

Intravascular Lymphoma with an Acute Course of Cerebellar Hemorrhage: A Case Report

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Abstract

Intravascular lymphoma (IVL) has been characterized in many case reports by multiple white matter lesions reflecting ischemic changes. In contrast, there are very few case reports of cerebral or cerebellar hemorrhage resulting from IVL. A 56-year-old woman was referred to our department with two-week history of headache, nausea, and poor appetite. Gadolinium (Gd)-enhanced magnetic resonance imaging (MRI) showed dilated veins on the cerebellar surface. No ischemic lesions were detected on diffusion-weighted images. Three days after admission, the patient had a large cerebellar hemorrhage, prompting emergency surgery. Unfortunately, the patient died on the 11th postoperative day. Massive CD20-positive lymphoma cells were recognized in the cerebellar veins, but not in the arteries or the parenchyma of the brain. This is the rare case report of a cerebellar hemorrhage complication from IVL that might have been caused by venous congestion. The dilated veins on the cerebellar surface recognized from the Gd-enhanced T1-weighted images were specific clues in this case.

Key words: intravascular lymphoma, venous involvement, cerebellar hemorrhage, central nervous system, congestion

Introduction

Intravascular lymphoma (IVL) is a rare subtype of extranodal non-Hodgkin lymphoma. It was first described in 1959 as systemic angioendotheliomatosis of skin blood vessels.¹⁾ This type of tumor was later reclassified as IVL and subsequently recognized as a distinct entity in the World Health Organization (WHO) classification.^{2,3)}

IVL is characterized by the proliferation of large CD20-positive B cells within the lumen of small and medium sized blood vessels, except for veins and large arteries. Blood vessels in the central nervous system (CNS) and skin are most frequently affected.⁴⁾ Clinical symptoms of IVL are generally non-specific and progression can be extremely rapid. Thus, the prognosis of IVL is still dismal. As for the CNS IVL, about 60% of cases were diagnosed post mortem examination.⁵⁾

Imaging studies of IVL in the brain are characterized by multiple hyperintense white matter

lesions on T2-weighted images, resembling ischemic or demyelinating lesions.⁶⁾ Cerebral or cerebellar hemorrhage resulting from IVL is extremely rare. Here, we report a case of IVL leading to devastating cerebellar hemorrhage.

Case Report

A 56-year-old female was referred to our department with a two-week history of headache, nausea, and appetite loss. She had no history of malignancy. Findings of neurological and general examination were normal. Laboratory workup revealed an elevated lactate dehydrogenase level (435 U/L) and soluble IL-2 receptor level (1850 U/ml). Blood coagulation was normal. Cerebrospinal fluid analysis revealed an elevated protein level (220 mg/dl) and cell count (18, mature lymphocytes); the cytological examination was normal.

Initial plain computed tomography (CT) images showed a low-density lesion in the left cerebellum with minimal mass effect. T2-weighted images and fluid-attenuated inversion recovery (FLAIR) MRI revealed multiple high intensity lesions in the left cerebellum and right frontal lobe (Figs. 1A and 1B) that

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were iso-intense on diffusion-weighted images (DWI) (Fig. 1C). Contrast-enhanced T1-weighted MR images revealed that those lesions were slightly enhancing, especially in the vermis and left cerebellar sulci (Figs. 1D–1F). Some dilated vessels were detected on the cerebellar and right frontal surface (Figs. 1G–1I). The patient's headache and nausea gradually worsened, and, on the third day of admission, she suddenly complained of severe headache and went into respiratory arrest immediately after the fluorodeoxyglucose-positron emission tomography (FDG-PET) examination. The CT scan revealed a

cerebellar hemorrhage with subdural hematoma (Fig. 2B). Despite an emergency surgical decompression, the patient did not recover from the brainstem damage and died on the 11th postoperative day.

