Pineal Malignant B-cell Lymphoma with Lower Cranial Nerve Involvement

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Abstract

A 62-year-old man was admitted to our hospital complaining of dysphagia and hoarseness that had persisted for five days. A neurological examination indicated bulbar palsy. Brain magnetic resonance imaging showed thickening of cranial nerves IX, X and XI, in addition to pineal body enlargement with diffuse contrast enhancement. A tumor biopsy overriding the spinal root of the right XIth cranial nerve was performed. The histologic analysis confirmed a diagnosis of diffuse large B-cell lymphoma. Malignant lymphoma should be considered in the differential diagnosis of pineal region tumors. Furthermore, obtaining histological confirmation is crucial for making proper management decisions.

Key words: malignant lymphoma, pineal gland, bulbar palsy

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Introduction

Approximately 1-2% of patients with non-Hodgkin’s lymphoma (NHL) present with primary central nervous system (CNS) disease at the initial diagnosis (1). Among them, the occurrence of malignant lymphoma in the pineal region is very rare, as only a few such cases have been reported (2-7). We herein report a case of pineal region malignant lymphoma with lower cranial nerve involvement and review the previous literature.

Case Report

A 62-year-old man was admitted to our hospital complaining of dysphagia and hoarseness that had persisted for five days. Most pronounced was a difficulty in swallowing liquids. He denied previously having similar episodes, fever, night sweats, weight loss, dizziness, altered vision, weakness or numbness. His past medical history was unremarkable, except for hypertension. His father had died of malignant lymphoma at 81 years of age. On a physical examination, there was no lymphadenopathy or abdominal organomegaly.

A neurological examination revealed a positive curtain sign (uvula deviated to the left side), hoarseness and a decreased gag reflex. The remainder of the neurological exam, including assessments of other cranial nerves, the motor and sensory systems, the cerebellar function and gait, was normal. The patient was admitted to the neurology department for a further investigation of his symptoms. The results of laboratory tests were as follows: white blood cell count=5.8×10^3/μL (4.8-8.5×10^3/μL); red blood cell count=4.53×10^6/μL (3.70-5.00×10^6/μL); hemoglobin=14.5 g/dL (12.0-16.0 g/dL); platelet count=14.1×10^4/μL (13-37×10^4/μL); lactate dehydrogenase (LDH)=175 IU/L (120-240 IU/L); angiotensin-converting enzyme (ACE)=6.0 IU/L (8.3-21.4 IU/L); cerebrospinal fluid (CSF) cell count=120/mm^3 (lymphocytes: 99%, neutrophils: 1%) (<5/mm^3); CSF protein=54 mg/dL (15-45 mg/dL); and CSF immunoglobulin G index=0.91. Blood and CSF cultures for bacteria and acid-fast bacilli were negative. The levels of serum beta-D-glucan as well as serum and CSF cryptococcal antigens were within the normal limits. HIV antibodies were negative. Fiber optic laryngoscopy showed a poor soft palate and vocal cord move-
ment on the right side. Brain magnetic resonance imaging (MRI) revealed thickening of cranial nerves IX, X and XI, in addition to pineal body swelling with diffuse contrast enhancement (Fig. 1). Although CSF cytology demonstrated few large atypical lymphocytes, a flow cytometric analysis of the CSF was non-diagnostic. In order to obtain a definitive diagnosis, we attempted to perform a biopsy of the cranial nerve lesion. We observed a whitish and thickened arachnoid membrane via posterior fossa craniotomy. Upon incision, soft, pinkish-white tumorous lesions diffusely infiltrated the subarachnoid space and formed a mass lesion overriding the spinal root of the right XIth cranial nerve (Fig. 2). The surface of the lesions was gently removed with a ring curette. After the procedure, the patient showed no symptoms suggestive of accessory nerve dysfunction. A histologic analysis of the mass revealed proliferation of large atypical lymphocytes with prominent nucleoli (Fig. 3). These atypical cells were positive for CD5, CD20, CD79a and bcl-2 and negative for CD3, CD10 and cyclin D1. The rate of Ki-67 positivity was over 95%. Based on these results, a diagnosis of diffuse large B-cell lymphoma was made. A whole-body computed tomography scan and bone marrow biopsy were negative for other sites of disease. The patient was initially treated with intravenous high-dose methotrexate, cytarabine and prednisolone. Intrathecal methotrexate and cytarabine were subsequently added to the treatment regimen. After four cycles of chemotherapy, the cranial nerve thickening and pineal gland enlargement on MRI improved, followed by a gradual recovery from the dysphagia. The patient was transferred to another hospital where he successfully received autologous hematopoietic stem cell transplantation.

**Discussion**

NHL may involve the CNS with either a primary tumor or hematogenously with systemic lymphoma. Only 1-2% of patients with NHL present with primary CNS disease at the initial diagnosis (1). Furthermore, the occurrence of malignant lymphoma in the pineal region is very rare, and there are few reports of pineal gland lymphoma (2-7).

