Malignant Transformation of Craniopharyngioma Associated With Moyamoya Syndrome
—Case Report—

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Abstract

A 32-year-old man presented with malignant craniopharyngioma associated with moyamoya syndrome manifesting as right visual disturbance. Magnetic resonance (MR) imaging revealed a parasellar mass lesion diagnosed as adamantinomatous craniopharyngioma. He underwent three surgical procedures and repeated courses of radiotherapy, and was able to resume his daily life. MR imaging demonstrated tumor regrowth and bilateral occlusions of the internal carotid arteries (ICAs) with basal moyamoya phenomenon, which might have been induced by irradiation and/or tumor compression, 10 years after the initial manifestations. Sufficient debulking was safely achieved via the transsphenoidal route and histological examination revealed squamous cell carcinoma, indicating malignant transformation of craniopharyngioma. The tumor relapsed after only one month, so transsphenoidal tumor debulking was tried again. However, the postoperative course was unfavorable because of intraoperative bleeding from the right ICA. Malignant transformation of craniopharyngioma may be included in moyamoya syndrome. The treatment strategy should be carefully considered in such a complicated situation.

Key words: craniopharyngioma, malignant transformation, moyamoya syndrome, surgical complication, transsphenoidal surgery

Introduction

Craniopharyngioma is a benign tumor that accounts for approximately 3–3.5% of all intracranial tumors. Craniopharyngioma is derived from the remnant of Rathke’s pouch and may arise within the sphenoid bone, the sella, or suprasellar region. The tumor often behaves in a malignant fashion due to local growth and infiltration of adjacent tissue, so the 5-year survival rate is about 80%. Almost all craniopharyngiomas have benign features, and histologically malignant craniopharyngiomas are extremely rare.

Moyamoya disease is an idiopathic disease entity characterized by progressive intracranial occlusion of the anterior circulation followed by the appearance of an abnormal collateral vascular network around the circle of Willis. Moyamoya vessels may also arise in patients with predisposed disorders such as parasellar tumors and cranial irradiation, which is known as moyamoya syndrome, quasi moyamoya disease, akin moyamoya disease, and moyamoya-like vasculopathy.

This report presents a case of malignant craniopharyngioma associated with moyamoya syndrome.

Case Report

A 32-year-old man presented with complaints of right visual disturbance. He was 160 cm in height, pale, edematous, and had no pubic hair. A diagnosis of hypothyroidism and hypogonadism was established. Magnetic resonance (MR) imaging revealed a mass lesion extending from the sella turcica to the bilateral cavernous sinuses and the suprasellar region. Carotid angiography showed occlusion of the right internal carotid artery (ICA) and cross flow from the left ICA (data not shown). Right frontal temporal open craniotomy and endoscopic transnasal biopsy were performed, but no adequate specimen could not be obtained because the tumor was bony, hard, and bled easily. Craniopharyngioma was highly suspected so the surgical procedure was followed by gamma knife radiosurgery (marginal dose 11 Gy, maximum dose 22 Gy).

His symptoms remained stable until he complained of loss of vision. MR imaging showed regrowth of the tumor 5 years after the first clinical manifestation (Fig. 1A, B).
Carotid angiography demonstrated bilateral ICA occlusions just distal to the opthalmic arteries and the development of bilateral basal moyamoya vessels (Fig. 2). Transsphenoidal biopsy was performed. The tumor was bony hard and prone to bleed. Histological examination revealed an odontogenic component (calcification similar to enamel matrix) and keratinization, but no malignant cells (Fig. 3A–C). These findings were consistent with the first histopathological investigation (data not shown). Therefore, the diagnosis was regrowth of adamantinomatous craniopharyngioma because of the similarity to odontogenic fibroma and adamantinoma. Conventional fractionated radiotherapy (50 Gy in 25 fractions) was delivered, and the tumor shrank markedly (Fig. 1C, D). He was able to resume his normal activities.

