Intracerebral ganglioglioma

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Ganglioglioma in the temporal lobe was encountered in 0.6% of a series of 998 patients undergoing biopsy for intracranial tumors. It was more frequent in young adults and children. Seizures were the main symptom and had been present over a long period of time in some patients. Clinical examination also revealed intracranial pressure, focal signs, and behavioral problems, but these symptoms were not always evident. Electroencephalography was not specific. Calcifications were visible on computerized tomography (CT) in five cases. The cystic and well-circumscribed aspects of these tumors were apparent on CT scans; these features were confirmed at operation and on magnetic resonance imaging (MRI), when it was also found that the tumors were partially solid. Therefore, MRI seems to be a useful diagnostic method, particularly when a cystic tumor is revealed on CT, and is also valuable for postoperative monitoring. Surgical treatment for ganglioglioma is recommended, with total extirpation if possible.

KEY WORDS • ganglioglioma • computerized tomography • temporal lobe • magnetic resonance imaging

Ganglioglioma has been considered a rare neoplastic tumor of the central nervous system (CNS). Zülch observed it in 0.4% and Cushing in 0.3% of comprehensive series of brain tumors. The incidence of ganglioglioma ranges from 1.2% to 7.6% in children and young adults with brain tumors. Despite the usual cystic presentation on computerized tomography (CT) scans, some lesions have proven to be solid at operation. This low-density CT appearance of the tumor presents difficulties not only for preoperative diagnosis but also for postoperative radiological follow-up monitoring. The tumor often has the same CT density as cerebrospinal fluid (CSF). It is therefore difficult on CT scans to distinguish the tumor or a recurrence from a CSF-filled cavity.

Magnetic resonance imaging (MRI) permits better delineation of cerebral tumors; however, no case of ganglioglioma has been reported diagnosed with this new technique. In this study, a series of six operated gangliogliomas is presented, four of which were investigated with MRI. The different modalities for radiological examination and their influence on diagnosis and treatment are discussed.

Clinical Material and Methods

We reviewed all brain-tumor biopsies obtained at the Department of Neuropathology, University of Göttingen, between January, 1978 (when the CT scanner was introduced), and December, 1984. The total number of patients with intracranial neoplasms was 998, six (0.6%) of whom had a ganglioglioma. Clinical and radiological information on the six patients was extracted from hospital charts. Electroencephalography (EEG), skull x-ray films, angiography, and CT scanning were performed in all patients. Pneumoencephalography (PEG) and CT scanning were also performed in one case, and four underwent MRI. All patients had recent clinical and radiological studies.

Magnetic resonance images were obtained using a Siemens Magnetome at 0.35/0.49 Tesla. The matrix was 256 × 256 pixels with two averages. Slice thickness was 10 mm, with no space between slices. The pictures were taken using the spin-multiple echo mode with a TR of 1600 msec (1400 msec in Case 6), a TE of 400

* Magnetome manufactured by Siemens Corp., Medical/Industrial Groups, Iselin, New Jersey.
msec, a $T_{E1}$ of 35 msec, and a $T_{E2}$ of 140 msec (70 msec in Case 6). In Case 6, an additional scan was made with a 2100-msec repetition time and a 200-msec echo. All slices were obtained in both the coronal and axial projections.

Histological diagnosis of the ganglioglioma was based on the criteria of Russell and Rubinstein. In addition to conventional stains, histological examination included immunohistochemical stains for glial fibrillary acidic protein (GFAP) and neurofilaments using alcohol-fixed sections. Electron microscopic examination was also performed on sections fixed in 3% glutaraldehyde.

Results

Clinical Findings

The clinical findings are summarized in Table 1. There were three males and three females, ranging in age between 14 and 48 years at diagnosis. The duration of symptoms prior to surgery was 3 months to 34 years. All patients presented with seizures, which in Cases 2, 3, and 6 were difficult to control. The seizures were mostly stereotypical, evoking temporal seizures and sometimes becoming generalized. The inter-ictal EEG suggested a focal process in all cases, with localized irregular slow waves (theta/delta activities) and/or spike and wave discharges. The neurological examination revealed symptoms of intracranial pressure in two patients (Cases 3 and 4), and all but one presented behavioral or emotional problems. Only one patient (Case 5) had a focal neurological sign.