Table compares the clinical, radiological and histological characteristics of our case with those of previous cases found in the literature that were described in detail. Com-
pared to the previous reports, our case was characteristic, with the absence of headaches and hydrocephalus and the presence of lower cranial nerve signs on the initial presentation. Furthermore, meningeal dissemination was confirmed intraoperatively. The patient in Case 6 presented with a similar clinical course involving cranial nerve dysfunction (VIth cranial nerve), and a diagnostic endoscopic biopsy revealed disseminated lesions along the third ventricle. The patient in Case 4 also demonstrated dissemination along the ventricular wall, as well as subarachnoid spread at autopsy. In contrast, the patient in Case 1 showed involvement in the suprasellar region and dorsal medulla, which resulted in hypopituitarism. Case 5 included diffuse leptomeningeal involvement, which produced meningitis-like symptoms. Meanwhile, the patient in Case 2 developed a mass lesion in the cauda equina 10 months after radiotherapy of a pineal tumor.

According to these data, it is likely that pineal malignant lymphoma is able to easily disseminate through the CSF and may present with neurological symptoms originating at sites distant from the pineal gland. Because less than 20% of cases of primary central nervous system lymphoma (PCNSL) are associated with meningeal dissemination, the close proximity of the pineal gland to the third ventricle may be responsible for the high rate of meningeal dissemination. In fact, other types of pineal region tumors, such as germ cell tumors, are known to spread locally and metastasize to the CSF (8). As observed in Case 1, germ cell tumors and malignant lymphoma may be indistinguishable clinically and radiologically (9). Obtaining a histologic diagnosis is thus very important for making appropriate management decisions.

In the present case, MRI revealed multiple cranial nerve abnormalities. There are previous reports of cranial nerve neurolymphomatosis in which the patient presented with MRI abnormalities that are quite similar to those observed

Figure 2. Biopsy of the tumor. Via posterior fossa craniotomy, a whitish and thickened arachnoid membrane was observed (A). Upon incision, soft, pinkish-white tumorous lesions diffusely infiltrated the subarachnoid space and formed a mass lesion overriding the spinal root of the right XIth cranial nerve (B). The surface of the lesions was gently removed with a ring curette (C).

Figure 3. Histologic analysis. Hematoxylin and Eosin staining (A) and CD20 immunohistochemistry (IHC) (B). The proliferation of large atypical lymphocytes with prominent nucleoli was observed (A). IHC was positive for various B cell-lineage markers, including CD20 (B).
in the present case (10-12). Although there is ongoing controversy regarding the use of cranial nerve biopsies due to the high risk of adverse events (13), the intraoperative findings and results of the histopathological analysis confirmed the presence of meningeal dissemination in our patient.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

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References


Table. Summary of Clinical, Radiological and Histological Characteristics of Pineal Gland Lymphoma

<table>
<thead>
<tr>
<th>Case</th>
<th>Age / sex</th>
<th>Clinical feature</th>
<th>Peripheral nerve involvement</th>
<th>MRI (CT)</th>
<th>MD</th>
<th>Histology</th>
</tr>
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<tbody>
<tr>
<td>Case 1 1</td>
<td>21/M</td>
<td>Headache, emesis, hypopituitarism, Parinaud’s sign</td>
<td>None</td>
<td>Hydrocephalus Gd-enhancement</td>
<td>+ (?)</td>
<td>Malignant T-cell lymphoma</td>
</tr>
<tr>
<td>(2)</td>
<td></td>
<td></td>
<td></td>
<td>Dorsal medulla and suprasellar lesion</td>
<td></td>
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<tr>
<td>Case 2 3</td>
<td>15/M</td>
<td>Headache, gait disturbance, Parinaud’s sign</td>
<td>Cauda equina</td>
<td>Hydrocephalus Gd-enhancement</td>
<td>+</td>
<td>Immunoblastic lymphoma</td>
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<td></td>
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<tr>
<td>Case 3 4</td>
<td>52/M</td>
<td>Headache, obtundation</td>
<td>ND</td>
<td>No hydrocephalus Homogenous enhancement on CT</td>
<td>ND</td>
<td>Lymphoma (no detail)</td>
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<tr>
<td>Case 4 5</td>
<td>72/F</td>
<td>Confusion, visual and gait disturbance</td>
<td>None</td>
<td>Gd-enhancement Brain parenchyma and subependymal lesion</td>
<td>+</td>
<td>High grade, large B-cell lymphoma</td>
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<td>Case 5 6</td>
<td>4/M</td>
<td>Seizure, fever, headache, emesis, neck stiffness, altered mental status</td>
<td>None</td>
<td>No hydrocephalus Gd-enhancement Bilateral frontal and leptomeningeal spread</td>
<td>+</td>
<td>ALK-1 positive ALCL</td>
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<td>Case 6 7</td>
<td>31/M</td>
<td>Diplopia, headache, nausea</td>
<td>Cranial nerve VI</td>
<td>Hydrocephalus Cystic mass with Gd-enhanced nodule</td>
<td>+</td>
<td>Malignant B-cell lymphoma</td>
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<tr>
<td>Our case 8</td>
<td>62/M</td>
<td>Dysphagia</td>
<td>Cranial nerve IX, X, and XI</td>
<td>No hydrocephalus Gd-enhancement</td>
<td>+</td>
<td>Diffuse large B-cell lymphoma</td>
</tr>
</tbody>
</table>

MD: meningeal dissemination, Gd: gadolinium, ALCL: anaplastic large cell lymphoma, ND: no description