Intravascular large B-cell lymphoma is a rare subtype of extranodal diffuse large B-cell lymphoma characterized by the presence of lymphoma cells in the lumen of small vessels in the skin, CNS, lungs, kidneys, and other organs. Tumor cells can occlude the small vessels in various organs. Dementia and focal neurological deficits are known as ischemic symptoms of the CNS. Nevertheless, we could not find any reports in which tumor cells were verified in the cerebral aneurysms in patients with intravascular large B-cell lymphoma. We found only 2 reports in which the authors referred to any subtype of lymphoma.

Abbreviations used in this paper: CNS = central nervous system; MCA = middle cerebral artery; SAH = subarachnoid hemorrhage.

Case Report

History. This 69-year-old woman presented with a transient left-handed weakness on August 1, 2005, and was referred to our hospital on the same day. When she was in her 5th decade of life she had undergone a cesarean section. When she was 55 years old, she underwent an aortic valve replacement, and a year later she had a graft replacement for a thoracic aortic aneurysm. Warfarin potassium was administered. She had no specific family history.

Examination. The patient’s body temperature was 38.1°C. She had a weak left grip and left facial numbness, but no other neurological deficits were observed. Diffusion weighted MR imaging revealed a small high
signal lesion in the right frontal lobe (Fig. 1A). Another high signal intensity was detected by FLAIR and T2-weighted MR imaging in the right occipital lobe. Head (Fig. 1B) and cervical MR angiography demonstrated no abnormality in the major cervical and cerebral arteries. Initial laboratory studies showed a normal white blood cell count of $5.7 \times 10^3/\mu l$, and an elevated C-reactive protein of 6.8. The prothrombin time international normalized ratio was 2.97. Transesophageal echocardiography demonstrated no intracardiac thrombus. Levofloxacin was administered for a urinary tract infection. A blood culture was negative for bacteria. Cardioembolism was suspected as a cause of cerebral infarction, and anticoagulation treatment was continued. As she subsequently sometimes suffered transient left-handed weakness, intravenous injection of sodium oxagrel and oral administration of cilostazol were added. Intermittent fever and an elevated C-reactive protein persisted, so levofloxacin was replaced by cefozopran hydrochloride. Two weeks after onset, the transient ischemic attack disappeared; however, diffusion weighted MR imaging demonstrated enlargement of the right frontal lesion, although MR angiography revealed no abnormality in the circle of Willis. On August 22, she was found to be stuporous, and she had a left hemiparesis. A CT scan showed a hematoma in the right parietal lobe and SAH (Fig. 2A), and digital subtrac-

![Fig. 1. A: Diffusion weighted MR image demonstrating a small high signal lesion in the right frontal white matter (arrow). B: An MR angiogram demonstrating no abnormality.](image1)

![Fig. 2. A: A CT scan demonstrating the hematoma in the right parietal lobe and adjacent SAH. B: A digital subtraction angiogram obtained after intravenous injection of contrast medium, suggesting an aneurysm in the distal portion of the right MCA (arrow).](image2)
tigation angiography after intravenous injection of contrast medium suggested an aneurysm in the distal portion of the right MCA (Fig. 2B). A mycotic cerebral aneurysm was suspected. Vitamin K was administered, platelet and fresh-frozen plasma were transfused, and an operation was performed on August 23.

**Operation.** After induction of general anesthesia, a parietal craniotomy was performed. After dissecting the distal right sylvian fissure and evacuating the subarachnoid clots, 2 aneurysms were identified near the intracerebral hematoma. The lesions were unusual fusiform dilations of 2 branches of the distal MCA adjacent to one diverging branch (Fig. 3). Both vascular lesions were resected, and a superficial temporal artery–MCA anastomosis was done at the distal side of 1 of the interrupted MCA branches. Under histological examination, clusters of atypical large cells with irregular nuclei were recognized in the dilated arterial lumen (Fig. 4A and B). The cell membrane was immunopositive for CD20 (Fig. 4C) and CD79α (the markers of B-cell lymphocytes) and immunonegative for CD45RO, (the marker of T-cell lymphocytes). The diagnosis was diffuse large B-cell lymphoma.

**Postoperative Course.** On September 22, a ventriculoperitoneal shunt was placed for normal-pressure hydrocephalus. She could speak and her hemiparesis was also gradually improving. A laboratory study demonstrated an elevated soluble interleukin-2 receptor of 1680 U/ml. The lesion appeared as a high signal on FLAIR and T2-weighted images, which was the same as on the initial MR images. Positron emission tomography did not reveal an abnormal accumulation of fluorodeoxyglucose in her entire body. Unfortunately, secondary bleeding occurred on October 11, and she died on October 24.

