

## Case Report

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# Primary Cerebellar Hodgkin's Lymphoma

Authors report a very rare case of primary Hodgkin's lymphoma limited to the cerebellum. A 64-year-old female patient presented with headache, nausea, and vomiting. Magnetic resonance imaging of the brain revealed a nodular enhancing mass in the left cerebellar hemisphere. Tumor was removed totally with retromastoid suboccipital approach. Diagnosis was Hodgkin's lymphoma of mixed cellularity type, consisting of a dense mixed inflammatory infiltrate containing scattered large atypical mononuclear Hodgkin cells and multinucleated Reed-Sternberg cells. Systemic work-up for the Hodgkin's lymphoma was followed with negative result. Postoperative radiation therapy was given and the patient is disease-free at 16 months after the operation.

**KEY WORDS :** Cerebellar tumor · Hodgkin's lymphoma · CNS involvement .

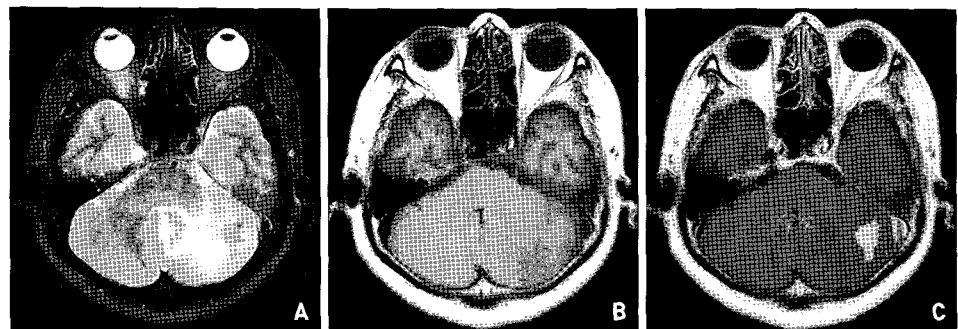
## INTRODUCTION

Hodgkin's lymphoma with central nervous system (CNS) involvement is uncommon, even in the HIV-positive population, and usually appears as a late manifestation in patients who have relapsed with widespread disease<sup>1,5</sup>. Retrospective and prospective cohort studies suggest that CNS involvement occurs in 0.5% of patients with systemic Hodgkin's lymphoma<sup>15,16</sup>. Primary CNS Hodgkin's lymphoma is extremely rare with only 12 cases reported in the literature<sup>3-5,8-12,17,20,22,23</sup>. Tumors have been described as isolated cerebral or cerebellar masses or, less commonly, parenchymal disease with attachment to the dura or bone. We describe a patient with primary cerebellar Hodgkin's lymphoma without systemic involvement.

## CASE REPORT

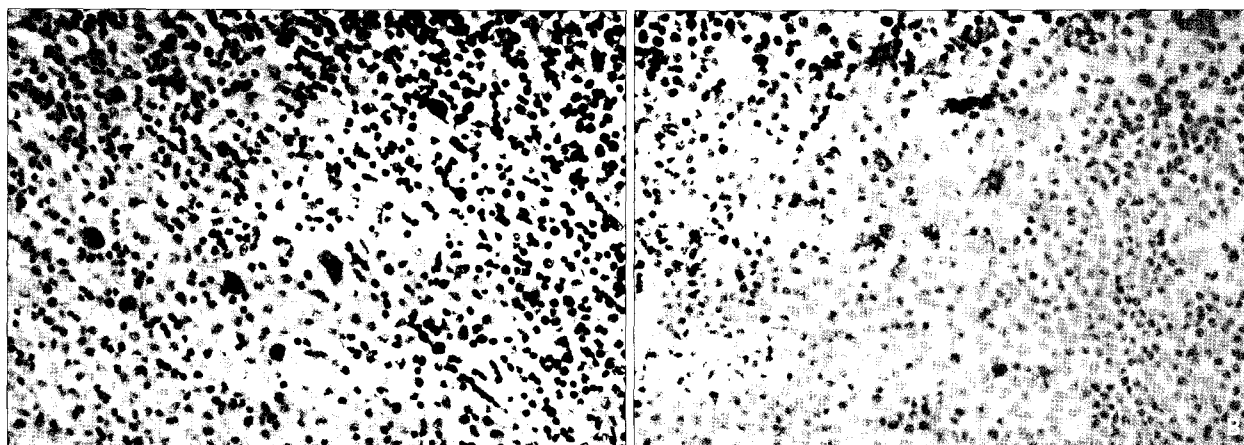
A 64-year-old female patient presented with headache, nausea and vomiting for one month. Functional inquiry was negative for fatigue, weight loss, pruritis, fever, and night sweat. Physical examination revealed no evidence of peripheral lymphadenopathy or hepatosplenomegaly. Past medical history was unremarkable and neurological assessment of cranial nerves, motor and sensory system, and coordination revealed no abnormalities.

