Primary intracranial germ-cell tumors

A clinicopathological study of 14 cases

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Fourteen cases of primary intracranial germ-cell tumors are presented. Histologically, there were eight germinomas, three teratomas, and three germ-cell tumors of more than one histological type. Immunohistochemical studies revealed alpha-fetoprotein in yolk-sac tumor components in two cases and beta human choriogonadotropin in syncytiotrophoblastic giant cells in one case. One teratoma contained an unusual pleomorphic sarcomatous portion with features of early myoblastic differentiation. Comparison of intracranial with gonadal germ-cell tumors shows that the same subtypes are found in both locations with comparable incidence and similar biological behavior. The detailed World Health Organization classification of testicular germ-cell tumors should be applied to the histopathological classification of intracranial germ-cell tumors. Despite the critical location of intracranial germ-cell tumors, a good outcome can be achieved by optimal surgical excision. A primary microsurgical approach provides a histopathological diagnosis, which is indispensable for the proper choice of postoperative management.

KEY WORDS • germinoma • germ-cell tumor • teratoma • alpha-fetoprotein • human choriogonadotropin

The World Health Organization classification of intracranial germ-cell tumors is based on the much more detailed classification of testicular tumors. However, it has not been established if the subtypes described for the testicular location are found with the same relative incidence intracranially and if they show the same biological behavior. These questions can only be answered when a direct surgical approach is used. There is a controversy about management of these tumors between proponents of primary surgical excision and supporters of conservative therapy, including ventricular shunting and radiotherapy.

We report here our experience with primary direct microsurgical techniques for removal of tumors in the pineal region to support increasing evidence of the benefits of this approach.

Summary of Cases

This series included eight patients with pure germinomas, three with teratomas, and three with mixed germ-cell tumors. The clinical data, including the patient's age and sex, main clinical symptoms, site of tumor, pre- and postoperative treatment (shunting, radiotherapy, chemotherapy), operative procedure, recurrences, survival time, and histopathological diagnosis, are given in Tables 1 and 2. Typical pre- and postoperative computerized tomography scans are presented from Cases 12 and 14 in Figs. 1 and 2.

From a histopathological point of view, two cases were of special interest. In Case 9, immunohistochemical staining revealed alpha-fetoprotein (AFP) in the yolk-sac component (Fig. 3 left), and syncytiotrophoblastic giant cells were found within the germinoma component. These giant cells stained positive for beta-human choriogonadotropin (HCG, Fig. 3 right). The second patient (Case 12) had an immature teratoma. In addition to the glandular structures, the tumor contained areas of haphazardly arranged spindle-shaped malignant cells (Fig. 4 left) that stained positive with phosphotungstic acid hematoxylin (PTAH); no definite cross striations were evident (Fig. 4 right).

Discussion

The incidence of primary intracranial germ-cell tumors is about 0.5% in adults and 2% in children.
Primary intracranial germ-cell tumors

FIG. 1. Computerized tomography scans in Case 12. a: Preoperative scan showing a mass in the right basal ganglia with deviation of midline structures to the left. b: Scan 6 days postoperatively showing the fluid-filled resection cavity. There is no evidence of residual tumor. A hygroma can be seen in the right frontal region with shift of the midline.

FIG. 2. Computerized tomography scans in Case 14. a: Preoperative scan showing a cystic and focally calcified paraventricular tumor causing compression and shifting of the third ventricle to the left. b: Scan 5 weeks postoperatively showing a small resection cavity at the right border of the third ventricle. There is no evidence of residual tumor.


FIG. 4. Photomicrographs of a mixed germ-cell tumor removed from Case 12. Left: Section showing teratomatous glandular structures and sarcomatous components of the tumor. H & E, × 123. Right: Section from the sarcomatous part of the tumor showing several large spindle-shaped cells. PTAH, × 350.

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TABLE 1
Primary intracranial germinomas

