Large Hypothalamic and Optic Chiasm Gliomas in Infants: Difficulties in Distinction

Hypothalamic and optic chiasm gliomas may be indistinguishable clinically, radiographically, and pathologically. Ten children with giant gliomas of the hypothalamus and optic pathway, all under age 2 years, had masses greater than 3 cm in diameter. Pathologically all proven cases (seven) were cytologically benign fibrillary astrocytomas. Previous authors have recognized the difficulty in distinguishing these lesions; in this series, using previously suggested criteria, masses of optic chiasm could not be differentiated from hypothalamic origins. Likewise, at surgery and autopsy, the origin of these large masses was indeterminate. These tumors were more aggressive, invasive, and less responsive to therapy than the relatively benign orbital and optic nerve gliomas of older children and adults.

The optic pathways include the optic nerves, chiasm, and tracts; lateral geniculate bodies; and optic radiations to the occipital lobes. The optic chiasm is immediately adjacent to and embedded in the floor of the hypothalamus [1]. The hypothalamus forms the floor and part of the lateral walls of the third ventricle, with its anterior boundary at the level of the mid optic chiasm and posterior boundary immediately caudal to the mammillary bodies [2].

Fibrillary astrocytomas of the juvenile type may arise in the optic nerves, optic chiasm, optic tracts, and hypothalamus. Such tumors show variable extension from their site of origin to the adjacent structures and may infiltrate the brain substance itself [2-4]. They may become symptomatic at any stage of growth. They may be massive at presentation, with the exact site of origin indeterminate [4, 5]. The biologic behavior of large astrocytomas of the optic chiasm, optic tracts, and hypothalamus is unpredictable [6-12], although some investigators have stated that such tumors are less amenable to therapy than gliomas of the optic nerves [11, 13, 14].

We retrospectively reviewed gliomas of the hypothalamus and optic pathways seen at our institution from 1975 to 1982. Of 24 patients with optic pathway lesions, we identified 10 patients presenting with large (>3 cm in diameter) suprasellar masses. All presented at or before 2 years of age. In this group, we were unable to differentiate gliomas arising in the intracranial optic pathways from those arising in the hypothalamus. These patients were similar by clinical, radiologic, and pathologic criteria. Despite aggressive therapy, these patients carried a worse prognosis than reported for older children and adults with optic pathway gliomas [10-16].

Materials and Methods

Ten patients with chiasmal masses greater than 3 cm in diameter at presentation were studied. All of these patients with large lesions developed symptoms before 2 years of age (mean age at presentation, 10.1 months; range, 3–19 months). In seven of 10, the diagnosis was confirmed by surgery and histologic examination; of these, two were studied at autopsy.
One additional child was studied at autopsy only. We included two children with excellent neuroradiologic evidence of tumor but no surgical verification. Eight of the 10 patients had computed tomographic (CT) scans before therapy; the other two patients were diagnosed before CT with pneumoencephalography. Four were studied with angiography. Duration of clinical and radiologic follow-up ranged from 11 months to 11.5 years.

Patients with optic nerve involvement alone or with chiasmal lesions less than 3 cm in diameter at presentation were excluded from this study. These patients with smaller lesions ranged in age from 3 years to 44 years (mean, 23 years), although several reported unilateral blindness "since birth." Sequential CT studies were generally not available for patients in this group; whether this represents stability of clinical course or loss to follow-up is unknown. No known deaths attributable to these smaller optic pathway and/or hypothalamic lesions have occurred.

Results

All patients developed symptoms before 2 years of age. Presenting symptoms are given in table 1. Despite the large size of the suprasellar mass at presentation, only two patients initially presented with hydrocephalus. Seven patients underwent craniotomy with biopsy for confirmation of the diagnosis. At surgery, the optic chiasm, proximal optic nerves, and hypothalamus were engulfed and obliterated by tumor, so that the site of origin was indeterminate in all cases. Ten patients received radiation therapy; five received chemotherapy. Tumor locations at presentation, at follow-up, and at autopsy are given in table 2.