The FDG-PET scan showed increased glucose uptake in the left cerebellar lesion (Fig. 2A), and also in the pelvis. The right frontal lesion was cold on the FDG-PET scan. The cerebellar biopsy obtained during surgery revealed extensive infiltration of CD20-positive large B cells in the veins (Figs. 3A and 3B), but not to the arteries and resected cerebellar parenchyma (Fig. 3F). Most of the tumor cells were also immunopositive for

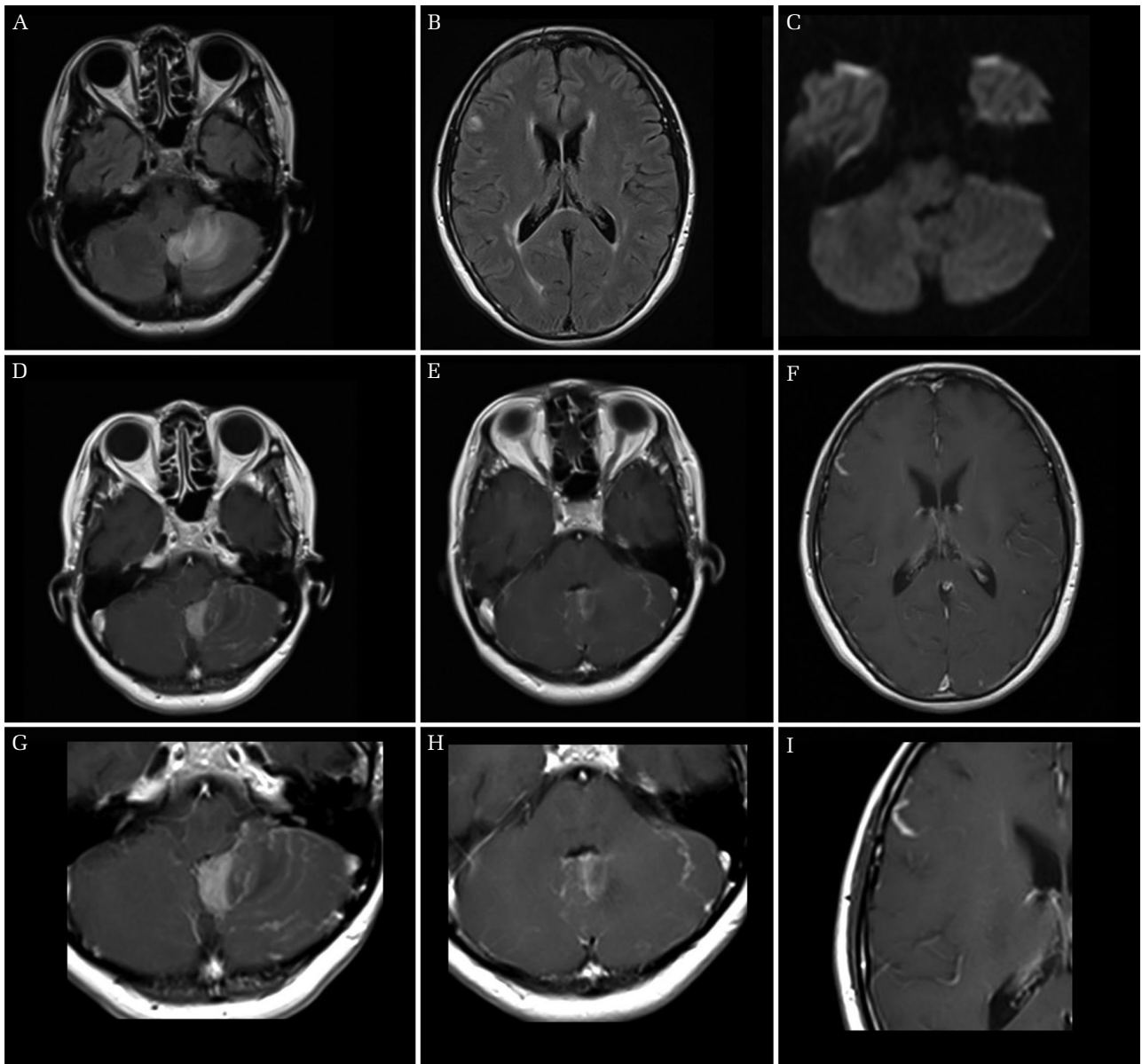


Fig. 1 (A, B) FLAIR MR images obtained on the day of admission reveal high-signal intensity lesions in the left cerebellum and right frontal lobe. (C) The vermis was iso-intensity on DWI. (D–F) The left cerebellar and right frontal lesion shows enhancement on T1-weighted, Gd-enhanced scan. (G–I) Some enhancing string-like lesions on the cerebellar surface that resembled meningeal carcinomatosis and dilated vessels were recognized.