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Symptoms</th>
<th>Tumor Site</th>
<th>Shunting</th>
<th>Surgical Treatment</th>
<th>Radiotherapy Dose</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14, M</td>
<td>headaches, squint to lt, double vision</td>
<td>lt thalamus</td>
<td>yes</td>
<td>radical extirpation</td>
<td>5400 cGy, 6000 cGy (to spinal cord)</td>
<td>alive 6 yrs (spinal cord metastasis)</td>
</tr>
<tr>
<td>2</td>
<td>7, M</td>
<td>vomiting, rt-sided hemiparesis, visual disturbances</td>
<td>lt parapineal region</td>
<td>yes</td>
<td>radical extirpation</td>
<td>1800 cGy</td>
<td>died 4 mos postop from tumor recurrence alive &amp; well 5 yrs postop</td>
</tr>
<tr>
<td>3</td>
<td>50, M</td>
<td>dizziness, headaches, double vision, rt-sided hemiparesis</td>
<td>pineal region</td>
<td>yes</td>
<td>radical extirpation</td>
<td>5500 cGy</td>
<td>died 5 yrs postop from tumor recurrence alive &amp; well 3 yrs postop</td>
</tr>
<tr>
<td>4</td>
<td>12, F</td>
<td>nausea, vomiting, polydypsia, visual disturbances</td>
<td>suprasellar region</td>
<td>no</td>
<td>subtotal extirpation</td>
<td>3000 cGy</td>
<td>alive &amp; well 5 yrs postop</td>
</tr>
<tr>
<td>5</td>
<td>23, M</td>
<td>nausea, vomiting, polydypsia, visual disturbances, incompetence</td>
<td>pineal region</td>
<td>no</td>
<td>radical extirpation</td>
<td>4140 cGy</td>
<td>alive &amp; well 3 yrs postop</td>
</tr>
<tr>
<td>6</td>
<td>11, F</td>
<td>retarded growth, weight loss, visual &amp; sleep disturbances</td>
<td>suprasellar region</td>
<td>no</td>
<td>radical extirpation</td>
<td>5200 cGy</td>
<td>alive &amp; well 3 yrs postop</td>
</tr>
<tr>
<td>7</td>
<td>13, F</td>
<td>polyuria, retarded growth, weight gain, dizziness, visual disturbances</td>
<td>hypothalamus</td>
<td>no</td>
<td>radical extirpation</td>
<td>5600 cGy</td>
<td>alive &amp; well 2 yrs postop</td>
</tr>
<tr>
<td>8</td>
<td>17, M</td>
<td>polyuria, retarded growth, weight gain, dizziness, visual disturbances</td>
<td>suprasellar region</td>
<td>no</td>
<td>stereotaxic biopsy</td>
<td>none</td>
<td>alive &amp; well 2 yrs postop</td>
</tr>
</tbody>
</table>

* None of these patients underwent chemotherapy.

We are aware of only four other cases of primary intracranial germ-cell tumors with syncytiotrophoblastic giant cells.\textsuperscript{13,18-20} This variant may be clinically important; in a recent report, precocious puberty in a child was attributed to the presence of syncytiotrophoblastic giant cells in an otherwise typical germinoma.\textsuperscript{19} Germ-cell tumors with elevation of both AFP and beta-HCG are commonly associated with the diagnosis of embryonal carcinomas. However, in the mixed germ-cell tumor in our Case 9, AFP production was restricted to the yolk-sac components and beta-HCG expression to syncytiotrophoblastic giant cells in the germinoma component. This illustrates that it is possible by immunohistochemical examination to localize the AFP- and beta-HCG-producing tissue in particular components of a tumor.

A further argument in favor of the value of histological and immunohistochemical diagnosis lies in the observation that there are false-negative serum measurements. This may be due to the fact that the tumor cells produce the markers, but do not secrete them into the bloodstream, or simply because the tumors do not produce AFP or beta-HCG at all.\textsuperscript{29} In our 14 cases, only three had demonstrable expression of tumor markers. In addition, elevated serum levels of AFP and beta-HCG can be found in conditions other than germ-cell tumors, such as associated with hepatocellular carcinoma or during pregnancy.\textsuperscript{24} All of the above-mentioned examples illustrate that the information given by histological diagnosis and immunohistochemical tests leads to better documented diagnosis than serum screening alone.

