

Primary Angiitis of the Central Nervous System Mimicking Tumor-Like Lesion

—Case Report—

Takafumi TANEI,^{1,2} Norimoto NAKAHARA,¹ Shigenori TAKEBAYASHI,¹
Masafumi ITO,³ Yoshio HASHIZUME,⁴ and Toshihiko WAKABAYASHI²

¹Department of Neurosurgery, Nagoya Central Hospital, Nagoya, Aichi;

²Department of Neurosurgery, Nagoya University Graduate School of Medicine, Nagoya, Aichi;

³Department of Pathology, Japanese Red Cross Nagoya Daiichi Hospital, Nagoya, Aichi;

⁴Department of Neuropathology, Institute for Medical Science of Aging,
Aichi Medical University, Nagakute, Aichi

Abstract

A 60-year-old man presented with a rare case of primary angiitis of the central nervous system mimicking a tumor-like lesion and manifesting as slight disorientation, left hemiparesis, and motor aphasia. Computed tomography showed multiple low density lesions in the left frontal lobe, brain stem, and right parietal lobe. Magnetic resonance images revealed a slightly enhanced mass lesion in the right parietal lobe with surrounding brain edema. Serum, cerebrospinal fluid, and other image examinations did not show any abnormal findings, so surgical removal of the right parietal mass was performed. Histological examination revealed that the mass consisted of hemorrhagic infarction without cellular atypia. Proliferations of endothelial cells in small and medium arteries, and infiltration of macrophages in the perivascular space were detected in the infarction tissues. The histological diagnosis was primary angiitis of the central nervous system.

Key words: primary angiitis of the central nervous system, multiple infarctions, endothelial proliferation, intracerebral hemorrhage, mass lesion

Introduction

Primary angiitis of the central nervous system (PACNS) is a rare disease,^{9,15,17} with incidences of 1–2.4 per million per year reported in Europe and America.^{15,16} The etiology and pathogenesis of PACNS remain unclear. PACNS is characterized by inflammation of the intracranial small and medium arteries without systemic disease. We describe a rare case of PACNS presenting as a tumor-like lesion.

Case Report

A 60-year-old man presented with disturbance of gait, and a few days later, symptoms of abnormal speech. He was transferred to our hospital in October 2009. On admission, his Glasgow Coma Scale score was 13 (E4V3M6) with slight disorientation, hemiparesis dominant in the left lower limbs, and motor aphasia. He had a history of hypertension, diabetic mellitus, and surgery for renal cancer 10 years earlier.

Computed tomography (CT) showed multiple low density lesions in the left frontal lobe, brain stem, and right

parietal lobe, and the right parietal region contained a mass lesion (Fig. 1A). Magnetic resonance (MR) imaging revealed a slightly enhanced mass lesion in the right parietal lobe with surrounding brain edema (Fig. 1B–F). Diffusion-weighted MR imaging showed the right parietal mass as a slightly heterogeneously hyperintense area and the left frontal lobe lesion as a homogeneously hyperintense area (Fig. 1G). Susceptibility-weighted MR imaging showed the right parietal mass as hypointense (Fig. 1H). [¹⁸F]fluoro-2-deoxyglucose positron emission tomography showed low accumulation of whole body and right parietal lesion (Fig. 1I). Cerebral angiography showed no evidence of vascularity around the lesions. Chest radiography and CT showed no abnormalities. Laboratory examinations demonstrated no abnormalities, and tumor markers such as carcinoembryonic antigen, alpha-fetoprotein, and carbohydrate antigen 19–9 were all negative. Serum angiotensin-converting enzyme was negative and markers for infectious diseases such as tuberculosis, human immunodeficiency virus, lues venerea, and hepatitis viruses B and C were also negative. Cerebrospinal fluid (CSF) examination revealed cell count of 1 mononuclear cell, total protein 50.0 mg/dl, and sugar 72 mg/dl. The initial pressure of the CSF was 7 cmH₂O, and the color was slightly yellow. These examinations did not show any ab-

