Occurrence of Basal Ganglia Germ Cell Tumors Without a Mass

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Objective: To report a case series in which basal ganglia calcifications without mass effect proved to be germ cell tumors.

Design: Case series.

Setting: Tertiary care hospital.

Patients: Four patients.

Interventions: Computed tomography, magnetic resonance imaging, positron emission tomography, biopsy, chemotherapy, and radiation therapy.

Main Outcome Measures: Recognition of clinical syndrome and radiological features.

Results: All patients had progressive hemiparesis, and 1 patient also had frontal lobe dementia. Imaging demonstrated progressive asymmetric signal abnormality with basal ganglia calcification and associated brainstem atrophy. Fludeoxyglucose F 18–positron emission tomography showed hypometabolism in contrast to malignant glioma.

Conclusion: Germ cell tumor should be considered in patients with an indolently progressive neurological course, particularly if basal ganglia calcification is present with or without enhancement, asymmetric brain atrophy, or a mass.

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From 4% to 12% of all pediatric central nervous system tumors in the Asian population are germinomas. The incidence in the Western world is much lower at 1% but is increasing, which may in part be explained by immigration trends. From 76% to 90% of germinomas develop in the midline, mainly in the pineal and suprasellar regions, but occurrence in the basal ganglia (BG) and thalamus has also been documented in up to 8% of all intracranial germinomas in Asian populations. Patients with central nervous system germinomas arising outside the pineal or suprasellar regions may present with nonspecific symptoms and signs and subtle radiologic findings, which may delay diagnosis unless a high level of consideration is maintained. We describe a series of children with atypical germ cell tumors (GCTs) presenting with BG calcifications without mass effect and with or without atrophy of the cerebral peduncle.

REPORT OF CASES

PATIENT 1

An 11-year-old Chinese boy presented with a 2-year progressive history of academic decline and behavioral dysfunction. He was presumed to have attention-deficient/hyperactivity syndrome and had been administered dextroamphetamine sulfate as treatment. Neurological evaluation revealed left hemiparesis and hemiatrophy of the right pons and cerebral peduncle and calcification of the right caudate nucleus (Figure 1). This was interpreted as the result of a remote insult. For 6 months, frontal lobe dementia, progressive hemiparesis, and ataxia developed.

Follow-up magnetic resonance imaging (MRI) with contrast media showed increased signal changes in the white matter of the right hemisphere, right cerebellum, and left internal capsule, with progressive right frontal white matter loss without mass effect or enhancement. This was interpreted as multifocal progressive white matter disorder. Positron emission tomography with fludeoxyglucose F 18 (FDG-PET) showed right frontal decreased activity. Test results for serum and cerebrospinal fluid (CSF) tumor markers were normal, and findings from the cytologic examination were negative. Right frontal lobe biopsy revealed germinoma (Figure 2). The patient received 6 cycles of carboplatin-based chemotherapy followed by 20 Gy (to convert to rad, mul-
tiply by 100) of craniospinal radiation. The hemiparesis and ataxia resolved; however, he had persistent, although improved, cognitive impairment 30 months later.

PATIENT 2

A 9-year-old Tongan boy presented with static mild mental handicap and progressive hemiparesis of 6 months’ duration. Computed tomographic scanning showed calcification of the left BG extending to the midbrain without mass effect (Figure 3). The left cerebral peduncle and pons were slightly smaller than those on the opposite side, suggesting atrophy. There was no dissemination. Based on the results of computed tomographic scanning with contrast (in particular, the BG calcification and secondary wallerian degeneration) and on our previous experience, GCT was considered. His CSF chorionic gonadotropin, β subunit, and α-fetoprotein (AFP) levels were normal in CSF, and serum AFP was 16 ng/mL (normal range, 0-11 ng/mL) (to convert to micrograms per liter, multiply by 1.0). The FDG-PET scan showed decreased uptake. She received hyperbaric oxygen, but the hemiparesis worsened, serum AFP increased to 37 ng/mL, and progression was noted on MRI with mass effect. She was diagnosed as having recurrent malignant GCT, and chemotherapy was commenced with a reduction in AFP. On chemotherapy, status epilepticus secondary to hyponatremia developed. Chemotherapy was stopped on parental request. She died of progressive tumor 2 months later.

PATIENT 3

A 6½-year-old white girl presented with headache and panhypopituitarism. She had a suprasellar mass, and tests for tumor markers were normal, and the results of the biopsy showed germinoma. She had a complete response to 2 cycles of carboplatin and etoposide. This was followed by focal radiotherapy with 30.6 Gy. One year later, progressive right hemiparesis, emotional lability, and dysarthria developed during a 5-month period. Computed tomographic scanning and MRI with contrast media suggested new neuronal tissue damage and calcification involving the left posterior limb of the internal capsule and lentiform nucleus. Chorionic gonadotropin, β subunit, and α-fetoprotein (AFP) levels were normal in CSF, and serum AFP was 16 ng/mL (normal range, 0-11 ng/mL) (to convert to micrograms per liter, multiply by 1.0). The FDG-PET scan showed decreased uptake. She received hyperbaric oxygen, but the hemiparesis worsened, serum AFP increased to 37 ng/mL, and progression was noted on MRI with mass effect. She was diagnosed as having recurrent malignant GCT, and chemotherapy was commenced with a reduction in AFP. On chemotherapy, status epilepticus secondary to hyponatremia developed. Chemotherapy was stopped on parental request. She died of progressive tumor 2 months later.

