Malignant astrocytoma following radiotherapy of a craniopharyngioma

Case report

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A 9-year-old schoolgirl received 6007 rads to the suprasellar region for craniopharyngioma. Five years later, a malignant astrocytoma developed in the right temporal lobe. We cite clinical and experimental evidence to support our suspicion that the glioma may have been induced by radiation.

Key Words • craniopharyngioma • Rathke's pouch tumor • suprasellar cyst • malignant astrocytoma • malignant brain tumor • radiation-induced tumor • computerized tomography

Radiation-induced brain tumors are well known. Benign tumors have occurred many years after irradiation for benign conditions. Malignant head and neck tumors resulting from irradiation for benign conditions and for acromegaly have been reported. However, a report in 1969 could cite only six instances in which human glioma occurred following therapeutic irradiation. The spontaneous coexistence of histologically different brain tumors in different sites is well known. Specifically, Carson and Hellwig reported the association of a suprasellar craniopharyngioma with a cystic astrocytoma of the left temporal lobe in the absence of irradiation. The particular association of irradiated craniopharyngioma with a glioma has not previously been reported.

Case Report

This 9-year-old schoolgirl presented in November, 1970, with a 6-month history of progressive abdominal pain, nausea, vomiting, and diplopia.

First Admission. Physical findings included visual acuities of 20/100 and 20/50 in right and left eyes, respectively, a right Marcus Gunn pupil, almost complete left lateral rectus paresis, and far advanced bilateral papilledema. Tomography revealed intrasellar and suprasellar calcifications. Ventriculography disclosed hydrocephalus, obstruction of the foramen of Monro, and a 4 × 3 cm mass deforming the floor of the third ventricle. Right frontal craniotomy was performed and golden-yellow fluid was aspirated from a cyst. One month later, the
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Fig. 1. Photomicrograph of craniopharyngioma cyst wall. Keratotic debris with foreign body giant cell reaction. Fragments of squamous epithelium with peripheral palisading of cells. Core of gliosis. H & E, × 70.

The surgical site bulged, and a pneumoencephalogram revealed increasing hydrocephalus. A bifrontal craniotomy was performed, the cyst was drained, and the cyst wall biopsied. The histological diagnosis was that of craniopharyngioma (Fig. 1). The patient then received 6007 rads in 46 days to the suprasellar area in a 5 × 6 cm field, using a 360° rotation from a 4.8 MeV linear accelerator (Table 1, Fig. 2). Following radiation, her vision improved to 20/30 and 20/25 despite profound optic atrophy, and her general clinical state improved. Growth arrest and hypothyroidism required the institution of replacement therapy with growth hormone and Synthroid (sodium levothyroxine).

Second Admission. She did well until April, 1976, when she developed nausea, vomiting, and increasing fatigue. Left homonymous hemianopia was more dense in the upper quadrants and computerized tomographic (CT) scan revealed an enhancing doughnut-shaped right temporal lobe mass (Fig. 3). Angiography confirmed the mass effect. A right temporal craniotomy revealed a malignant glioma in the right middle temporal gyrus (Fig. 4). The patient

Fig. 2. Radiation treatment plan of craniopharyngioma. Schematic location of craniopharyngioma within the cranium indicated by broken line. Isodose curves for the radiation of the craniopharyngioma are expressed as percentages of the isodose. 100% = 6007 rads.

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received 5100 rads in 39 days to the right temporal lobe (Table 1), as well as vincristine and 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU).

Third Admission. In October, 1976, a new periventricular lesion surrounding the left frontal horn was revealed on CT scanning, and rapidly increased in size over the next 17 days (Fig. 5). A left frontal burr hole, performed to exclude a possible brain abscess, revealed a malignant glioma, histologically indistinguishable from the right temporal lesion (Fig. 6). Further radiation was given to the left frontal lobe (Table 1), as well as weekly treatments with VM-26 (4'-demethylepipodophyllotoxin 9-[4,6-O-ethenylidene-D-glucopyranoside]). A ventriculoatrial shunt was required to control postoperative aseptic meningitis and hydrocephalus.

