Intraventricular neurocytoma: clinicopathological features of six cases

SHUNJI NISHIO, M.D., TAKATOSHI TASHIMA, M.D., IWAO TAKESHITA, M.D., AND MASASHI FUKUI, M.D.

Department of Neurosurgery, Neurological Institute, Faculty of Medicine, Kyushu University, Fukuoka, Japan

The clinical and pathological features of six patients with so-called “intraventricular oligodendroglioma” are reported. The tumor had no predilection for sex, and the patients’ age at diagnosis ranged from 15 to 39 years. The lesions were located in the lateral and/or third ventricles. Total removal of the tumor was performed in three patients, and the remaining three underwent partial resection. Postoperative irradiation was given to five patients. A follow-up study revealed that five patients were free of recurrent tumor at 15 to 227 months after treatment, and one was alive with disease 25 months after surgery. Histologically, all tumors were composed of small uniform cells, with perinuclear halos and regular round nuclei. Tumor cells were sometimes arranged around nucleus-free fibrillary zones. Mitoses were infrequent. Ultrastructurally, neoplastic cells had round nuclei with dispersed heterochromatin and organelle-sparse cytoplasm containing occasional microtubules, 20 to 25 nm in diameter, and scattered dense-core vesicles, 100 to 200 nm in diameter. Cell processes containing dense-core and clear vesicles were frequently present. Thus, these neoplasms should be considered neuronal in origin, and should be classified as “intraventricular neurocytomas.”

KEY WORDS • neurocytoma • intraventricular neoplasm • ultrastructural study

Primary neuronal tumors of the central nervous system (CNS) most often occur in the cerebral parenchyma in children. Identification of these tumors by light microscopy alone is often difficult, and many have been confused with oligodendrogliomas, ependymomas, or undifferentiated primary sarcomas. With the availability of ultrastructural and immunohistochemical techniques, tumor diagnosis has been refined beyond the capability of routine light microscopy. In 1982, Hassoun, et al., described two cases of intraventricular tumor which on light microscopy resembled oligodendroglioma and which showed the ultrastructural characteristics of neuronal neoplasms. They coined the term “central neurocytoma” for these tumors. This neoplasm has not become a distinct clinical and pathological entity because of its rare occurrence and its rather recent recognition. In this paper, the cases of six patients with so-called “intraventricular oligodendroglioma” are reviewed, and the ultrastructural resemblance of these tumors to central neurocytoma is confirmed.

Clinical Material and Methods

Six patients with intraventricular tumors, which were diagnosed as “oligodendroglioma” on light microscopic examination, form the basis of this report. All six patients were seen, diagnosed, and treated at the Kyushu University Hospital between 1968 and 1985. The clinical charts were reviewed and the surgical materials were reexamined. For histopathological examination, tumor tissues obtained at surgery were fixed in 10% formalin and embedded in paraffin. Sections were cut at 5 μm and stained with hematoxylin and eosin, phosphotungstic acid-hematoxylin, and Bodian’s silver impregnation for neurofibrils. For immunochemistry, paraffin sections from five cases were prepared with primary antisera directed against glial fibrillary acidic protein (GFAP), S-100 protein, myelin basic protein, γ-enolase, and neurofilament proteins (68 kD, 160 kD, and 210 kD), according to the avidin-biotin-peroxidase complex method of Hsu, et al. Samples for electron microscopic examination were fixed in cold 2% glutar-
TABLE 1
Clinical profiles in six patients with intraventricular neurocytoma

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs),*</th>
<th>Sex</th>
<th>Involved Ventricle</th>
<th>Surgical Removal</th>
<th>Postop Radiation</th>
<th>Follow-Up Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15, M</td>
<td>M</td>
<td>lateral</td>
<td>total</td>
<td>yes</td>
<td>2 yrs 5 mos 100</td>
</tr>
<tr>
<td>2</td>
<td>22, F</td>
<td>F</td>
<td>lateral &amp; 3rd</td>
<td>partial</td>
<td>yes</td>
<td>18 yrs 11 mos 80</td>
</tr>
<tr>
<td>3</td>
<td>22, F</td>
<td>F</td>
<td>lateral</td>
<td>total</td>
<td>no</td>
<td>4 yrs 8 mos 50</td>
</tr>
<tr>
<td>4</td>
<td>24, M</td>
<td>M</td>
<td>both lateral &amp; 3rd</td>
<td>total</td>
<td>yes</td>
<td>1 yr 3 mos 80</td>
</tr>
<tr>
<td>5</td>
<td>30, M</td>
<td>M</td>
<td>both lateral &amp; 3rd</td>
<td>partial</td>
<td>yes</td>
<td>1 yr 3 mos 90</td>
</tr>
<tr>
<td>6</td>
<td>39, F</td>
<td>F</td>
<td>both lateral</td>
<td>partial</td>
<td>yes</td>
<td>2 yrs 1 mos 50</td>
</tr>
</tbody>
</table>

* Age at diagnosis.
† Results assessed by Karnofsky performance scale.