**Postmortem Examination.** No cerebral neoplastic lesions were found. Proliferation of atypical cells with large irregular nuclei abounding in chromatin was verified only in the intimal layer that had grown on the luminal side of the aortic artificial graft (Fig. 5). Immunohistochemically, these tumor cells were positive for CD20 and CD79α, and they were similar to those found in the ruptured aneurysms. Other neoplastic lesions were not verified, and it was decided that the patient had had intravascular large B-cell lymphoma.

**Discussion**

Our patient experienced repeated ischemic symptoms despite antithrombotic therapy and later suffered SAH. Her clinical course was very different from that of patients who have suffered common cerebral artery stroke. It was also surprising that clusters of tumor cells were identified in the resected cerebral aneurysms, and the final autopsy diagnosis was intravascular large B-cell lymphoma. Although cerebral infarction has been reported in patients with intravascular lymphoma, there have been no reports referring to SAH or cerebral aneurysms in intravascular lymphoma. There are a few case reports in which the authors have referred to cerebral aneurysms in all subtypes of malignant lymphoma. Several months after the rupture of saccular cerebral aneurysms or after treatment of preexisting aneurysm, it was reported that 3 patients presented with CNS lymphoma. In every case, the cerebral aneurysm and malignant lymphoma

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**Fig. 3.** Intraoperative photograph showing the aneurysms (arrows).

**Fig. 4.** Photomicrographs of the resected aneurysms. **A:** Atypical cells are noted in thrombus and intima of aneurysmal wall of the MCA. **B:** Atypical cells have large oval to round nuclei and pale eosinophilic cytoplasm. **C:** The membrane of atypical cells are immunopositive for CD20. H & E (A and B), original magnification × 100 (A) and × 400 (B). Immunohistochemical stain for CD20 (C), original magnification × 400.
were regarded as purely coincidental. We found only 2 case reports in which malignant lymphoma cells infiltrating the walls of cerebral aneurysms were discovered on histopathological analysis.

Rahko et al.\textsuperscript{16} reported that lymphoma cells were infiltrating the wall of a ruptured MCA aneurysm in a 55-year-old woman whose spleen and abdominal lymph nodes had been affected by malignant lymphoma. Roitberg et al.\textsuperscript{17} reported on a 65-year-old man who had a brain tumor next to an anterior communicating artery aneurysm that had been embolized with a coil 6 months previously. The resected tumor was diagnosed as a primary CNS large cell lymphoma B-cell type, and the lymphoma cells had invaded all layers of the aneurysm wall resected at the same time. Except for malignant lymphoma, similar cases have been reported, and in almost all, choriocarcinoma and cardiac myxoma were the responsible neoplasms.\textsuperscript{2,4–7,9–13,15,20,22} The aneurysms have been reported to be molded by the tumor cells and are called neoplastic cerebral aneurysms. The mechanism by which neoplastic cerebral aneurysms are formed reportedly consists of arterial occlusion by a tumor embolism, infiltration of tumor cells into vessel walls, arterial recanalization, and ballooning of fragile vessel walls by hemodynamic stress, and these 2 neoplasms are suggested to have the potential for aneurysm formation.

In the aforementioned 2 reports of cerebral aneurysms in malignant lymphoma, the authors suggested that lymphoma cell infiltration into the walls of a preexisting cerebral aneurysm could result in late aneurysm enlargement and ultimate rupture. In one of the cases, the distal portion of the MCA dilated in a fusiform manner where ordinary saccular aneurysms rarely occur, and lymphoma cells were identified in the lumen and wall of the lesion. The preceding stroke in the same perfusion territory of the right MCA could be due to occlusion of the vessel by the tumor embolism. The remaining cluster of lymphoma cells in the vessel lumen could later invade the vascular wall in some way, making the vessel dilate as an aneurysm, disrupt it, and lead to an SAH.

Intravascular lymphoma should be considered for patients who have fever of unknown origin, increased inflammatory response, and recurring ischemic symptoms regardless of antithrombotic treatment. Early diagnosis and treatment for intravascular lymphoma can prevent aneurysm formation and subsequent rupture.

**Conclusions**

We have documented a 69-year-old woman who presented with SAH 3 weeks after the initial onset of cerebral stroke. Although this case is thought to be extremely rare, for patients with unusual cerebrovascular disease, further examination to check for the possibility of malignant neoplasm is warranted.

**Disclaimer**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

**References**


diffusion-weighted magnetic resonance imaging characteristics. *Acta Radiol* 46:246–249, 2005

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