His left visual acuity was decreased 5 years after the second procedure. MR imaging again showed growth of the tumor (Fig. 4A, B). The transsphenoidal approach to the parasellar tumor was performed with an operating microscope, navigation system, and endoscope. The lesion was partially removed and his symptoms improved somewhat.
Table 1 Summary of the reported cases of malignant craniopharyngioma

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Sex</th>
<th>Age of OS (yrs)</th>
<th>Age of TF (yrs)</th>
<th>Surgeries</th>
<th>Histology (Precursor/TF)</th>
<th>Irradiation</th>
<th>Chemotherapy</th>
<th>Prognoses (Period to death and/or postoperative course)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akachi et al. (1987)</td>
<td>F</td>
<td>10</td>
<td>13</td>
<td>subtotal resection</td>
<td>AC/SCC</td>
<td>cobalt 30 Gy, LINAC 36 Gy</td>
<td>NA</td>
<td>8 mos</td>
</tr>
<tr>
<td>Nelson et al. (1988)</td>
<td>F</td>
<td>14</td>
<td>49</td>
<td>subtotal resection</td>
<td>AC/SCC</td>
<td></td>
<td>NA</td>
<td>11 wks (due to upper gastrointestinal bleeding, pneumonia)</td>
</tr>
<tr>
<td>Suzuki et al. (1989)</td>
<td>M</td>
<td>3</td>
<td>11</td>
<td>subtotal resection</td>
<td>AC/SCC</td>
<td>40 Gy plus 30 Gy</td>
<td>local bleomycin</td>
<td>2 mos</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>9</td>
<td>14</td>
<td>subtotal resection</td>
<td>AC/atypical change/SCC with invasion</td>
<td>RT 50 Gy</td>
<td>NA</td>
<td>4 mos (due to respiratory failure)</td>
</tr>
<tr>
<td>Virik et al. (1999)</td>
<td>M</td>
<td>24</td>
<td>34</td>
<td>subtotal resection</td>
<td>AC twice/malignant epithelial tumor</td>
<td>RT 50 Gy, palliative RT</td>
<td>carboplatin and etoposide, CCNU and PCZ</td>
<td>10 mos</td>
</tr>
<tr>
<td>Kristopaitis et al. (2000)</td>
<td>F</td>
<td>27</td>
<td>42</td>
<td>subtotal, craniofacial, endoscopic resection, TSS</td>
<td>AC/SCC</td>
<td>RT 52 Gy, iodine 125 SRS</td>
<td>paclitaxel and carboplatin</td>
<td>continuous growth at 6 mos after the diagnosis</td>
</tr>
<tr>
<td>Plowman et al. (2004)</td>
<td>F</td>
<td>6.5</td>
<td>21</td>
<td>subtotal resection</td>
<td>AC/SCC</td>
<td>RT 50 Gy, SRT 16 Gy</td>
<td>cisplatin and etoposide</td>
<td>tumor relapsed 6 mos after the chemotherapy, patient died abroad</td>
</tr>
<tr>
<td>Yue and Da (2006)</td>
<td>M</td>
<td>17</td>
<td>NA</td>
<td>surgical resection</td>
<td>none/SCC</td>
<td>RT</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Rodriguez et al. (2007)</td>
<td>M</td>
<td>31</td>
<td>NA</td>
<td>subtotal resection</td>
<td>none/odontogenic ghost cell carcinoma</td>
<td>NA</td>
<td>NA</td>
<td>11 days (due to SIADH and multiple organ failure)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>58</td>
<td>62</td>
<td>subtotal resection</td>
<td>AC/SCC</td>
<td>RT</td>
<td>NA</td>
<td>2 mos</td>
</tr>
<tr>
<td>F</td>
<td>14</td>
<td>22</td>
<td>subtotal resection</td>
<td>AC/myoepithelial carcinoma</td>
<td>RT, brachytherapy</td>
<td>NA</td>
<td>1 yr</td>
<td></td>
</tr>
<tr>
<td>Boongird et al. (2008)</td>
<td>F</td>
<td>46</td>
<td>NA</td>
<td>partial removal and emergent removal of tumor and clot</td>
<td>none/SCC</td>
<td></td>
<td>NA</td>
<td>6 wks (due to intratumoral hemorrhage and sepsis)</td>
</tr>
<tr>
<td>Present case</td>
<td>M</td>
<td>32</td>
<td>42</td>
<td>open biopsy, TSS</td>
<td>AC/SCC</td>
<td>SRS 11 Gy, RT 50 Gy</td>
<td>NA</td>
<td>43 days (due to intraoperative ICA injury)</td>
</tr>
</tbody>
</table>

postoperatively (Fig. 4C, D). Histological examination revealed apparent malignant components such as atypical cell proliferation, mitosis, hypervascularity, and necrosis (Fig. 3D–F). Wet keratin, calcification, and some other characteristic features of craniopharyngiomas were found (Fig. 3C). Immunostaining for p63 protein (Fig. 3H) and cytokeratin markers (data not shown) highlighted malignant squamous cell components. Computed tomography (CT) with contrast medium detected no other extracranial primary lesions, which was consistent with malignant transformation of craniopharyngioma.