FIG. 1. Case 5. Computerized tomography scans revealing a well-circumscribed mass (left), which is moderately enhanced after intravenous administration of contrast material (right).

Results

Clinical Features

The clinical features of the six cases described here are summarized in Table 1. Four patients presented with symptoms and signs of increased intracranial pressure, such as headache, nausea, and papilledema. The duration of clinical symptoms before diagnosis ranged from 4 to 10 months, averaging 7.5 months. The other two patients (Cases 1 and 6) were discovered to have an intraventricular tumor as an incidental finding on computerized tomography (CT) scans taken after minor head trauma; neither patient showed any neurological deficits related to the tumor.

The tumors were supratentorial, located in the lateral ventricles with or without extension into the third ventricle. The pineal zone and the cerebellum were not involved. On CT scans the tumors in five patients were round with an irregular margin and showed intratumoral low-density areas of various sizes. Calcification within the tumor was observed in only one patient. On injection of contrast medium, the tumors enhanced slightly to moderately. Unilateral or bilateral ventricular dilatation due to obstruction of the foramen of Monro was commonly seen (Fig. 1).

All six patients underwent surgery, via an anterior interhemispheric transtemporal route in four and transfrontally in two. Three tumors were totally removed and three were partially excised. They were relatively well circumscribed and were mainly intraventricular. Five tumors involved the septum pellucidum, and four involved the fornix. They were usually attached to the lateral walls of the ventricles without invasion. At surgery, five tumors were interpreted as originating from the septum pellucidum or fornix, and one from the choroid plexus. Postoperative radiotherapy was given to five patients, and none received chemotherapy.

All patients are alive from 1 to nearly 19 years after treatment. Follow-up CT scans showed no tumor in five patients; the remaining patient (Case 6) had residual tumor without new clinical symptoms 25 months after treatment.

Light Microscopic and Immunohistochemical Findings

The tumors were composed of a uniform cell population, with round and occasional polygonal cell contours and central round nuclei. Cell cytoplasm was clear to eosinophilic, and was uniform in appearance (Fig. 2 left). Mitotic figures were infrequent. The cells were gathered into groups bound by capillaries or very thin bands of connective tissue. No Homer Wright rosettes were seen, but tumor cells were sometimes arranged about wide, round fibrillary patches (Fig. 2 right). Neither ganglion cells nor endothelial proliferation was identified. The histological features of the semithin sections were similar to those seen in paraffin sections, but areas of round fibrillary patches were not contained in the Epon blocks.

Immunocytochemical examination revealed no evidence of staining of tumor cells for GFAP, S-100 protein, myelin basic protein, γ-enolase, or neurofilament proteins. In the peripheral areas of the tumor in Case 5, scattered astrocytic cells were stained with...
Intraventricular neurocytoma


GFAP; no participation of astrocytes was noted in the other tumors.

Electron Microscopic Findings

Electron microscopic examination (Fig. 3) revealed essentially a similar population of tumor cells with relatively uniform structures in all cases. The nuclei were round or ovoid. They contained clear, sparsely dispersed chromatin, which was finely clumped in some areas. Nucleoli could sometimes be visualized and these were usually single and conspicuous. The cell cytoplasm was sparsely populated with polysomes and mitochondria. Small amounts of rough endoplasmic reticulum were also present. Occasional cells had abundant smooth or rough endoplasmic reticulum, some of which formed concentric whorls in the cytoplasm. Golgi apparatus were occasionally seen but were not prominent. In addition, some electron-dense, irregular, ovoid, or dumbbell-shaped lysosomes, and occasional membrane-bound dense-core vesicles, 100 to 200 nm in diameter, were identified. Microtubules were sparse, and intermediate filaments were not seen (Fig. 4). Between the tumor cells, numerous cytoplasmic processes were present. These processes sometimes contained parallel bundles of microtubules, a varied number of dense-core vesicles, and occasional clear vesicles. Some simple desmosomes were observed between the tumor cells, but no well-formed synapses were identified within the neoplasm.

FIG. 3. Low-power electron micrograph of the tumor in Case 4 showing tumor cells and many cell processes. Cell processes are filled with microtubules (arrows) as well as dense-core vesicles (arrowheads). A Golgi apparatus (asterisk) and many lysosomes are also present. × 4630.
Discussion

The six cases in this series showed clinical and histological similarities. All occurred in the ventricles of relatively young patients. Sheets of uniform round cells with perinuclear halos and rare mitotic figures were characteristic histological features. Except for the presence of patchy nucleus-free fibrillary zones, there were no apparent differences in histological features between oligodendrogliomas and the intraventricular tumors in these patients.

