Primary Germinoma in the Medulla Oblongata
—Case Report—

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Abstract

A 27-year-old woman presented with a case of primary medulla oblongata germinoma manifesting as sleep apnea, aspiration pneumonia, and left hemiparesis. Magnetic resonance (MR) imaging revealed a dorsal mass in the medulla oblongata with heterogeneous enhancement by gadolinium (Gd). Emergent biopsy and foramen magnum decompression with C1 laminectomy were performed because of rapid worsening of her symptoms. The histological diagnosis was germinoma. Subsequently she received chemoradiation therapy with subsequent amelioration of her neurological deficits and disappearance of enhancement on MR imaging with Gd. Primary medulla oblongata germinoma is rare and difficult to diagnose preoperatively. However, correct diagnosis and subsequent adequate chemoradiation therapy is possible by understanding the common characteristics of the disease. Germinoma should be included in the differential diagnosis of midline medullary lesion in young patients, and biopsy should be considered.

Key words: β-human chorionic gonadotropin, foramen magnum decompression, germ cell tumor, medulla oblongata, sleep apnea

Introduction

Astrocytoma, ependymoma, hemangioblastoma, and cavernous angioma are common intra-axial tumors in the medulla oblongata.3) Germ cell tumor, teratoma, and germinoma have also been reported in the medulla oblongata,10) but not choriocarcinoma, embryonal carcinoma, or yolk sac tumor. Primary germinoma in the medulla oblongata is rare with only 9 cases reported.1,2,7–9,12–14) We describe a case of medulla oblongata germinoma manifesting as lower cranial nerve symptoms, dyspnea, and limb palsy.

Case Report

A 27-year-old woman initially presented with progression of left hemiparesis for over 1 year. Subsequently she suffered occasional episodes of high fever for 6 months. She was admitted to a nearby hospital for progressive dyspnea with hematemesis and high fever in January 2009. Laboratory data revealed possible infection, autoimmune abnormality, and hypopituitarism [white blood cell 16,000/μl [neutrophil 85%], red blood cell 450 × 10^6/μl, platelet 43 × 10^9/μl, C-reactive protein 3.2 mg/dl, immunoglobulin G 2,020 mg/dl, immunoglobulin E 4470 mg/dl, cardiolipin antibody +, growth hormone 0.1 ng/ml, thyroid-stimulating hormone 0.2 μU/ml, prolactin 33 ng/ml]. After hospital admission, dyspnea worsened rapidly. Both PO2 and PCO2 were about 60 mmHg in the daytime. Sleep apnea was particularly noticeable with low oxygen saturation. An assistor with biphasic positive airway pressure was used to support her breathing.

She was introduced to our department 4 days after admission. Neurological examination identified limb palsy dominant on the left (hand grip, right: 18 kg, left: 6 kg), numbness of the left limbs, direction-consistent nystagmus, lower cranial nerve palsy, and cerebellar ataxia. Magnetic resonance (MR) imaging revealed a diffusely infiltrative mass lesion in the dorsal medulla oblongata appearing as isointensity on T1-weighted images, slightly high intensity on diffusion-weighted images, and high intensity on T2-weighted and fluid-attenuated inversion recovery images (Fig. 1C, D). T1-weighted images with gadolinium (Gd) demonstrated heterogeneous enhancement of the mass lesion (Fig. 1E, G). Computed tomography (CT) revealed a slightly high density mass with mild enhancement (Fig. 1A, B). No supratentorial lesion or hydrocephalus was present. Cerebral angiography revealed no tumor staining with mild deviation of the left posterior inferior cerebellar artery. The preoperative differential diagnosis included astrocytoma, ependymoma, and medulloblastoma.

Rapid exacerbation of her symptoms required emergent surgical decompression. Midline suboccipital craniec-
Fig. 1  Neuroradiological images demonstrating the characteristics of germinoma. A, B: Computed tomography (CT) scan without contrast medium (A) revealing a slightly high density lesion and CT scan with contrast medium (B) demonstrating mild enhancement. C–H: Magnetic resonance images demonstrating swelling of the medulla oblongata and the mass lesion located at the dorsal medulla oblongata appearing as isointensity on T1-weighted (C) and high intensity on T2-weighted images (D), with heterogeneous enhancement on T1-weighted images with gadolinium (E, G), but no enhancement at 11 months after discharge (F, H).