Chemotherapy was planned but the tumor markedly relapsed within one month (Fig. 4E, F). A fifth surgery was performed in a semi-emergency situation due to progressive loss of consciousness and uncontrollable hypopituitarism. Tumor debulking was easily performed, but intractable bleeding from the ICA during the transsphenoidal surgery required endovascular trapping of the right ICA. Postoperative CT revealed massive subarachnoid hemorrhage and global ischemia of the brain. The patient died 43 days after the last operation.

Discussion

Malignant transformation of craniopharyngioma is extremely rare, with only 13 reported cases (Table 1).1,3,7,14,17,18,20,23,24 The patients were aged 11 to 62 years (median 31 years), and the male to female ratio is 6:7. Radiotherapy was administered in all but the three patients with de novo tumor, and may have been one of the causes of the subsequent malignant transformation. The oncogenic effects of therapeutic irradiation are thoroughly documented.11 Radiation-induced deoxyribonucleic acid damage may cause carcinogenesis but the precise mechanism is not fully understood. Overexpression of p53 is observed in malignant craniopharyngioma.7,17 p53 immunohistochemical overexpression does not always indicate mutation of p53, but mutation of p53 may have important effects, such as loss of cell cycle control, genomic instability, and neoplastic growth, involved in carcinogenesis. This immunohistochemical finding may be an effective surrogate marker of malignant transformation.3,7,17,18 Positive immunostaining for p63, a homologue of p53 protein, was also observed in the present case, although this issue remains to be elucidated.

De novo cases of malignant craniopharyngioma have been reported from three different institutions.3,18,24 Such tumors should possibly be considered as a World Health Organization grade 3 tumor, a new variant of malignant craniopharyngioma,3,10 although whether the tumors are derived from the remnant of Rathke’s pouch is debatable. De novo tumor is histologically similar to odontogenic tumors, so that the tumor is an odontogenic ghost cell carcinoma.18 Other de novo tumors contain components of adamantinomatous craniopharyngioma.3,24 The current case presented similar diagnostic problems. No adequate specimens could be obtained for definitive diagnosis before malignant transformation because of the hardness of the tumor and the difficulty in hemostasis. The final diagnosis was malignant craniopharyngioma based on the adamantinomatous craniopharyngioma component of the first three biopsy specimens, and the adamantinomatous craniopharyngioma components in the fourth and last specimens (Fig. 3).

Evidence-based adjuvant therapy is difficult to establish in such a rare type of disease. The previous patients were treated with salvage irradiation, stereotactic radiosurgery, stereotactic radiotherapy, and brachytherapy, but the effects on malignant craniopharyngiomas are uncertain.1,7,14,17,18,20 Therefore, we hesitated to perform a third irradiation in the present case. Several chemotherapy regimens were reported as effective, but all patients either died or experienced tumor recurrence.7,17,23 Therefore, the prognosis is unknown, but is thought to be extremely poor.

The poor outcome in the present case may have been related to the moyamoya vessel formation. Radiation is known to induce vascular injuries such as endothelial damage, degeneration of internal elastic tissue, and degeneration of vascular wall, and moyamoya syndrome is a potential complication after irradiation.2,5,12,16 Tumor compression could also cause ICA occlusion, so moyamoya syndrome may occur in patients with brain tumors including craniopharyngioma.8,9,13,19,22 These conditions could explain the pathogenesis of moyamoya vessel formation in the current case.

In general, surgical approaches including pterional craniotomy may be strictly limited by the fragile moyamoya vessels and transdural anastomosis.9,13,22 An interhemispheric approach and radical resection with revascularization may be another option, but transsphenoidal surgery is highly recommended.6 A transsphenoidal approach was applied in the current case with all available surgical instruments, and safely achieved tumor debulking in the fourth surgery. Fragile perforators might have been torn from the right ICA causing intraoperative bleeding. Moyamoya vessels might contribute to bleeding, although the true cause cannot be determined because the family did not provide consent for an autopsy.

Malignant transformation of craniopharyngioma may be involved in moyamoya syndrome. The treatment strategy should be carefully contemplated in such a complicated situation.

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References

Malignant Craniopharyngioma With Moyamoya Phenomenon

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2) Ballonoff A, Kavanagh B: Complications of cranial irradiation, in Basow DS (ed): UpToDate ver 17.3. Waltham, Mass, UpToDate, 2009


