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Case Report

Primary Central Nervous System Lymphoma of the Cerebellopontine Angle That Initially Occurred as Neurolymphomatosis of the Acoustic Nerve

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We report a rare case of a primary central nervous system lymphoma (PCNSL) of the cerebellopontine angle (CPA) with infiltration into the pyramidal tract that initially presented as neurolymphomatosis (NL) of the acoustic nerve. A 60-year-old male suffered from right-side deafness and was referred to an otolaryngologist. Magnetic resonance imaging (MRI) showed fusiform enlargement of the right acoustic nerve with a hyperintense signal on a T_2-weighted image (T_2WI) and with gadolinium (Gd) enhancement, without an evidence of parenchymal CNS involvement. Although he was treated with steroids, his symptoms deteriorated. MRI was performed again and showed the mass lesion at the right CPA with enhancement. In addition to this, a lesion with slightly high intensity on a T_2WI with Gd enhancement was observed along the right pyramidal tract. Despite steroid pulse therapy, the lesion rapidly progressed. We performed a tumor biopsy, and the histological diagnosis was diffuse large B-cell lymphoma. Pelvic, abdominal, and chest computed tomography scans, gallium cintigraphy, and bone marrow biopsy failed to detect any other evidence of lymphomatous involvement of other organs. We attempted high-dose methotrexate therapy (3.5 g/m^2). We found a discrepancy in the therapeutic effect between the CPA lesion and the infiltrated lesion along the pyramidal tract; the lesions were chemo-resistant and chemo-sensitive, respectively. After completion of the second courses of chemotherapy, we began radiotherapy (total dose: 36 Gy). Four months after radiotherapy, the CPA tumor completely disappeared. Thirty-three months after the biopsy, he is doing well with a normal daily life and no signs of recurrence.

Keywords: malignant lymphoma, acoustic nerve, neurolymphomatosis, pyramidal tract, cerebellopontine angle

Introduction

Primary central nervous system lymphoma (PCNSL) accounts for 2.2% of all primary central nervous system tumors.[1)] Neurolymphomatosis (NL) is a lymphoma entity that affects cranial and peripheral nerves and roots. NL represents 10% of the primary lymphomas of the nervous system.[2)] NL often presents as a diagnostic challenge, particularly when it involves isolated cranial nerves. The gold standard for diagnosis is a biopsy of the affected nerve with demonstration of malignant lymphocytes in the nerve. However, if the only lesion noted is within a cranial nerve, the decision to perform a biopsy may be difficult because the biopsy may result in permanent neural dysfunction. The correct diagnosis may only be obtained after empiric treatment, because the other disease may also result in radiologic nerve thickening or enhancement. Thus, in cases of primary NL, the diagnosis is often delayed. Some patients with NL may develop parenchymal brain involvement during disease progression.[3)] We have encountered an extremely rare case of PCNLS of the cerebellopontine angle (CPA) region with infiltration into the pyramidal tract that initially presented as NL of the acoustic nerve.

Case Report

A 60-year-old male with diabetes mellitus suffered from right-side deafness and was referred to an otolaryngologist. An audiogram showed sensory neural hearing loss. Facial palsy was not observed. He was medically treated with a diagnosis of sudden deafness, but his symptoms did not improve. Magnetic resonance imaging (MRI) performed 2 weeks after the onset of symptom showed fusiform enlargement of the right acoustic nerve with a hyperintense signal on a T_2-weighted image (T_2WI) and with gadolinium (Gd) enhancement (Fig. 1) without evidence of parenchymal CNS involvement, suggesting mononeuropathy due to an inflammatory disease such as Ramsay Hunt's syndrome. Although he was treated with steroids, his symptoms deteriorated to dysarthria and an unsteady gait. Two months after the onset of symptoms, he was admitted to the Department of Neurology in our hospital for detailed examination. He was alert and had right-side deafness, right hemiparesis, and right side dominant cerebellar ataxia. Ophthalmological examination showed mild bilateral cataract and mild right vitreous clouding suggesting uveitis, which was followed-up by ophthalmologist. Laboratory examination showed no remarkable findings. The cerebrospinal fluid data were within normal ranges except for the increased level of beta-2 microglobulin (3,729 ng/ml: normal range; 440–1,240 ng/ml). MRI was performed again 6 weeks after the initial MRI and showed a