Complete blood count, liver function test, and other laboratory findings were within normal limits. Magnetic resonance imaging (MRI) of the brain revealed an ill-defined nodular enhancing mass in the left cerebellar hemisphere, which was not visible on T1-weighted image (Fig. 1). Whole body 18F-FDG PET was performed to evaluate this lesion in detail and to rule out lymphoma or metastasis. The mass was proved to be hypermetabolic, with lesion to background ratio of 4.4, suggesting malignancy. No abnormal lesions were found



**Fig. 1.** Preoperative magnetic resonance images. T2-weighted axial (A), T1-weighted (B) and Gd-enhanced T1-weighted axial (C) images show a contrast enhancing mass with peritumoral edema in the left cerebellar hemisphere.

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**Fig. 2.** Histopathologic findings. Some large atypical mononuclear Hodgkin cells and multinucleated Reed-sternberg cells (arrow) are scattered in dense inflammatory background (A : H&E,  $\times 400$ ). These cells are immunoreactive for CD30 (B : IHC for CD30,  $\times 400$ ).

outside of the brain.

Operation was done by retro-mastoid suboccipital approach. Exposed cerebellar hemisphere appeared normal. Cerebellar cortex was excised, and tumor was verified subcortically, which was a little hard in consistency and relatively well-demarcated. En-bloc removal was done without any difficulty, and surgical specimen was sent for histopathological examination.

The histopathological examination showed a dense mixed inflammatory infiltrate containing scattered large atypical mononuclear Hodgkin cells and multinucleated Reed-Sternberg cells. These cells are immunoreactive for CD30 (Fig. 2). They were negative for CD45, CD20, and CD3. The findings were consistent with Hodgkin's lymphoma, mixed cellularity type.

Subsequent work-up for staging was done. Bone marrow aspiration and biopsy were normal. Lumbar puncture yielded clear CSF characterized by normal white cell count, normal protein and glucose level. The cytospin of CSF was negative for malignant cells. Computed tomography scan of the chest, abdomen and pelvis revealed no significant abnormality.

Postoperatively, the patient received irradiation of 30 Gy to the whole brain with a boost of 6 Gy to the original sites. Chemotherapy was reserved for the tumor recurrence, and the patient was discharged without neurological deficit.

Whole body  $^{18}\text{F}$ -FDG PET scan taken 12 months after operation revealed hypometabolism in the local site and no evidence of abnormalities through the entire body. MRI of the brain taken 15 months after operation did not show the evidence of recurrence (Fig. 3). The patient was followed



**Fig. 3.** Follow-up magnetic resonance images 15 months after operation. T2-weighted axial (A), T1-weighted axial (B) and Gd-enhanced T1 weighted axial (C). Preoperative enhanced mass is removed totally. There is no evidence of local recurrence.

regularly, and enjoy disease-free survival at the 16 months after the operation.

### DISCUSSION

The term "Hodgkin's lymphoma", previously known as Hodgkin's disease, encompasses a group of lymphoid neoplasms that differ from non-Hodgkin's lymphoma (NHL) in several respects. While NHLs frequently occur at extranodal sites and spread in an unpredictable fashion, Hodgkin's lymphoma arises in a single node or chain of nodes and spread first to the anatomically contiguous nodes<sup>7,21</sup>. Lymph nodes, bones, bone marrow, and lungs are the most common concurrent sites of the disease<sup>19</sup>. Most patients present with palpable lymphadenopathy that is non-tender. Approximately one-third of patients present with fever, night sweat, and weight loss<sup>6,21</sup>.

Hodgkin's lymphoma can occasionally present with unusual manifestations. These include pruritis, cutaneous manifestation, alcohol-related pain, nephrotic syndrome, hemolytic anemia, idiopathic thrombocytopenia purpura, CNS involvement, and others<sup>6</sup>. Neurologic manifestations

are very uncommon in Hodgkin's lymphoma. They are mainly due to direct CNS involvement, but can be the expression of a paraneoplastic syndrome or of an infectious complication<sup>14,21</sup>. Direct CNS involvement is rare with an estimated frequency of 0.5%<sup>15</sup>. Sapozink et al.<sup>19</sup> reviewed 2185 patients with Hodgkin's lymphoma and found only 12 cases (0.5%) with intracranial Hodgkin's lymphoma. Akyuz et al.<sup>1</sup> identified only 3 patients (0.4%) in a review of their Hodgkin's lymphoma series which includes 780 cases.