Tumor extent was best appreciated with CT. In eight patients, CT before therapy demonstrated an isodense (six patients) or hypodense (two) mass in the suprasellar cistern with marked contrast enhancement (fig. 1A). At presentation, in addition to a suprasellar mass, CT defined tumor extent in the optic nerves (fig. 2A), optic tract, and lateral geniculate bodies. Enhancing mass was present in the anterior cranial fossa, middle cranial fossa/temporal lobe, and infratentorial cisterns (fig. 3). It was difficult to determine whether or not enhancing mass was purely intra- or extraxial by CT criteria, particularly in the subfrontal and medial temporal regions.

All 10 patients were followed with sequential CT scans. Progressive increase in tumor size and extent was noted in seven of the 10 patients. Rate of growth varied; some masses seemed to temporarily stabilize or regress at intervals, whereas one patient showed marked progression in tumor size and intraparenchymal extent over a 5-month period (fig. 4). Eight of the 10 patients eventually developed hydrocephalus and required ventricular shunting. Four patients had direct coronal images; all four of these demonstrated a "capping" appearance of the third ventricular interface with adjacent tumor [17, 18] (fig. 3C). Intraaxial tumor extension was identified by CT in the thalamus, basal ganglia, midbrain, pons, and medulla (table 2). Characteristically exophytic tumor masses were present immediately adjacent to the chiasm in the middle cranial fossa and in the interpeduncular and preoptic cisterns. By CT criteria, it was difficult to differentiate intra- and extraaxial tumor in the subfrontal and medial temporal lobes, although pathologically, intraparenchymal invasion by tumor was present in the frontal and temporal lobes in all three autopsied patients. Widening of the sylvian cisterns was identified only after treatment (two patients). One patient developed an isolated focus of enhancing mass about 1 cm in diameter in the superior aspect of the right lateral ventricle; presumably this was a neoplastic deposit, although it was not pathologically proven. Initially most tumors demonstrated homogeneous contrast enhancement; after treatment, the enhancement pattern became mottled and inhomogeneous.

Calcification developed within and/or around the margins of tumor in seven patients after therapy; one patient who remained undiagnosed until age 3 had tumor calcification at the time of diagnosis. In one child, extensive parenchymal calcification occurred in the temporal and frontal lobes (figs. 1C and 1D). By CT criteria, this child had previously infarcted temporal lobes bilaterally.

Three patients developed nonenhancing cystlike masses immediately adjacent to or within tumor (fig. 2B). Of these, one required surgical drainage. In this child at autopsy at the

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**TABLE 1: Summary of Signs and Symptoms at Presentation**

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>No. of Patients (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≤ 2 years</td>
<td>10</td>
</tr>
<tr>
<td>Decreased visual acuity</td>
<td>9</td>
</tr>
<tr>
<td>Abnormal eye movements</td>
<td>7</td>
</tr>
<tr>
<td>Proptosis</td>
<td>1</td>
</tr>
<tr>
<td>Delayed development</td>
<td>5</td>
</tr>
<tr>
<td>Diencephalic syndrome</td>
<td>3</td>
</tr>
<tr>
<td>Seizures</td>
<td>2</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>2</td>
</tr>
<tr>
<td>Neurofibromatosis</td>
<td>1*</td>
</tr>
</tbody>
</table>

* Two others had questionable family history.

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**TABLE 2: Tumor Extension at Presentation, Follow-up, and Autopsy**

