states that in all cases of optic glioma no form of therapy, including surgery, alters the prognosis either for life or for vision. In some cases the tumor does not extend while in others extension is significant and will lead to death.

However, I separate out a group of patients in which the tumor has not extended to the chiasm, which can be identified clinically, and can be completely resected. Follow up of these patients has indicated an excellent prognosis.

In a number of patients in this series extension of the tumor into the chiasm was confirmed at operation and no resection was attempted. In some there was no progression while others had progression, further visual loss, and death. There was no clinical, radiologic, surgical, or histologic finding which indicated whether extension would or would not occur. A blind study of the pathologic material in 30 cases showed no microscopic change that could be related to either progression or nonprogression.

If neurological signs of extensive cranial involvement are present, including hemiplegia and hydrocephalus, no treatment other than shunting procedures and radiation is indicated. But, if the diagnostic signs

suggest the tumor is still unilateral, within the orbital or intracranial portion of the nerve, then surgical intervention is indicated. In these patients total excision of the tumor is possible and should be undertaken.

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