PATIENT 4

A 13-year-old white boy underwent a total resection of a third ventricular tumor, consisting of immature teratoma with a small focus of germinoma. Test results for tumor markers in serum and CSF were normal. He received focal radiotherapy of 41.4 Gy. At age 21, progressive right hemiparesis developed. Computed tomo-
graphic scanning and MRI revealed bilateral BG calcification with regional enhancement extending into the left cerebral peduncle without mass effect. Injury secondary to previous radiation was the primary differential rather than tumor recurrence in the absence of mass effect. Eight months later, he was dysarthric and more hemiparetic. Magnetic resonance imaging showed a mass in the left BG and thalamus extending to the midbrain. Test results were negative for AFP and chorionic gonadotropin, β-subunit, levels in serum and CSF and positive for c-kit. The results of the biopsy examination demonstrated a germinoma. The patient received 2 cycles of high-dose chemotherapy (etoposide, cyclophosphamide, and carboplatin) and then fractionated stereotactic focal radiotherapy of 36.2 Gy. He is stable at 4-year follow-up.

Systemic workup for GCT was performed in patients 1, 2, and 3, and the results were normal. The patients were not immunocompromised at presentation of BG GCTs, and brain biopsy did not reveal any evidence of viral infection, including John Cunningham virus.

**Comment**

The MRI findings of typical pineal and suprasellar intracranial germinomas are a mass with signal intensity similar to adjacent cerebral tissue on both T1- and T2-weighted images with intense homogeneous contrast enhancement. Tumor calcification on computed tomography is reported in up to 50% of patients. The imaging appearance in germinomas outside the pineal and suprasellar regions consists of isodense or hyperdense lesions with heterogeneous enhancement in the solid component and associated cysts and calcification.

In germinomas of the BG and thalamus, the radiologic findings are usually subtle initially. Cerebral atrophy of the brainstem and ipsilateral cerebral hemisphere might be the only abnormal finding, along with nonspecific increased signal changes in the cerebral white matter. The incidence of cerebral atrophy ranges between 20% and 33%. The cerebral atrophy is hypothesized to be due to either infiltration of tumor cells into the internal capsule or involvement of thalamic ganglionic cells, with infiltration of afferent and efferent nerve fibers from the thalamus and subsequent antegrade and retrograde wallerian degeneration. As the tumor progresses, it may produce mass effect, but, if the process is diffusely infiltrative, it may cause progressive atrophy as occurred in patient 1. Heterogeneity on T1- and T2-weighted magnetic resonance images are also more commonly seen in atypical germinomas, reflecting concomitant solid and cystic portions of the tumor.

The indolent progression of germinomas occurring outside the pineal and suprasellar areas has commonly resulted in delayed diagnosis, as was the case in 3 of our 4 patients. The progressive neurological dysfunction and dementia in patient 1 raised the possibility of a neurodegenerative disorder, a tumor, progressive vasculopathy, or chronic encephalitis. The lack of mass effect associated with the BG lesion and the atrophy of the cerebral peduncle suggested a diagnosis other than tumor. Similar radiologic findings for patient 2 were interpreted correctly because of our experience with patient 1.

Positron emission tomography with FDG measures metabolic activity of tumors, with malignant tumors having increased FDG uptake; benign tumors and radiation necrosis demonstrate reduced uptake. Our 2 patients (patients 1 and 3) showed FDG-PET hypometabolism,
Intracranial GCTs must be considered in those presenting with indolently progressive neurological dysfunction, with asymmetric progressive brain abnormalities. Atypical GCTs may cause calcification in BG and atrophy of the ipsilateral cerebral hemisphere and midbrain. An FDG-PET scan of BG GCTs demonstrates hypometabolism in contrast to malignant gliomas. It is important to diagnose GCTs before the development of major neurological deficits, because delayed treatment results in irreversible neurological dysfunction.

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REFERENCES


Table. Causes of Basal Ganglia Calcification

<table>
<thead>
<tr>
<th>Cause</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic</td>
<td>Familial basal ganglia calcification</td>
</tr>
<tr>
<td>Congenital</td>
<td>Toxoplasmosis, cytomegalovirus, rubella</td>
</tr>
<tr>
<td>Infection</td>
<td>Chickenpox, cysticercosis, AIDS, tuberculosis</td>
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<tr>
<td>Endocrine</td>
<td>Hypothyroidism, hyperparathyroidism,</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Mitochondrial cytopathy</td>
</tr>
<tr>
<td>Vascular</td>
<td>Hypoxia, SLE, radiation</td>
</tr>
<tr>
<td>Toxic</td>
<td>CO intoxication, lead poisoning, methotrexate use</td>
</tr>
<tr>
<td>Tumors</td>
<td>Germ cell tumor, glioma, ependymoma, meningioma, craniopharyngioma</td>
</tr>
<tr>
<td>Syndrome</td>
<td>Down syndrome, Cockayne syndrome</td>
</tr>
</tbody>
</table>

Abbreviations: CO, carbon dioxide; SLE, systemic lupus erythematosus.