<table>
<thead>
<tr>
<th>Location</th>
<th>CT at Presentation</th>
<th>Follow-up CT</th>
<th>Autopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optic nerves (orbital)</td>
<td>4/4‡</td>
<td>4/9</td>
<td>NE</td>
</tr>
<tr>
<td>Optic chiasm/ hypothalamus</td>
<td>8/8</td>
<td>10/10</td>
<td>3/3</td>
</tr>
<tr>
<td>Optic tracts/lateral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>geniculate</td>
<td>7/8</td>
<td>9/10</td>
<td>2/3</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>2/8</td>
<td>8/10</td>
<td>2/3</td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>2/8</td>
<td>6/10</td>
<td>1/3</td>
</tr>
<tr>
<td>Thalamus</td>
<td>2/8</td>
<td>6/10</td>
<td>3/3</td>
</tr>
<tr>
<td>Caudate</td>
<td>0/8</td>
<td>3/10</td>
<td>1/3</td>
</tr>
<tr>
<td>Frontal lobe/subfrontal</td>
<td>6/8</td>
<td>8/10</td>
<td>2/3</td>
</tr>
<tr>
<td>Temporal lobe/middle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cranial fossa</td>
<td>6/8</td>
<td>8/10</td>
<td>3/3§</td>
</tr>
<tr>
<td>Pituitary gland</td>
<td>0/8</td>
<td>0/10</td>
<td>2/3</td>
</tr>
<tr>
<td>Midbrain</td>
<td>2/8</td>
<td>6/10</td>
<td>2/3</td>
</tr>
<tr>
<td>Pons</td>
<td>0/8</td>
<td>4/10</td>
<td>2/3</td>
</tr>
<tr>
<td>Medulla</td>
<td>0/8</td>
<td>2/10</td>
<td>1/3</td>
</tr>
<tr>
<td>Infratentorial cisterns/</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>meninges</td>
<td>3/8</td>
<td>6/10</td>
<td>3/3</td>
</tr>
</tbody>
</table>

Note.—NE = not evaluated.
‡ Two patients were diagnosed with pneumoencephalography before CT was available.
◊ All patients received radiation therapy; five of 10 received various forms of chemotherapy.
§ Orbital parts of optic nerves were not seen on four initial scans.
§§ Pathologically temporal lobe intraxial invasion by tumor was identified in all three patients.
A site of surgical drainage, tumor cells were identified within the cyst wall along with gliosis and fibrosis. All autopsied masses contained small macro- and microscopic cysts.

Five patients were studied with angiography. All showed marked elevation of the supraclinoid internal carotid arteries bilaterally. Four of the five had significant attenuation of the supraclinoid internal carotid arteries; three of these patients demonstrated arterial attenuation before radiation or chemotherapy. In the patient with bilateral cerebral infarcts, severe internal carotid arterial attenuation was identified bilaterally with collateral supply to the middle cerebral artery distribution from the posterior cerebral artery and from the external carotid distribution (fig. 1B). Enlargement of the lenticulostriate arteries mimicked moyamoya disease in two patients [19-21]; one of these carried the diagnosis of moyamoya for several years before the advent of CT. Minimal tumor blush was present in two patients; however, no beaded or irregular arteries were noted.

Three patients were studied at autopsy. All had large, histologically benign fibrillary astrocytomas with complete gross and microscopic obliteration of the optic chiasm and hypothalamus. No malignant change was present. In these patients, the internal carotid arteries were completely obliterated within the tumor mass by gross and histologic study. All three patients had intra- and extraaxial tumor spread. The extent of tumor at autopsy is given in table 2.

Discussion

Computed tomography has become the single most useful method of evaluating and following gliomas of the optic pathways and hypothalamus [1, 17, 18]. Due to hypovascularity,
tumor extent may be underestimated with angiography. In addition, CT is useful for identification of intraorbital extension and optic canal enlargement.

Although optic nerve gliomas occur with neurofibromatosis, only one of our patients had definite clinical stigmata of neurofibromatosis. Two had suspicious family histories. Other cranial stigmata of neurofibromatosis, such as dysplasia of sphenoid bone and enlargement of the internal auditory canal, were not identified. Since all patients presented at less than 2 years of age, perhaps other stigmata of neurofibromatosis had not yet developed.

A congenital origin has been postulated for optic gliomas [22-24]. In one series [15], 80% of the optic gliomas identified were diagnosed in infants and preschool children. Our experience supports this theory, since all children with extensive masses were symptomatic before 2 years of age. In our experience, no children presenting later with optic gliomas had masses of the size or extent of those in this series.