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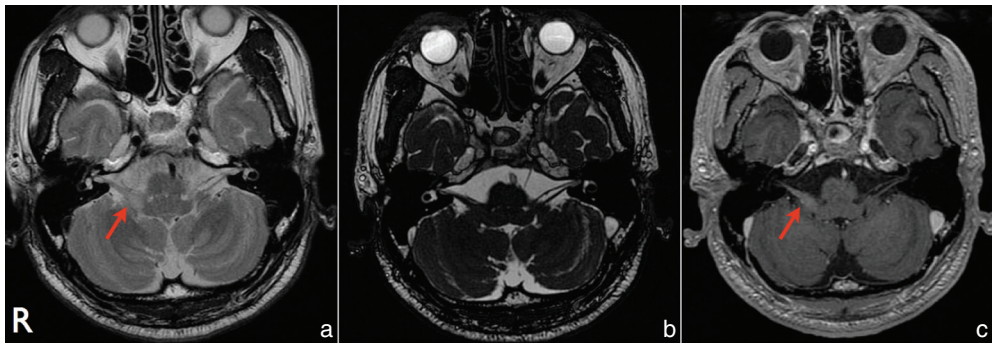

Fig. 1 a: T_2WI showed fusiform enlargement of the right acoustic nerve with a hyperintense signal (arrow). b: Fast imaging employing steady-state acquisition showed no lesion in the right facial nerve. c: Gadolinium-enhanced T_1WI showed enhancement of the enlarged right acoustic nerve (arrow). WI: weighted image.

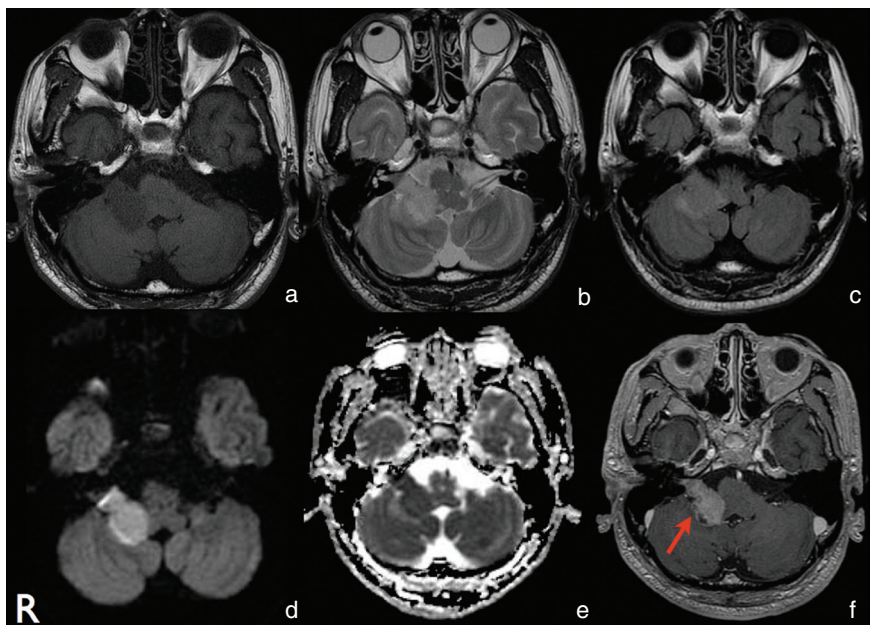

Fig. 2 a: T_1WI, b: T_2WI, c: fluid-attenuated inversion recovery image, d: diffusion-weighted image, e: apparent diffusion coefficient map, and f: Gadolinium-enhanced T_1WI showed the cerebellopontine angle lesion (arrow). WI: weighted image.