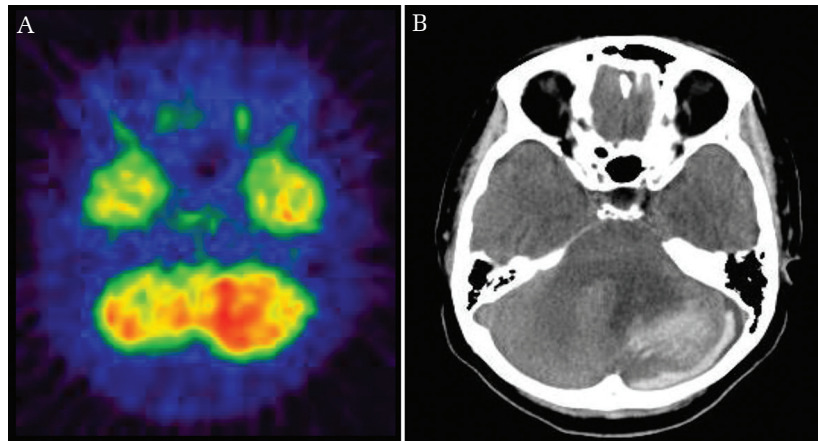


Fig. 2 (A) FDG-PET study showed uptake at the left cerebellar lesion. (B) The hemorrhage in the left cerebellum recognized from plain CT images. A subdural hematoma is also apparent, as is tight compression of the brainstem.