Radiological Findings

Calcifications were present in two patients on skull x-ray films and in five patients on CT scans. The tumors were demonstrated on CT to lie in the temporal lobe in five patients and in the temporoparieto-occipital area in one (Case 3). The tumor in this last case showed signs of infiltration, particularly into the thalamus. Three cases revealed mass effect with displacement of the ventricular system. The lesions were hypodense in all patients except Case 4, and there was no enhancement after administration of contrast material in these five cases. Case 4 showed a high-density process with contrast enhancement. Well-circumscribed lesions were seen in all cases.

At angiography all but two patients were shown to have an avascular mass. In Cases 3 and 5 pathological vessels were revealed in the arterial phase and irregular veins were shown in the capillary and venous phases. Pneumoencephalography was performed in Case 2 in 1950 and was described as normal. In this case no CSF communication was demonstrated between the cyst and the ventricular system.

In MRI the tumors had high echo intensity in the $T_1$-weighted images and low echo intensity in the $T_2$-weighted images. The tumor recurrence is well defined for planning an operative approach.

![Fig. 1. Case 6. Upper Left: Preoperative computerized tomography (CT) scan showing a large low-density region in the temporal lobe. Upper Right: Control CT scan 3 years after the first operation showing the skull with a nonhomogeneous low-density structure in the temporal lobe, indicating a recurrence. Lower: Coronal $T_2$-weighted magnetic resonance image showing a high-signal area below the ventricular system. The tumor recurrence is well defined for planning an operative approach.](image1.png)

![Fig. 2. Case 2. Left: Computerized tomography scan showing a low-density lesion with calcification in the temporal lobe. Right: Preoperative $T_2$-weighted magnetic resonance image showing a high-signal cystic area in the temporal lobe with the same appearance as cerebrospinal fluid. Below this region, the small tumor is clearly delineated from the surrounding tissue.](image2.png)
Intracerebral ganglioglioma

**TABLE 1**

*Clinical findings in six cases of intracerebral ganglioglioma*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age* &amp; Sex</th>
<th>Presenting Symptom</th>
<th>Duration of Symptoms</th>
<th>Neurological Findings</th>
<th>Tumor Location</th>
<th>Treatment</th>
<th>Follow-Up Period &amp; Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25, M</td>
<td>seizures</td>
<td>3 mos</td>
<td>normal</td>
<td>rt temporal, anterior</td>
<td>total extirpation</td>
<td>9 mos: normal, seizure-free</td>
</tr>
<tr>
<td>2</td>
<td>48, F</td>
<td>seizures, behavioral problems</td>
<td>34 yrs</td>
<td>emotional difficulties</td>
<td>rt temporal, posterior</td>
<td>subtotal extirpation</td>
<td>9 mos: behavioral problems, seizure-free, hemiparesis</td>
</tr>
<tr>
<td>3</td>
<td>30, F</td>
<td>seizures, headache</td>
<td>19 yrs</td>
<td>papilledema</td>
<td>rt temporoparietal, thalamic infiltration</td>
<td>subtotal extirpation, radiotherapy</td>
<td>21 mos: seizures, hemianopsia</td>
</tr>
<tr>
<td>4</td>
<td>23, F</td>
<td>seizures, headache</td>
<td>5 yrs</td>
<td>papilledema</td>
<td>rt temporal, anterior</td>
<td>total extirpation</td>
<td>15 mos: normal, seizure-free</td>
</tr>
<tr>
<td>5</td>
<td>25, M</td>
<td>seizures, hemiparesis, dysphasia</td>
<td>7 yrs</td>
<td>depression, dysphasia, hemiparesis</td>
<td>lt temporal</td>
<td>total extirpation, radiotherapy</td>
<td>21 mos: seizures</td>
</tr>
<tr>
<td>6</td>
<td>14, M</td>
<td>seizures</td>
<td>8 yrs</td>
<td>normal</td>
<td>rt temporal</td>
<td>subtotal extirpation (recurrence 3 yrs later, total extirpation)</td>
<td>14 mos: seizure-free, hemiparesis</td>
</tr>
</tbody>
</table>

* Age (in years) at diagnosis.