mass lesion in the right CPA with enhancement (Fig. 2a–f). Abnormalities of the internal auditory canal were not observed. In addition to the mass lesion, a lesion with slightly high intensity on a T_2WI and fluid attenuation inversion recovery (FLAIR) image with Gd enhancement was observed along with right pyramidal tract spreading to the cerebral peduncle (Fig. 3a–e). Despite steroid pulse therapy, the lesion progressed rapidly. He was referred to our department for a surgical biopsy because of the possibility of a neoplastic lesion. We performed a tumor biopsy through a lateral suboccipital craniotomy. The pathological diagnosis during surgery revealed a malignant lymphoma. Hematoxylin and eosin staining of the surgical specimen showed diffuse infiltration by cohesive sheets of undifferentiated lymphoid cells with hyperchromatic nuclei that are round and occasionally cleaved (Fig. 4a). Most of these cells were positive for L-26 monoclonal B-cell marker (Fig. 4b). The final histological diagnosis was diffuse large B-cell lymphoma (DLBCL). Pelvic, abdominal, and chest computed tomography scans, gallium scintigraphy, and a bone marrow biopsy failed to detect any evidence of lymphomatous involvement of other organs. Antibody to the human immunodeficiency virus type 1 was negative. We attempted high-dose methotrexate (HD-MTX) therapy. Intraveneous MTX (3.5 g/m^2) was administered on a rapid (3-hour) infusion schedule with leucovorin rescue in 2–3 week cycles according to the recommended regimen.[4,5] After completion of one course, MRI performed 1 month after the second MRI showed mild enlargement of the CPA tumor (Fig. 5a–c). In contrast, disappearance of the lesion along the pyramidal tract was seen (Fig. 5d–g). Then we performed a second course of HD-MTX therapy. After completion of two courses, MRI performed 3 weeks after the third MRI showed further enlargement of the CPA tumor (Fig. 6a), deterioration of perifocal edema, and no lesion along the

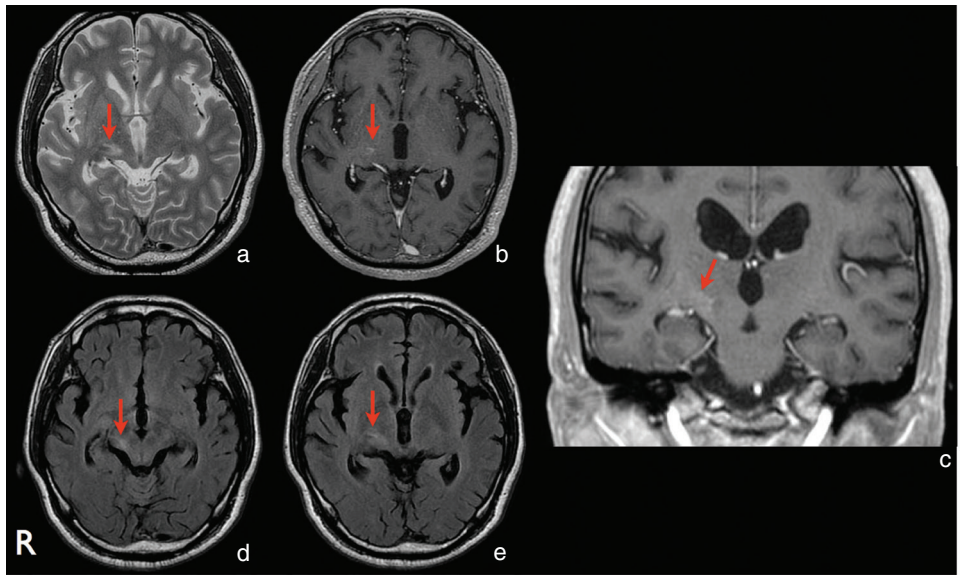

Fig. 3 a: T_2WI showed a lesion with slightly high intensity along the right pyramidal tract. b: Gd-enhanced T_1WI. c: A coronal view of Gd-enhanced T_1WI showed the enhanced lesion along with right pyramidal tract spreading to the cerebral peduncle (arrow). d, e: Fluid-attenuated inversion recovery image showed a lesion with slightly high intensity along the right pyramidal tract (arrow). WI: weighted image, Gd: gadolinium.

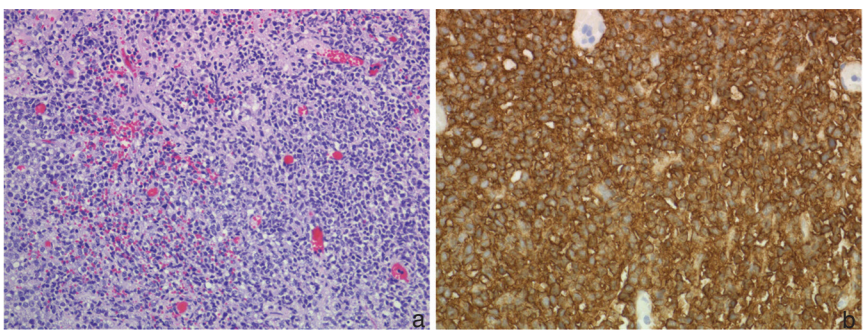

Fig. 4 a: Hematoxylin and eosin staining of the surgical specimen showed sheets of cells, many with vesicular nuclei and prominent nucleoli, and large numbers of mitotic figures (original magnification ×200). b: Most of the cells were positive for L-26 monoclonal B-cell marker, which was consistent with a B-cell type lymphoma (original magnification ×400).