Although there was dramatic regression of the tumor sites by January, 1977 (Fig. 7), her general course deteriorated and she died in May, 1977.

Postmortem Findings. No residual viable craniopharyngioma epithelial cells were found in the region of the tuber cinereum; however, partially keratinized ghost-like areas were seen, and the surrounding brain was gliotic, as is typical for this tumor. The medial right temporal glioma had no microscopic connection with the craniopharyngioma, nor was there an area of transitional cytology. The glioma showed subepen-
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**Fig. 6.** Photomicrograph of the malignant glioma of the left frontal lobe, showing highly cellular, hyperchromatic pleomorphic astrocytes. Smear preparation from needle biopsy. H & E, × 300.

**Fig. 8.** Horizontal section of brain cut in plane of the computerized tomography scan (Fig. 7). Glioma is present in the left frontal and right occipital horns of lateral ventricles, and clot in the left occipital horn. Calcified angiomatosis in basal ganglia can be seen on the right (arrow).

dymal spread throughout the ventricular system and meningeal spread throughout the spinal subarachnoid space. An area of calcified angiomatosis in the right basal ganglia represented an incidental finding.

Grossly, there was considerable hydrocephalus present and a fresh blood clot in the left occipital horn (Fig. 8).

**Discussion**

This glioma may have been induced by irradiation. Similar doses of irradiation have produced gliomas in primates, but no human glioma has been reported after similar irradiation for craniopharyngioma.

We suspect this association for several reasons. 1) Superimposition of the isodose curves from the original irradiation on the site of the right temporal lobe glioma shows that site received 80% to 95% of the original 6007 rads (Figs. 2 and 9). 2) Malignant brain tumors have been reported to follow irradiation to the head in intervals as short as 7
TABLE 1

Summary of radiation treatment

<table>
<thead>
<tr>
<th>Date Begun</th>
<th>Date Ended</th>
<th>No. of Treatments</th>
<th>Tumor Dose (Source)</th>
<th>Region</th>
<th>Port Size (cm)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/29/71</td>
<td>5/14/71</td>
<td>30</td>
<td>6007 rads, 4.8 MeV, photons</td>
<td>suprasellar</td>
<td>5 x 6</td>
<td>360° rotation</td>
</tr>
<tr>
<td>6/14/76</td>
<td>7/23/76</td>
<td>28</td>
<td>5100 rads, 6 MeV, photons</td>
<td>rt temporal region</td>
<td>8.5 x 8 each</td>
<td>3-field right lateral &amp; wedged anterior &amp; posterior pair</td>
</tr>
<tr>
<td>11/26/76</td>
<td>1/10/77</td>
<td>25</td>
<td>5000 rads, 4 MeV, photons</td>
<td>lt frontal lobe</td>
<td>12 x 8</td>
<td>2-field, anterior &amp; left lateral wedged pair</td>
</tr>
</tbody>
</table>

years. 3) The craniopharyngioma is surrounded by gliotic brain. Induction of a glioma is more probable in such gliotic brain tissue than in other nervous tissue. 4) The presence of such congenital lesions as craniopharyngioma and angiomatosis suggests that this patient’s brain was at increased risk for induction of neoplasia by a specific carcinogen (radiation).

We re-emphasize that there was no microscopic connection between the glioma and the craniopharyngioma. Without such continuity, we can establish no more definite connection between the two lesions.

Fig. 9. Correlation of craniopharyngioma irradiation with subsequent tumor. *Left:* Schematic location of the two intracranial tumors. *Right:* Superimposition of isodose curves for the treatment of the craniopharyngioma, showing the overlap of the 95% dose curve with the site of origin of the right temporal lobe glioma. 100% = 6007 rads.
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References


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