Fig. 2 Intraoperative photos (A, B) and photomicrographs (C, D) revealing typical germinoma. A: Glossy grayish-yellow tumor (arrowhead) was sited below the cerebellar tonsils. B: The tumor was biopsied without severe bleeding (arrowhead). C: Hematoxylin and eosin staining demonstrating the typical ‘two cell pattern’ with relatively large tumor cells and small lymphocytes. ×100. D: Immunostaining revealing strong immunoreactivity to c-kit, the receptor of stem cell factor. ×100.

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tomy with C1 laminectomy and partial removal of the tumor were performed at 1 week after admission. Before surgery, cardiovascular specialists implanted a temporary pacing device. Functions of the brain stem and lower cranial nerves were monitored by somatosensory evoked potentials and the Nerve Integrity Monitor (NIM®) system (Medtronic, Inc., Minneapolis, Minnesota, USA) during the operation. The glossy grayish-yellow mass was found on the surface of the medulla oblongata below the cerebellar tonsils (Fig. 2A). After opening of the cerebellomedullary cistern for drainage of cerebrospinal fluid (CSF), the mass was biopsied (Fig. 2B). Intraoperative frozen specimen examination demonstrated the two cell pattern with relatively large tumor cells and small lymphocytes, typical of germinoma (Fig. 2C). Finally, decompressive dural plasty was performed using Gore-Tex® sheet (WL Gore & Associates, Inc., Newark, Delaware, USA). After the operation, her symptoms were slightly ameliorated. Immunohistochemical investigations revealed that the lesion was pure germinoma with strongly positive staining for c-kit (Fig. 2D), partially positive staining for cytokeratin, and negative staining for leukocyte common antigen.

Subsequently, ICE chemotherapy with ifosfamide, cisplatin, and etoposide was started. Additional laboratory data revealed α-fetoprotein level of 2.8 ng/ml and β-human chorionic gonadotropin (β-HCG) level of 8.2 IU/l. We decided that this tumor should be aggressively treated because of the atypical location, progressive deterioration of symptoms, and high level of β-HCG. Hence, we planned to perform 3 courses of ICE therapy with subsequent radiotherapy and 1 additional course of ICE therapy. After the initial ICE therapy, remarkable shrinkage of the enhanced tumor was confirmed by MR imaging with Gd. Af-
mild sleep apnea and left hand weakness (hand grip: 21 kg, left: 13 kg). She was carefully followed up without recurrence for 11 months (Fig. 1F, H).

**Discussion**

Medullary astrocytoma or ependymoma were the most probable preoperative diagnoses in the present case of primary medullary germinoma. With the rapid exacerbation of her symptoms, surgical intervention was performed with subsequent histological diagnosis of germinoma. Her postoperative course was good with chemoradiation therapy. Initially we considered that this case might be rare and difficult to be diagnose preoperatively. Preoperative differential diagnosis between germinoma and glioma is quite difficult. However, this case was clearly medullary germinoma, so we can include germinoma in the preoperative differential diagnosis.

The 9 previous cases of primary medullary germinoma and the present case are summarized in Table 1. The 5 men and 5 women aged 12 to 33 years (mean 21.5 years) included 7 cases in Japan. Lower cranial nerves were usually affected with disturbances of cerebellar function and breathing. Neuroradiologically, all germinomas appeared as high intensity on T2-weighted MR imaging with enhancement on T1-weighted MR imaging with gadolinium; CSF, or immunohistochemically in 3 patients, who had antibodies on T1-weighted MR imaging.4) High intensity of germ cell tumors appear as mixed low and intermediate intensity might depend on the cell density. Expression of β-HCG Therapy Outcome