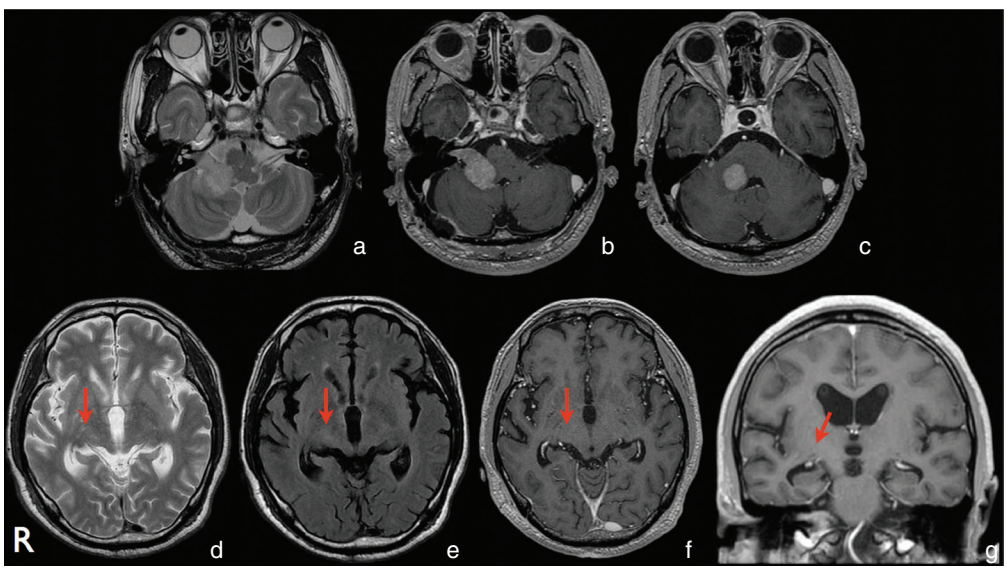

Fig. 5 a: T_2WI. b, c: Gd-enhanced T_1WI showed enlargement of the cerebellopontine angle tumor after chemotherapy. d: T_2WI, e: Fluid-attenuated inversion recovery image, f: Gd-enhanced T_1WI, and g: a coronal view of Gd-enhanced T_1WI showed disappearance of the infiltrated lesion along the pyramidal tract after chemotherapy (arrow). WI: weighted image, Gd: gadolinium.

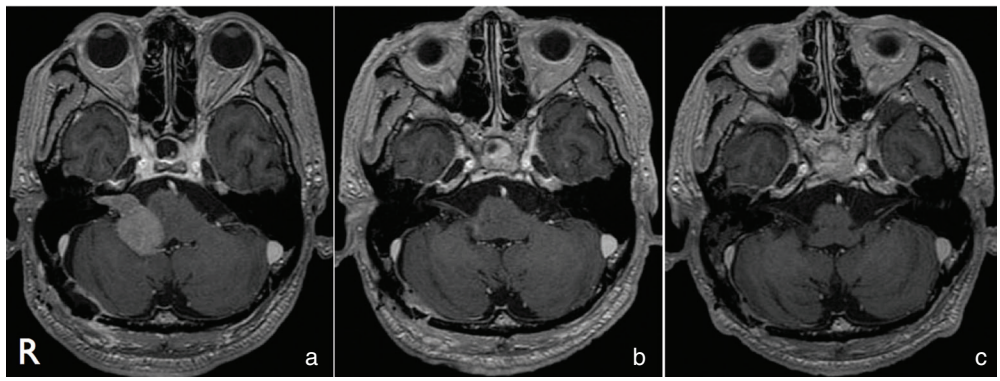

Fig. 6 Serial gadolinium-enhanced T_1-weighted image. a: After two courses of chemotherapy, magnetic resonance imaging showed further enlargement of the cerebellopontine angle tumor. b: One month after radiotherapy, the tumor had remarkably decreased in size. c: Four months after radiotherapy, tumor had completely disappeared.

pyramidal tract. The symptoms also worsened. As the tumor of the CPA seemed to be resistant to HD-MTX therapy, we abandoned the chemotherapy and began total dose of 36 Gy of whole brain radiotherapy, fractionated into 2 Gy/day administered 5 times per week. One month after radiotherapy, the tumor had remarkably decreased in size (Fig. 6b). Four months after radiotherapy, the tumor had completely disappeared (Fig. 6c), and the patient's symptoms had improved. Two years after the biopsy, malignant intraocular lymphoma was diagnosed by ophthalmologist and the intravitreal injection of MTX was performed in another hospital and achieves clinical remission and followed-up carefully. Thirty-three months after the biopsy, the patient is doing well with a normal daily life without cognitive disturbance and no sign of recurrence.