Primary CNS Hodgkin's lymphoma is even more uncommon. The number of published cases is exceedingly small<sup>3-5,8-12,17,20,22,23</sup>. This patient may be the first case reported in Korea to our knowledge. The existence of primary CNS Hodgkin's lymphoma, however, is still controversial<sup>12</sup>. From today's view, it remains uncertain whether all these cases were true Hodgkin's lymphomas and whether the lesions were primarily located in the brain. Some authors doubt that the histologic criteria for the diagnosis of Hodgkin's lymphoma of published cases are fulfilled because of limited immunohistochemical evidence<sup>12</sup>. Actually, some case reports provide inadequate diagnostic information or have been reclassified as NHL<sup>5,12</sup>.

There might be arguments of CNS Hodgkin's lymphoma in this patient, since it was the only site of involvement. The diagnosis of Hodgkin's disease is based on characteristic morphological findings and immunohistochemical studies. Identification of Reed-Sternberg cells and their variants is essential for the histologic diagnosis. Diagnostic Reed-Sternberg cells are large and have either multiple nuclei or a single nucleus with multiple nuclear lobes, each with a large inclusion-like nucleolus about the size of a small lymphocyte<sup>12,15</sup>. The tumor cells have a characteristic immunophenotype: positive for CD15 and CD30 and negative for CD45 and B-cell and T-cell markers<sup>6,11,12</sup>. In this patient, some large atypical mononuclear Hodgkin cells and multinucleated Reed-Sternberg cells are scattered in dense inflammatory background. These cells are positive for CD30 and negative for CD45, CD20, and CD3 in the immunohistochemical staining (Fig. 2). The histologic morphology and immunohistochemical reactions in this case supported a diagnosis of Hodgkin's lymphoma, the mixed cellularity type.

Pathogenesis and risk factors for primary CNS Hodgkin's lymphoma have not been determined, although some reports have suggested an increased involvement of CNS with mixed cellularity histology in up to 44% of cases reported<sup>1,2,15</sup>. Like its systemic counterpart, it may be related to Epstein-Barr virus infection<sup>12,15</sup>. Epstein-Barr virus antigens have been demonstrated in Reed-Sternberg cells in approximately half of systemic cases and strongly associated with mixed cellularity type<sup>18</sup>. Their presence was recently described in Reed-Sternberg

cells in a case of primary CNS Hodgkin's lymphoma<sup>13</sup>. The frequent presence of EBV antigens in the Reed-Sternberg cells of many cases of mixed cellularity Hodgkin's lymphoma and the tendency of mixed cellularity type to involve CNS may be one important clue of the pathogenesis for intracranial Hodgkin's lymphoma. In this case, however, the presence of EBV antigens was not investigated.

Treatment and prognosis of primary CNS Hodgkin's lymphoma have not been established. Management should always include biopsy of the CNS lesion for the exact diagnosis. Intracranial relapse in the presence of systemic disease is usually treated with cranial radiotherapy and systemic chemotherapy. Primary CNS involvement of Hodgkin's lymphoma requires modification of this treatment protocol and involves consideration of surgery in combination with radiation therapy<sup>1,9</sup>. The role of systemic chemotherapy is under active investigation in primary CNS lymphoma because of disappointing results with radiotherapy alone<sup>5,12</sup>. Meningeal involvement or the presence of Reed-Sternberg cells in the CSF may warrant intrathecal therapy but the evidence to support this approach is minimal<sup>4</sup>. When Hodgkin's lymphoma relapses with brain involvement, the prognosis is poor with a median survival of 2-3 years following diagnosis of intracranial disease, but the prognosis of primary CNS Hodgkin's lymphoma appears to be superior with adequate surgical resection<sup>3-5,8,9,11,12,17,20,22,23</sup>.

## CONCLUSION

Primary Hodgkin's lymphoma limited to the CNS is exceedingly rare. Little is known regarding etiologic factors, optimal management, and prognosis. Here, we report an extremely rare case of a primary CNS Hodgkin's lymphoma without any evidence of systemic involvement.

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