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Author (Year)</th>
<th>Age (yrs), Sex</th>
<th>Affected nerves and symptoms</th>
<th>Neuroradiological evaluations</th>
<th>Expression of β-HCG</th>
<th>Therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pounyvarin et al. (1991)</td>
<td>17, M</td>
<td>IX, X, intermittent apnea</td>
<td>pCT: calcified mass</td>
<td>N/A</td>
<td>PR + RT</td>
<td>death</td>
</tr>
<tr>
<td>2*</td>
<td>Hashimoto et al. (1992)</td>
<td>19, M</td>
<td>IX, X, sleep apnea</td>
<td>pCT: iso, eCT, enhanced, T1: low, Gd: enhanced</td>
<td>(−) in serum</td>
<td>PR + RT³</td>
<td>no rec. for 2 mos</td>
</tr>
<tr>
<td>3</td>
<td>Sugiyama et al. (1994)</td>
<td>32, F</td>
<td>X, numbness of limbs, ataxia</td>
<td>eCT: enhanced</td>
<td>(+) with STGC in IH</td>
<td>PR + RT²</td>
<td>no rec. for 9 yrs</td>
</tr>
<tr>
<td>4</td>
<td>Nakajima et al. (2000)</td>
<td>18, F</td>
<td>hiccups</td>
<td>Gd: enhanced</td>
<td>(−) in serum</td>
<td>PR + CT² + RS</td>
<td>no rec. for 8 mos</td>
</tr>
<tr>
<td>5</td>
<td>Yoshida et al. (2003)</td>
<td>33, M</td>
<td>V, VI, VII, VIII, ataxia</td>
<td>eCT: enhanced, T1: iso, T2: high, Gd: enhanced</td>
<td>(−) in serum, CSF, IH</td>
<td>PR + CT²</td>
<td>no rec. for 7 mos</td>
</tr>
<tr>
<td>6</td>
<td>Yen et al. (2003)</td>
<td>16, F</td>
<td>headache, double vision, ataxia</td>
<td>T1: iso cystic lesion, T2: high, Gd: enhanced</td>
<td>(−) in IH</td>
<td>PR + RT¹</td>
<td>no rec. for 7 yrs</td>
</tr>
<tr>
<td>7</td>
<td>Yang et al. (2009)</td>
<td>12, M</td>
<td>IX, X, XII, lethargy, appetite loss</td>
<td>Gd: enhanced cystic lesion</td>
<td>(+) in CSF</td>
<td>PR + CT¹ + RT</td>
<td>no rec.</td>
</tr>
<tr>
<td>8</td>
<td>Akiyama et al. (2009)</td>
<td>30, F</td>
<td>VI, IX, X, XII</td>
<td>pCT: slightly high, T1: low-iso, T2: high, Gd: enhanced</td>
<td>N/A</td>
<td>PR + CT + RT (focal)</td>
<td>no rec. for 1 yr</td>
</tr>
<tr>
<td>9</td>
<td>Present case</td>
<td>24, M</td>
<td>headache, nausea (hydrocephalus)</td>
<td>pCT: slightly high, T1: low, T2: high, Gd: enhanced</td>
<td>N/A</td>
<td>PR + CT + RT (focal)</td>
<td>no rec.</td>
</tr>
<tr>
<td>10</td>
<td>Present case</td>
<td>27, F</td>
<td>VIII, IX, X, XII, ataxia, sleep apnea, numbness of limbs, weakness</td>
<td>pCT: iso, eCT: enhanced, T1: low, T2: high, FLAIR: high, DWI: slightly high, Gd: enhanced</td>
<td>(−) in serum</td>
<td>biopsy + CT³ + RT³</td>
<td>no rec. for 6 mos</td>
</tr>
</tbody>
</table>

*Klinefelter syndrome. β-HCG: β-human chorionic gonadotropin; CSF: cerebrospinal fluid; CT: chemotherapy; CT*: cisplatin, cyclophosphamide, pegfilgrastim; CT²: carboplatin, etoposide; CT³: ifosfamide, cisplatin, etoposide; DWI: diffusion-weighted image; eCT: enhanced computed tomography; F: female; FLAIR: fluid-attenuated inversion recovery image; Gd: T1-weighted image with gadolinium; IH: immunohistochemical staining; M: male; N/A: non-applicable; pCT: plain computed tomography; PR: partial resection; rec.: recurrence; RS: radiosurgery (gamma knife); RT: radiotherapy; RT¹: total 50 Gy to the posterior fossa (30 Gy to the craniospinal axis); RT²: posterior fossa 44 Gy, spinal cord 20 Gy; RT³: brain 30 Gy, focal 30 Gy, spinal cord 35 Gy, STGC: syncytiotrophoblastic giant cells; T1: T₁-weighted image; T2: T₂-weighted image.
was short in some cases including our case. One of the important lessons from previous reports might be the fair prognosis of medullary germinoma, if the appropriate therapy is chosen. We should think of the possibility of germinoma in cases of midline medullary lesion in young patients, although the lesion looks like glioma, for which biopsy is sometimes omitted because of the advancement of diagnostic technology and the avoidance of the side effects of surgery. Additionally, the wide exposure and biopsy of an adequate amount of the tumor might lead to the correct histological diagnosis with subsequent determination of the optimum treatment protocol. Therefore, aggressive biopsy for correct diagnosis should be considered in cases of midline lesion of the brain stem.

References


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