Although a specific immunological indicator that characterizes oligodendroglioma or CNS neuronal tumors has not so far been found, immunohistochemical staining for GFAP, γ-enolase, neurofilament proteins, and myelin basic protein was performed in the hope of clarifying the histogenesis of these tumors. The presence of GFAP-positive neoplastic oligodendrocytes has been reported in about 50% of oligodendrogliomas; however, none of the five tumors so examined contained this cell. No cells stained positive for myelin basic protein or neurofilament protein. None of the tumors examined showed any reaction for γ-enolase, which has been reported both in neuronal cells and in oligodendrogliomas. Thus, there is no immunohistochemical evidence suggesting that the tumors in our series were derived from oligodendrocytes or from neuronal cells.

Since the first ultrastructural observations on oligodendrogliomas by Luse, many authors have reported on the ultrastructure of the tumor. Although it is not as homogeneous as was thought from the light microscopy studies, the characteristic ultrastructural features have been reported to include: numerous and sometimes abnormally enlarged mitochondria; abundant microtubules; prominent Golgi apparatus; and occasional polygonal crystalline bodies. Concentric laminar structures, which were first thought to reflect the myelin-forming capacity of oligodendroglioma, are now not considered to be specific to this tumor. Five of the six tumors in our series had these structures. Ultrastructurally, the tumor cells of these six tumors resemble neither normal oligodendrocytes nor cerebral oligodendroglioma cells.

Dense-core vesicles in the tumors described here are identical to those seen in the cytoplasm and process of the neurons in the normal peripheral, central, and autonomic nervous systems, and in APUD (amine precursor uptake and decarboxylation) cells. These vesicles have been reported to be present in ganglioneuromas, gangliocytomas, gangliogliomas, ganglio-neuroblastomas, neuroblastomas, pheochromocytomas, glomus jugulare tumors, carotid body tumors, paragangliocytomas, and even in small-cell carcinomas. The presence of these vesicles in non-neuronal neoplastic cells was accepted as a possible aberrant expression of cellular differentiation. In neuronal neoplastic cells, these vesicles are reported to be abundant in the nerve process and fewer in the perikaryon, as in our tumors. As mentioned above, microtubules rarely occur in tumors other than of neuronal origin and oligodendrogliomas. Ultrastructural features, such as abundant cell processes containing microtubules and dense-core and clear vesicles, indicate the neuronal nature of our neoplasms.

Intraventricular tumors of neuronal cell origin, al-

---

FIG. 4. High-power electron micrographs. **Left**: Tumor section in Case 3 showing several dense-core vesicles and microtubules within the cell processes, × 25,000. **Right**: Tumor section in Case 5 showing a process containing dense-core vesicles that forms a junction with another process, × 29,000.
Intraventricular neurocytoma

though rare, have been reported. Among these, neuroblastomas are characterized by process formation, intracytoplasmic microtubules, and clear and dense-core vesicles. A central neurocytoma is a slowly growing tumor composed of mature, small, and regular neuronal cells, not mature ganglion cells; its identification depends mostly on ultrastructural findings such as neurosecretory granules and well-formed synapses. The tumors described here were composed of a homogeneous population of cytologically bland cells, and were ultrastructurally identical to central neurocytomas except for the absence of well-formed synapses. Jerdan, et al., and Wilson, et al., reported tumors similar to ours, and designated them as "differentiated neuroblastomas." There may be a certain range of cell differentiation in this kind of tumor, and we consider that these tumors (including ours) may be placed into one tumor group. This type of tumor has a favorable postoperative prognosis. To avoid nosological confusion, we prefer the term "intraventricular neurocytoma."

The critical issue in these tumors is their biological activity. Two of the six tumors were incidental findings on CT. Five of these patients have no evidence of recurrence, and all six are alive 15 to 227 months after treatment. The histological appearance may reflect the benign biological behavior of these tumors. Further study is needed with more extensive use of electron microscopy to reveal the true incidence, the actual site of origin, and the spectrum of differentiation, including the presence of synapses. Neuronal neoplasms of the CNS are known to show a wide spectrum of differentiation.

References


J. Neurosurg. / Volume 68 / May, 1988

Manuscript received June 26, 1987.
Accepted in final form October 5, 1987.
Address reprint requests to: Shunji Nishio, M.D., Department of Neurosurgery, Neurological Institute, Faculty of Medicine, Kyushu University 60, 3-1-1, Maidashi, Higashiku, Fukuoka 812, Japan.