Growing Teratoma Syndrome in a Patient With a Non-germinomatous Germ Cell Tumor in the Neurohypophysis —Case Report—

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Abstract

A 16-year-old woman presented with a non-germinomatous germ cell tumor in the neurohypophysis manifesting as progressive visual disturbance, amenorrhea, hydrosipsia, and polyuria. Her serum α-fetoprotein and human chorionic gonadotropin levels were elevated. She experienced sudden, rapid visual deterioration and underwent emergency partial tumor removal to decompress the optic nerves. Her vision subsequently improved. Histological examination of the surgical specimens confirmed immature teratoma. She received chemotherapy (ifosphamide 900 mg/m², cisplatin 20 mg/m², etoposide 60 mg/m²) for 5 consecutive days. Although the tumor marker levels decreased remarkably, her vision again declined rapidly due to enlargement of the tumor after the first course of chemotherapy. A second radical operation resulted in vision improvement. The tumor specimen showed only mature teratoma elements. This phenomenon, called the growing teratoma syndrome, is very rare in intracranial non-germinomatous germ cell tumors.

Key words: germ cell tumor, growing teratoma syndrome, teratoma, suprasellar tumor, neurohypophyseal tumor

Introduction

Primary intracranial germ cell tumors are rare and more common in children than adults, accounting for 0.5–1.0% of all intracranial neoplasms in Western countries and for 2.0–5.0% in Japan.5,8,10,21) The incidence of teratoma, including the malignant type, is reported as 0.4% of all intracranial neoplasms.20) Intracranial germ cell tumors tend to arise in the pineal region or neurohypophysis,6,10,20) and can be divided into germinomas and non-germinomatous germ cell tumors (NGGCTs) including mature or immature teratoma, embryonal carcinoma, yolk sac tumor, and choriocarcinoma. The disease status and the malignant nature of these tumors can be monitored by tumor marker assay (α-fetoprotein [AFP] and human chorionic gonadotropin-β [β-HCG]).10,20)

NGGCT responds poorly to radiotherapy, as the reported 5-year survival rate is 20–30%.21) Chemotherapy, especially with cisplatin, is more effective.9,8,12,19) A good response of 78% has been achieved with a combination of cisplatin and etoposide.19) Chemotherapy resulted in reduced tumor size and normalized tumor markers. The residual masses contained mature teratoma or fibrotic and necrotic tissue in 40–45% of patients, and persistent carcinoma in 15%,1,7,17,21)

Growing teratoma syndrome manifests as an increase in the tumor size and the presence of mature teratoma in resected specimens despite decreased or normalized tumor marker levels during or after chemotherapy in patients with NGGCT.10) The first reported case arose from the testes.4) Most other cases were associated with retroperitoneal tumors. The incidence of growing teratoma syndrome is 1.9–7.6% in patients with metastatic NGGCT,1,2,7,13,18) Only a few cases of this syndrome have been reported in patients with intracranial germ cell tumors.8,15,21,22)

We treated a 16-year-old Japanese woman with intracranial growing teratoma syndrome associated with a NGGCT in the neurohypophysis.
Case Report

A 16-year-old woman complained of impaired mental concentration, a one-month history of progressive visual disturbance, and a 2-year history of amenorrhea, hydrodipsia, and polyuria. Her past and family histories were unremarkable.

On admission she was alert but showed moderate disorientation and memory disturbance. Her ability to concentrate was impaired. She had been completely blind in the left eye for about a month, and her right visual acuity was 0.02. Neurological examination disclosed temporal hemianopsia. Her full blood cell count was normal. The serum sodium level was slightly elevated (144 mEq/l). The urinary volume was increased (about 4000 ml/day) and low urinary density (1.003 g/cm³) was suggestive of diabetes insipidus. Endocrine function tests revealed panhypopituitarism. The serum AFP level was 69 ng/ml (normal < 10) and the serum β-HCG level was 4.8 mIU/ml (normal < 0.5). The results of other biochemical tests were normal.

Magnetic resonance (MR) imaging disclosed a huge mass appearing as heterogeneous intensity with enhancement in the suprasellar region. The tumor occupied the interpeduncular cistern and the third ventricle. Both anterior horns of the lateral ventricle contained disseminated lipid-like fragments (Fig. 1). Spinal MR imaging revealed no evidence of tumor dissemination. Five days after admission, she suddenly lost all vision in her right eye. Computed tomography showed no intratumoral hemorrhage or hydrocephalus.

She underwent emergent partial removal of the tumor via the basal interhemispheric approach. Operative findings revealed that the tumor was fibrous and hard without adherence to the surrounding tissues. The tumor bled easily and strongly compressed the bilateral optic nerves and chiasma. Histological examination of the large specimens showed mature teratoma mixed with immature elements that were negative for AFP or β-HCG. The diagnosis was immature teratoma (Fig. 2).