In our series, we were unable to differentiate masses of hypothalamic and optic pathway origin on the basis of previously suggested criteria [17, 18]. Other authors have noted the difficulty or impossibility of distinguishing these masses. In our series, presenting symptoms included emaciation (diencephalic syndrome [25]) and visual abnormalities. Chiasmal gliomas are a recognized cause of the diencephalic syndrome due to hypothalamic extension [26], as are masses originating in the hypothalamus. Hypothalamic gliomas, likewise, are known to extend into the chiasm and optic nerves [17, 18]; thus, the similarities in clinical findings are understandable. Radiographically, optic gliomas are said to expand exophytically without invading the surrounding tissue; thus, the third ventricle is described as enlarged and appears as a cap over the exophytic subjacent tumor [17, 18]. The subarachnoid cisterns in classic descriptions of optic chiasm gliomas are enlarged mechanically or due to entrapment of the cistern. In our series, patients with known hypothalamic and/or optic
GIANT HYPOTHALAMIC–OPTIC CHIASM GLIOMAS

Fig. 3.—6-month-old boy with delayed development, decreased visual acuity, and abnormal eye movements. A, Contrast CT scan. Enhancing lobular suprasellar mass without hydrocephalus. B, Tumor mass extends exophytically into interpeduncular and preoptic cisterns and optic nerves bilaterally. C, coronal CT scan. Tumor is capped by third ventricle.

Chiasm disease had both extensive exophytic extraaxial masses and extensive intraparenchymal invasion. All children who had coronal studies had a third-ventricular-cap appearance.

By CT criteria, no child showed resolution of tumor after radiation therapy (10/10) or chemotherapy (5/10). In one patient, a decrease in tumor volume was present 1 year after diagnosis with interval radiation therapy; however, this child was subsequently lost to follow-up. In the three cases studied at autopsy, no evidence of malignant change of the originally diagnosed low-grade astrocytoma was present. Thus, these histologically benign masses showed progressive enlargement with both parenchymal invasion and exophytic extraaxial growth as described by other authors clinically and pathologically [2, 8, 11]. Diffuse meningeal involvement both adjacent to and remote from the site of tumor mass was identified. Eight of the 10 patients eventually developed obstructive hydrocephalus and required ventricular shunting. Four patients developed parenchymal infarcts by CT criteria. In correlating these with the marked attenuation of the suprachiasmatic internal carotids seen at angiography before therapy and the obliteration of the internal carotid arteries at autopsy, it is reasonable to conclude that ischemia was the likely cause, although radiation therapy has been implicated [10]. Three patients developed cysts within their tumors after treatment, one of which was surgically drained. Histologically, all three lesions studied at autopsy contained macro- and/or microscopic cysts; thus, presumably cyst formation was due to tumor necrosis.

Calcification after radiation in intracerebral tumors is well recognized [3, 17, 27]. One of our patients had intratumoral calcification before treatment. After irradiation, six additional patients developed intratumoral calcification. One of these developed extensive temporal lobe calcification after bitemporal infarcts.

Prognosis for these children is less favorable than for smaller optic nerve or optic pathway gliomas [10–16]. Of our 10 patients, five children died 9 months to 11 years after diagnosis (mean, 4.4 years); no deaths attributable to tumor have occurred in the patients with smaller lesions evaluated at our institution. Of the surviving children, the mean survival period from time of diagnosis to most recent follow-up is 5.7 years (range, 0.9–8 years). The surviving children have extensive residual tumor and multiple neurologic abnormalities including amblyopia, nystagmus, hemiparesis, brainstem abnormalities, and endocrine dysfunction. Although radiation and mass effect from suprasellar tumor are reasonable causes of pituitary dysfunction, two of three autopsied patients had tumor extension to the pituitary gland.

In summary, we identified a group of patients with optic chiasm and/or hypothalamic gliomas presenting with large suprasellar masses before 2 years of age. These lesions carry a less favorable prognosis when compared with smaller gliomas of the optic pathways due to extensive parenchymal and extraaxial growth. Tumor extension progressed despite radiation and chemotherapy. Clinical, radiographic, and pathologic criteria failed to differentiate hypothalamic from optic chiasm gliomas. With CT, masses characteristically were iso-
or hypodense, with marked contrast enhancement. After therapy, inhomogeneous enhancement, cyst formation, calcification, hydrocephalus, and progressive growth were noted.

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REFERENCES

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