Discussion

PCNLS are rare malignant lesions, constituting 2.2% of all primary central nervous system tumors.[1)] Only 14 cases of PCNLS occupying the CPA have been reported in the literature.[6)] NL is a lymphoma entity that affects cranial and peripheral nerves and roots.[7)] NL represents 10% of primary lymphomas of the nervous system.[2)] Typical manifestations of NL are neuropathies that may affect peripheral or cranial nerves. NL is difficult to diagnose because clinically it mimics nonneoplastic or paraneoplastic neuropathies. In cases of primary NL, the diagnosis is often delayed. When the diagnosis is delayed, the patient may develop parenchymal brain involvement during disease progression.[3)] In almost half of the reported cases, a clinical or histopathologic diagnosis of NL is not established until autopsy.[2)] As with PCNSL, most NL is due to DLBCL when classified by the REAL or WHO systems.[8)] In about 20% of patients with NL, the early disease course is characterized by isolated cranial neuropathy. Only one reported case showed mononeuropathy of the acoustic nerve as the initial presentation.[2)] NL ultimately tends to infiltrate into the parenchyma of the brain. With retrospective consideration, the initial appearance of our case was consistent with NL without brain or meningeal involvement, and later showed apparent progression to a CPA tumor and infiltration into the pyramidal tract. Our case was diagnosed at this stage following a biopsy. We speculate that NL may represent the initial presentation of a more severe and diffuse lymphomatous involvement of the CNS. PCNSL presenting as limited infiltration into the pyramidal tract is extremely rare. Only one case has been reported in which PCNSL presented as infiltration into the pyramidal tract without forming a mass.[9)] The affinity of PCNLS for the pyramidal tract in this case is a particularly unique finding. The site specificity of the lymphoma likely reflects differences in its molecular biology. As in normal lymphoid cells, adhesion receptors contribute to lymphoma aggressiveness and seem to determine the highly tissue-specific dissemination patterns of certain lymphoma subtypes.[10)] We cannot explain the exact mechanisms of the discrepancy in the therapeutic effect between the CPA lesion and the infiltrated lesion along the pyramidal tract. Some variability and heterogeneity may have been present in this lymphomatous involvement in the CNS, and this should be elucidated in the future. Another subtype of PCNSL exists in which rare cases of PCNSL with diffuse invasion without contrast enhancement are seen, a condition termed lymphomatosis cerebri (LC). Our case was different from LC, because the lesion along the pyramidal tract showed enhancement, and the infiltration was localized. Our case was an extremely rare presentation of PCNLS, as we could not find any similar cases in the English literature. To the authors' best knowledge, no reports have described a CPA tumor of the PCNLS that infiltrated into the pyramidal tract and initially occurred as NL of the acoustic nerve. The median overall survival of NL is 10 months from the initial diagnosis, with 12- and 36-month survival proportions of 46% and 24%, respectively.[7)] An aggressive multimodality therapy can prevent neurologic deterioration and is associated with prolonged survival in a subset of patients. A high index of suspicion and familiarity with the clinical manifestations of NL are necessary. Because it is a rare manifestation of hematologic malignancies, diagnosis is often delayed and leads to a fatal condition, as few patients respond to chemotherapy.[11)] Isolated peripheral nerve lymphomas behave aggressively and require radiation therapy combined with chemotherapy.[12)] Of all the diagnostic tools, imaging studies are of the greatest

clinical utility. The improved resolution of current imaging techniques can detect affected neural structures with increased precision. Patients with primary NL may have a more favorable outcome if the diagnosis and treatment are started earlier.

Conclusion

This is the first report describing a CPA tumor of PCNLS that infiltrated into the pyramidal tract and initially occurred as an NL of the acoustic nerve. Early recognition and proper management of this rare neurologic manifestation of lymphoma are necessary for improved outcome.

Conflicts of Interest Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices in the article.

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