No new neurological deficits developed after the operation. Her right-eye vision gradually recovered to 0.4. She received cortisol and antidiuretics for steroid hormone insufficiency and diabetes insipidus. Postoperative MR imaging showed that the tumor in the suprasellar area had been partially removed (Fig. 3A). Her serum AFP and β-HCG levels decreased to 35 ng/ml and 1.9 mIU/ml, respectively. A second-stage operation was planned after inten-
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AnICEregimenwasbegunconsistingofifosphamide(900mg/m²), cisplatin (20mg/m²), and etoposide (60mg/m²) for 5 consecutive days starting at 24 days after surgery. Her serum levels of the tumor markers continued to be high (9.4mIU/ml) just after completion of the first course, but gradually decreased during the 4-week interval between the first and second courses. This was thought to indicate a chemotherapeutic response. However, her right-eye vision again suddenly worsened to 0.05 on the day preceding the start of the second course. MR imaging disclosed remarkable enlargement of the tumor without elevation in the serum tumor markers (AFP 15ng/ml, β-HCG 0.5mIU/ml) (Fig. 3B).

She underwent a second emergency craniotomy. Gross total removal of the tumor was performed via the combined basal interhemispheric and transcannal transventricular approach. The tumor was mixed with hard and soft tissues and not strongly adherent to the surrounding tissues. Histological examination disclosed that all specimens were mature teratoma with no immature or malignant elements (Fig. 4). Subsequently, her right-eye vision improved to 0.3 with temporal hemianopsia.

She developed no new neurological deficits, but thermoregulatory disturbance was noted. MR imaging revealed that the tumor had been almost totally resected (Fig. 5). Only a small mass below the right optic nerve remained, which was not noticed during the operation because of the location behind the optic nerve. Her serum AFP and β-HCG levels were negative.

Prophylactic radiotherapy was started 4 weeks after the second operation because MR imaging on admission had revealed evidence of dissemination into the lateral ventricles. Initially, doses of 30 Gy to the whole brain and 24 Gy to the whole spine were delivered. This was followed by 14 Gy to the entire ventricle 9 days later, subsequently by 6 Gy to the local suprasellar region 3 days later. MR imaging showed no change in the size of the residual tumor. Tumor markers in both serum and cerebrospinal fluid were negative. Her concentration and memory disturbance persisted but then gradually improved. Her visual deficits were not exacerbated after the second operation and her diabetes insipidus and panhypopituitarism were well-controlled by sup-
Table 1  Reported cases of growing teratoma syndrome (GTS)

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Site of disease</th>
<th>First operation</th>
<th>Histological diagnosis</th>
<th>Time interval*</th>
<th>Treatment of GTS</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rustin et al. (1986)</td>
<td>9</td>
<td>F</td>
<td>neurohypophysis</td>
<td>biopsy</td>
<td>York sac tumor</td>
<td>3 mos</td>
<td>not performed</td>
<td>dead</td>
</tr>
<tr>
<td>Lee et al. (1995)</td>
<td>5</td>
<td>M</td>
<td>pineal</td>
<td>biopsy</td>
<td>Immature teratoma</td>
<td>3 mos</td>
<td>total removal, chemotherapy</td>
<td>NED</td>
</tr>
<tr>
<td>O’Callaghan et al. (1997)</td>
<td>19</td>
<td>M</td>
<td>pineal</td>
<td>biopsy</td>
<td>York sac tumor</td>
<td>6 wks</td>
<td>total removal, chemotherapy</td>
<td>NED</td>
</tr>
<tr>
<td>Hanna et al. (2000)</td>
<td>13</td>
<td>M</td>
<td>pineal</td>
<td>not done</td>
<td>Unknown</td>
<td>unknown</td>
<td>Subtotal removal, radiotherapy</td>
<td>NED</td>
</tr>
<tr>
<td>Present case</td>
<td>16</td>
<td>F</td>
<td>neurohypophysis</td>
<td>partial removal</td>
<td>Immature teratoma</td>
<td>4 wks</td>
<td>Total removal, chemotherapy, radiotherapy</td>
<td>NED</td>
</tr>
</tbody>
</table>

*Time interval from chemotherapy to presentation of GTS.  AWD: alive with disease, NED: no evidence of disease.

Discussion

Teratomas constitute approximately 0.5% of all intracranial neoplasms. The expected 10-year survival rates of patients with mature and immature teratomas are more than 90% and approximately 70%, respectively. However, the 5-year survival rate for patients with teratomas containing a malignant component is less than 50%.

Intracranial growing teratoma syndrome is very rare, with only four cases associated with intracranial NGGCT reported previously (Table 1). Repeat surgery and adjuvant therapy are now widely employed in the treatment of intracranial NGGCT. Therapeutic strategies must consider the possibility of growing teratoma syndrome in patients exhibiting rapid posttherapy tumor growth to lower the risk of debilitating or fatal treatment failure. This is especially important in patients with large malignant NGGCT.

References

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