Weighted images. In Cases 1 and 6 (Fig. 1), small areas with low echo intensity were seen in the T1-weighted images and high echo intensity in the T2-weighted images, which we interpreted as edema. In Cases 1 and 2 (Fig. 2), a zone above the tumor exhibited high signal intensity on the T2-weighted images; we interpreted this area as cystic. In Cases 3 (Fig. 3) and 6 (Fig. 1), there was a zone that produced a signal similar to that of CSF; in fact, it was the defect of the first operation which surrounded the rest of the tumor. In all cases there was good contrast between the lesion and the normal brain tissue. Calcifications seen on CT scans were not apparent on MRI, either with T1- or T2-weighted images; these regions showed low signal intensity.

**Histological Studies**

The tumor tissues were composed of gangliomatous and gliomatous components. Randomly oriented and diffusely scattered cells with polymorphous, slightly eosinophilic cytoplasm, eccentric large and distinct nuclei (sometimes binucleated), and prominent nucleoli were compatible with a ganglionic nature. Nissl's granules were poorly represented in all cases. Axons were swollen and irregularly intermingled on Bodian staining. The immunohistochemical reaction to the neuro-
filaments is shown in Fig. 4 left. Gliomatous cells were small and showed astrocytic differentiation; the parenchyma underwent microcystic degeneration. These cells, including the Rosenthal fibers observed in Case 1, were positive to GFAP (Fig. 4 center). Glial filaments and irregular small filaments were identified electron microscopically in gliomatous and gangliomatous tumor cells, respectively.

Capillary and reticulin fiber proliferation was fairly intense in half of the cases. In all cases, calcification deposits were observed at the periphery of the tumor or in the neighboring cortex. There was prominent perivascular lymphocytic cuffing inside the tumors from Cases 1, 4, and 6 (Fig. 4 right).

Treatment

The tumor was removed totally in four cases and subtotally in the other two. All tumors were partially cystic and solid; the dissection of tumor tissue from brain was easy in all cases, but the solid part of the lesion showed an infiltrative tendency, particularly in Case 3. Two patients whose tumors were infiltrative were treated postoperatively with local radiation therapy. All patients received 300 mg diphenylhydantoin daily after the operation.

Outcome

The two patients (Cases 1 and 4) with total extirpation without radiation therapy had normal findings 9 and 15 months after the operation. One patient (Case 2) showed some persistent behavioral problems and residual hemiparesis; however, no seizures were noted during the 9 months after surgery. One patient (Case 3) with thalamic infiltration and irradiation developed residual hemianopsia, psychomotor seizures (as often as three times a month), and early hydrocephalus 21 months after surgical treatment. The last patient (Case 6) developed increased seizures 2 years after a subtotal extirpation. The CT scan at that time revealed a cystic process, and MRI showed a partially cystic and solid tumor (Fig. 1); because of the recurrence, this patient underwent repeat surgery and an avascular tumor was totally extirpated. This child was seizure-free 14 months later, but had a postoperative hemiparesis.

Discussion

Ganglioglioma is a rare slow-growing tumor of the CNS, in which mature neuroglia and ganglion cells coexist. Hamartomas found in patients with a prolonged history of temporal lobe epilepsy since early childhood are congenital malformations which can subsequently grow or take on a neoplastic character. Only one of our patients (Case 6) had had clinical manifestations since early childhood. The histological features of the tumor specimens were those generally recognized as typical of ganglioglioma. This type of tumor is found anywhere in the CNS: spinal cord, brain stem, third and fourth ventricles, cerebellum, pineal region, thalamus, intrasellar region, and op-

Fig. 4. Left: Photomicrograph showing the immunohistochemical reaction to neurofilaments. Positive ganglioma cells are darkly stained. × 170. Center: Photomicrograph showing the immunohistochemical reaction of glial fibrillary acidic protein. Positive astrocytoma cells as well as abundant glial fibers are darkly stained, while ganglioma cells are not stained. × 170. Right: Photomicrograph showing marked perivascular cuffing of lymphocytes inside the tumor tissue. H & E, × 80.
Intracerebral ganglioglioma
tic nerve. However, in most of the reported cases the
tumors were located in the temporal lobe. 12,17,19,28,30