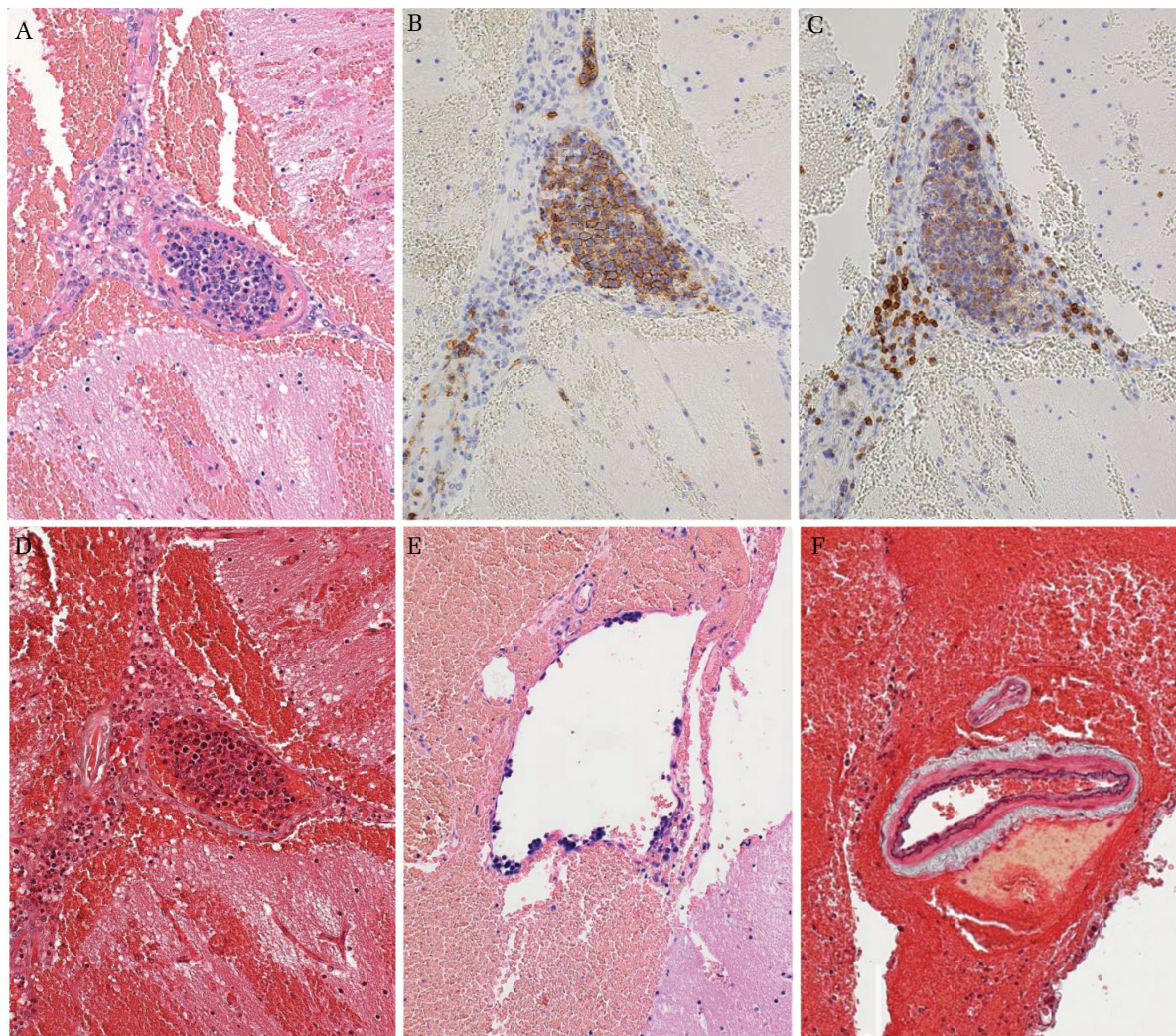


Fig. 3 (A) Surgical specimen stained with hematoxylin-eosin showing the presence of atypical lymphocytes in a cerebellar vein ($\times 200$). (B, C) Intravascular lymphoma cells are CD20 (B) and CD5 (C) positive. (D) The Elastica-Masson stain shows that the vessel is a vein due to the absence of elastic lamina. (E) The leptomeningeal vessels showing luminal dilation. (F) No tumor cells were recognized in the arterial vessels in the cerebellum (Elastica-Masson stain).

CD5 (Fig. 3C). In addition, microscopic observations revealed atypical lymphocyte infiltration, fibrinoid necrosis, and wall thinning (Fig. 3E). Deposition of hemosiderin and hemorrhage around the veins was also detected. Ischemic change of the cerebellum and subarachnoid dissemination was not observed. We could not confirm the tumor invasion to the vermis which was enhanced on MR images because the lesion was not resected.

Discussion

In the present report, we describe an extremely rare complication of IVL: a fulminant course of cerebellar hemorrhage with fatal outcome. MRI is considered essential for diagnosing IVL, although IVL-specific changes are scant. The most common reported findings are multiple hyperintense subcortical lesions on T2-weighted and FLAIR images, most likely representing small vessel ischemia. Hyperintense lesions on DWI also reflecting ischemia seems to be characteristic findings.^{6,7} Here, multiple hyperintense lesions on T2-weighted and FLAIR images, which were iso-intense on DW images, were recognized. Those lesions probably reflected a congestion phase secondary to venous occlusion. The most important radiographic findings in this case were the enhancing lesions on the left cerebellar surface that were later histologically identified as dilated veins congested by tumor infiltration. Differential diagnosis for such findings would include meningeal carcinomatosis, venous thrombosis, and vasculitis. Cerebellar angiography would have greatly aided the diagnosis but it was not available for this case.

Histopathologically, we found large lymphoid cells filling venous lumens, and capillary vessels. Despite the congestion of the blood vessels, ischemic changes were not observed. Therefore, we postulate that venous congestion from massive tumor cell infiltration directly caused the bleeding. Passarin et al. reported a case of IVL with intracerebral hemorrhage in which the cause of bleeding was never identified, even from the histopathological examination. They speculated that chronic degenerative or inflammatory changes of the vessel wall, such as hyalinization, fibrosis, and fibrinoid necrosis caused the hemorrhage.⁸

There was a hot spot lesion in her pelvis on the FDG-PET study just before the cerebellar hemorrhage. We could not perform further studies due to her poor condition. There is the possibility of the existence of the tumor mass in her pelvic organs. However, we could find tumor cells mainly in the cerebellar veins, thus we conclude the diagnosis was intravascular lymphoma.

Although the fulminant course of the disease prevented us from reaching the correct diagnosis before surgery, a skin biopsy should be considered if IVL is a possible diagnosis. Random skin biopsy is reportedly a highly sensitive diagnostic method for IVL, even in patients with normal appearing skin.⁹

The treatment strategy for IVL remains controversial. Some studies have shown that rituximab-containing chemotherapy in patients with IVL can be effective.¹⁰ In contrast, methotrexate did not change the overall survival time in a meta-analysis of 654 patients.¹¹ Future prospective studies are needed to establish best treatment for IVL.

This is the rare case of a cerebellar hemorrhage complication from IVL that might have been caused by venous congestion. The dilated veins on the cerebellar surface recognized from the Gd-enhanced T1-weighted images were specific clues in this case.

Conflicts of Interest Disclosure

The authors declare that they have no competing interests.

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