The presence of a sarcomatous component suggestive of early myoblastic differentiation within an immature...
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Symptoms</th>
<th>Tumor Site</th>
<th>Diagnosis*</th>
<th>Shunting</th>
<th>Surgical Treatment</th>
<th>Radiotherapy Dose</th>
<th>Chemotherapy Agent†</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>12, M</td>
<td>weight loss, thirst, headaches</td>
<td>suprasellar chiasmatic region</td>
<td>germinoma with STGC’s, yolk-sac tumor, &amp; embryonal carcinoma</td>
<td>no</td>
<td>subtotal extirpation</td>
<td>8650 cGy</td>
<td>methotrexate, CCNU</td>
<td>died 2 yrs postop</td>
</tr>
<tr>
<td>10</td>
<td>14, M</td>
<td>fever, nausea, vomiting, rapid loss of hearing, somnolence, double vision</td>
<td>pineal region</td>
<td>yolk-sac tumor, immature teratoma</td>
<td>yes</td>
<td>radical extirpation</td>
<td>6000 cGy</td>
<td>methotrexate, bleomycin, cis-platinum, cyclophosphamide, Vepesid, dacarbazine</td>
<td>alive 3 yrs postop (recurrence &amp; spinal cord metastases)</td>
</tr>
<tr>
<td>11</td>
<td>21, M</td>
<td>diabetes insipidus, headaches, vertigo, ear pains, rapid loss of hearing, impotence, epileptic seizures, upward gaze palsy</td>
<td>pineal region</td>
<td>germinoma, mature teratoma</td>
<td>yes</td>
<td>radical extirpation</td>
<td>?</td>
<td>none</td>
<td>alive &amp; well 3 yrs postop</td>
</tr>
<tr>
<td>12</td>
<td>8, M</td>
<td>left-sided hemiparesis, headaches, convergent strabismus</td>
<td>rt basal ganglia</td>
<td>immature teratoma with sarcomatous components</td>
<td>no</td>
<td>radical extirpation</td>
<td>4800 cGy (preop)</td>
<td>Holoxan, BCNU (preop)</td>
<td>died 5 mos postop</td>
</tr>
<tr>
<td>13</td>
<td>9, M</td>
<td>headaches, vertigo, vomiting, visual disturbances</td>
<td>posterior part of third ventricle</td>
<td>mature teratoma</td>
<td>yes</td>
<td>radical extirpation</td>
<td>none</td>
<td>none</td>
<td>alive &amp; well 4 yrs postop</td>
</tr>
<tr>
<td>14</td>
<td>11, M</td>
<td>headaches, vomiting, loss of concentration, loss of consciousness, incontinence, polydypsia, epileptic seizures, left-sided hemiparesis</td>
<td>pineal region extending into third ventricle</td>
<td>mature teratoma</td>
<td>yes</td>
<td>radical extirpation</td>
<td>5200 cGy (preop)</td>
<td>none</td>
<td>died 5 yrs postop</td>
</tr>
</tbody>
</table>

* According to the World Health Organization classification of the gonadal germ-cell tumors. STGC’s = syncytiotrophoblastic giant cells.
† CCNU = l-(2-chloroethyl)-3-cyclohexyl-[4-nitrosourea; BCNU = 1,3-bis(2-chloroethyl)-1-nitrosourea; Vepesid = etoposide; Holoxan = ifosfamide.

The presence of a sarcomatous component in teratomas leads to a poor prognosis. The patient of Glass and Culbertson died 1 day postoperatively, our patient survived 4 months, and survival time reported in the case of Preissig, et al., was 1 year. The same is reported for intragonadal examples of this rare entity. We thus can conclude that subtyping and biological behavior of intracranial germ-cell tumors are comparable to those of their gonadal counterparts. The more detailed histopathological classification of testicular germ-cell tumors should therefore be applied to intracranial germ-cell tumors. Some reports indicate that biopsy may increase the risk of spinal metastasis in germinomas. In our series of eight germinomas, seven were treated by primary microsurgical subtotal or total extirpation and postoperative radiotherapy. Only one case was diagnosed by a stereotactic biopsy and was treated by radiotherapy only. Of the eight patients, only one (Case 1) developed spinal cord metastasis but he is still alive after 6 years.

Two patients died from local tumor recurrences 4 months and 5 years after operation. Of the 14 patients, 75% have no evidence of recurrence during observation periods of 2 to 6 years. In the more heterogeneous groups of germ-cell tumors with mixed tumor components, two of three patients with highly malignant variants died 5 months and 2 years postoperatively; the third patient is living 3 years after the first operation but has a local recurrence and evidence of spinal cord metastasis. Of the three patients with mature teratomas, one died 5 years after surgery, while two others are living and well 3 and 4 years postoperatively. Only two of our patients underwent preoperative radiotherapy. Both died, one within 5 months and the other within 5 years. Tumors not responding to conservative therapy (consisting of shunting and preoperative radiotherapy) may have grown to a stage where a total surgical extirpation is unlikely and the prognosis therefore worsened. These results indicate that primary microsurgical inter-

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vention, if performed by an experienced neurosurgeon, leads not only to a biopsy-proven diagnosis and exact classification of primary intracranial germ-cell tumors, but also represents the most effective therapeutic approach.

References


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