Because of this location, some authors report that
most of their patients presented with intellectual and
behavioral difficulties and seizures. 17,24,28 In most cases,
the seizures were generalized, became increasingly dif-
ficult to control with anticonvulsant therapy, and had
often been present for several years. Electroencephalo-
grams were locally abnormal in most of these patients.
Symptoms of intracranial pressure are described in the
literature as rare; however, papillary stasis, nausea,
and headache were noted in two patients.

Neuroradiological findings are not specific for this
type of tumor. As reported by Imanaga, et al.,17 and
Katz, et al., the plain skull x-ray films sometimes show
calcifications, and angiography reveals an avascular
mass without other pathological findings. Pneumo-
encephalography does not seem to be useful in identifying
this lesion.17,19 The CT findings described by Zimmer-
man and Bilaniuk29 and confirmed by others17,21,24,28
showed the lesions to be isodense or with increased
density. As reported here, most tumors have a cystic
appearance, are well circumscribed, and show CSF
density on CT scanning. They present with calcifi-
cations and reveal no mass effect, suggesting a slow
rate of growth. All studies suggest possible confusion
with a diagnosis of arachnoid cyst or porenceph-
aly.12,17,18,21,24,28,29

The discrimination of pathological and normal tissue
in four of the present cases was more reliable with MRI
than with CT scanning. As noted by Bydder, et al., it
is possible to differentiate tumor, edema, and normal
tissues in T1- and T2-weighted images. Furthermore,
MRI enables good imaging of the tumor and surround-
ing space, which is an advantage for planning the op-
eration. In all four cases so examined, MRI showed the
same signal behavior with a high echo intensity in the
T1-weighted image.

According to Johannsson, et al., the histological
appearance is highly variable; cell density and pleomor-
phism of both the neural and the glial components
varied from case to case, and showed an inconsistent
relationship between the histological appearance of the
lesion, the clinical course, and the prognosis of the
disease. However, the reactive lymphocytic inflamma-
tion observed in the tumor tissue of Cases 1 and 6 may
be correlated with the perifocal edema seen on MRI,
while Case 2 showed neither inflammation on the
histological sections nor edema on the MRI scans.
Anaplastic changes may take place in the glialomatous
component, and the gangliomatous component may
develop into primitive neuroblastic forms. 9,16,25 How-
ever, anaplastic transformation is very rare. 23,31 and this
malignancy was not found in the present cases.

In accordance with the literature, surgical treatment is
recommended with total extirpation if possible, as
recurrence is frequent. However, since seizures are the
major problem associated with this tumor, it would be
desirable to treat the tumor and the epilepsy together.
Some diagnostic studies, such as stereotaxic EEG
with the introduction of deep intracerebral electrodes,
should provide some indication not only of the volume
of the tumor but also of the "anatomofunctional"
organization of neighboring brain structures and the
localization of the epileptogenic area adjacent to the
tumor. 2,20 Unfortunately, these investigations were not
possible in our patients (particularly Cases 2 and 6)
because of technical difficulties.

The value of radiation therapy in these tumors is not
well defined. 24 This tumor is quite radiosensitive and,
as proposed by some authors, irradiation should only
be used in cases where there is evidence of progressive
disease. 12,18,24,28 Several authors recommend radiation
therapy when tumor growth is evident on a follow-up
CT scan12,18 or in the case of residual tumor. 28 However,
Garrido, et al.,12 and Johannsson, et al., 18 reported
similar results whether the patients had radiation ther-
apy or not.

The outcome of all series is generally good and, as
noted by some authors,18,24 the rather variable course
of these tumors depends on their location. Further-
more, recurrence depends on the extent of surgical
extirpation and on the infiltrative potency of the tumor.
Because MRI allows better discrimination of patholog-
ical and normal tissue, it should not only help reduce
the risk of recurrence but also help follow the course of
this lesion with more precision.

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