Intravascular Large B-cell Lymphoma Following a Relapsing Stroke with Temporary Fever: A Brain Biopsy Case

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Intravascular large B-cell lymphoma (IVL) is a rare systemic disease that is characterized by massive intravascular growth of lymphoma cells with a predilection for the central nervous system. It is a subtype of diffuse large B-cell lymphoma as recognized by the World Health Organization classification (1). We report a case of IVL diagnosed by cerebral biopsy.

A 75-year-old woman having a history of hypertension and diabetes was admitted to our hospital with pseudobulbar palsy in February 2003. She complained of an acute onset of dysarthria and dysphagia. T2-weighted MR images of the brain showed a high signal intensity lesion in the white matter of the left frontal lobe. She was given ozaqrel, having cerebral infarction, and her pseudobulbar palsy vanished soon after. While she had a fever of 37.8°C on her admission day, it normalized after treatment of the stroke.

One month later, she was readmitted because of an acute onset of sensory aphasia. T2-weighted MR images of the brain showed a high intensity area in the left temporal lobe. After administration of argatroban for recurrent cerebral infarction, her sensory aphasia improved. Though she had a fever of 38.2°C, it normalized following the medication of the stroke.

Two months after the first onset, she had a slowly progressive consciousness disturbance and a fever of 38°C. Her conscious level was expressed as 11 points (E4, V2, M5) on the Glasgow Coma Scale, and she did not show any palsy in her limbs. The result of routine laboratory analysis of blood showed no abnormalities except mild elevation of lactate dehydrogenase (LDH) of 364 IU/l (normal: 106-211). T2-weighted MR images showed diffuse, large-sized high intensity areas in the subcortical white matter of bilateral frontal, temporal and parieto-occipital lobes (Fig. 1-A). Gd-enhanced T1-weighted images showed gyriform enhancement in the bilateral temporal lobes and nodular enhancement in the left parieto-occipital lobe (Fig. 1-B).

Additional laboratory data of blood tests revealed elevation of β2-microglobulin to 3.7μg/ml (normal: 1.3-2.2) and soluble interleukin-2 receptor to 1,540 U/ml (normal: 188-570). CT scans of her chest and abdomen revealed no abnormalities such as lymph node swellings and hypertrophy of adrenal glands. Atypical cells were not detected in her cerebrospinal fluid and bone marrow.

To determine the diagnosis, a brain biopsy was performed on the enhanced lesions of the left temporal and occipital lobes in June 2003. Histopathological examination revealed the proliferation of large atypical cells in the vessels, coexistent with the cerebral infarctions (Fig. 1-C1, 2). Immunohistochemically, they were positive for B-cell markers including CD 20 (Fig. 1-C3) and CD 79α; they were negative for CD 3, CD 5, CD 10, CD 23 and CD 45. The patient was diagnosed as having IVL and was treated with glycerol and prednisolone (40 mg/day) following a pulse of methylprednisolone (1,000 mg/day × 3 days). Chemotherapy was not performed because her general condition had deteriorated, and her family did not desire her to have aggressive treatment. The administration of steroid was partially effective, and her consciousness disturbance improved so that she could speak with her family. Though her neurological condition remained in remission, she died of a complication of pneumonia ten months after her first admission. The clinical course was shown in Fig. 2.

The diagnosis of IVL is difficult in life and is often made postmortem because of the absence of specific diagnostic procedures. While previous reports have shown that the invasion of lymphoma cells can be detected in brain, adrenal glands, kidney and skin in autopsy cases (2), it is difficult to diagnose in biopsy from these organs clinically. Because no other lesions were revealed except of cerebrum, we did the brain biopsy.

It has been reported that IVL sometimes indicates stroke-like symptoms (3, 4). The present case also showed that the symptoms closely resemble cerebral infarction, and she was medicated as having cerebral infarction. In our case, every time the patient came under stroke attack, she had a temporary fever that normalized as soon as her stroke symptoms improved. We suggest that relapsing stroke following a tem-

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Figure 1. A. T2 weighted images of MR (TR=4,000, TE=100) showing high intensity area in the subcortical white matter of bilateral frontal, temporal and pariet-occipital lobes when conscious disturbance was turned up. B. Gd-enhanced T1-weighted images of MR (TR=450, TE=15) showing gyriform enhancements in the bilateral temporal lobes and a nodular enhancement in the left parieto-occipital lobe. C. Histopathologic findings of a biopsy specimen revealing the proliferation of large atypical lymphoma cells positive for CD 20 within the vessels associated with cerebral infarctions in the surrounding tissue (1. HE stain, ×100, 2. HE stain, ×400, 3. immunohistochemical stain with CD 20, ×400).

Temporary fever is one of the distinctive features of IVL. Recently the efficacy of the systemic chemotherapy such as CHOP (5) and rituximab (6) has been reported; it is important to diagnose in the early stage.

References

Figure 2. Clinical course of the patient. Every time the patient came under stroke attack, she had a temporary fever that normalized as soon as her stroke symptoms improved.