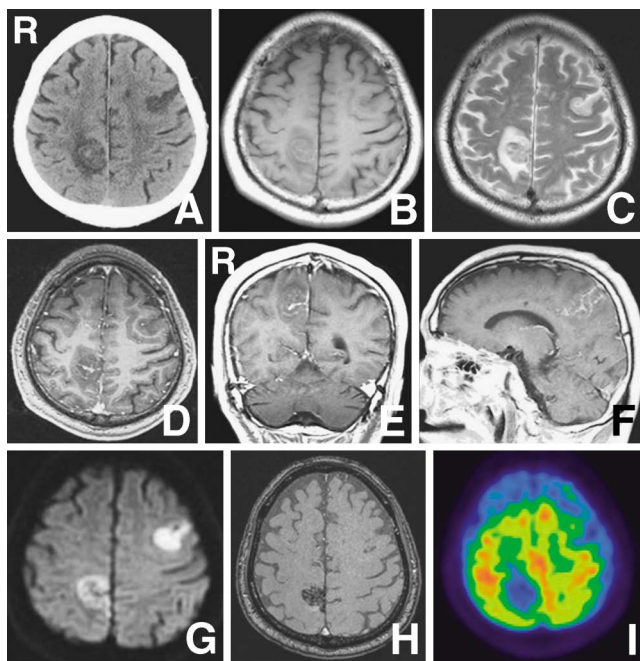


Fig. 1 Computed tomography scan (A) showing the left frontal low density lesion and the right parietal mass lesion. Magnetic resonance (MR) images showing the right parietal mass as isointense on the T₁-weighted image (B), and hyperintense with peripheral edema on the T₂-weighted image (C). Axial (D), coronal (E), and sagittal (F) T₁-weighted MR images with gadolinium revealing a slightly enhanced mass lesion. MR images showing the right parietal mass as slightly heterogeneously hyperintense on the diffusion-weighted image (G), and hypointense on the susceptibility-weighted image (H). [¹⁸F]fluoro-2-deoxyglucose positron emission tomography scan (I) showing low accumulation in the right parietal lesion.

normal findings. The mass lesion caused left hemiparesis, so surgical removal of the right parietal mass was performed in October 2009.

The mass lesion consisted of soft tissue and hematoma with an elastic capsule (Fig. 2). The border between the capsule and normal brain was clear. The lesion was totally removed without new neurological deficits. Histological examination revealed that the lesion contained mainly hemorrhagic infarction without cellular atypia (Fig. 3). In the infarction tissues, proliferations of vascular cells were detected in small and medium arteries, which caused narrowing of the intravascular lumen (Fig. 4A). Van Gieson's elastic stain revealed internal and external elastic lamina, and the proliferating cells were located between the internal elastic lamina and intravascular lumen (Fig. 4B). Therefore, the proliferating cells were endothelial cells. These cell proliferations were not seen in veins. Other immunohistochemical examinations showed positive staining for smooth muscle actin in endothelial cells (Fig. 4C), and staining for CD68 in the perivascular space (Fig. 4D). These findings indicated proliferation of fibroblast cells in the endothelium and infiltration of macrophages in the perivascular space. Staining for amyloid was negative. The histological diagnosis was PACNS.

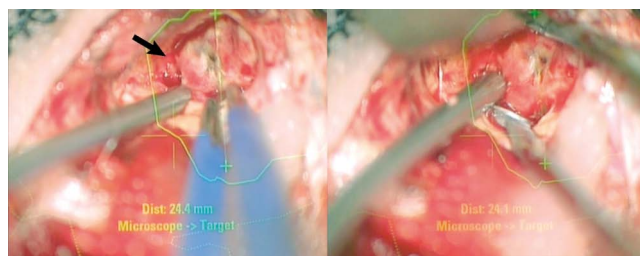


Fig. 2 Intraoperative photographs showing the lesion with surrounding elastic capsule (arrow).

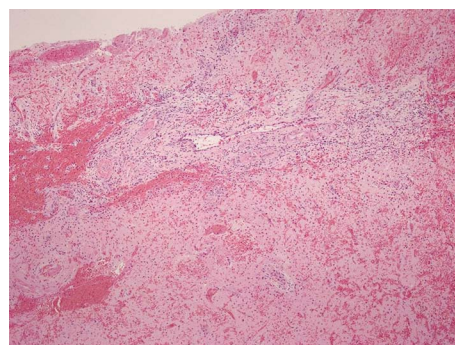


Fig. 3 Photomicrograph of contents of the right parietal mass showing the hemorrhagic infarction without cellular atypia. Hematoxylin-eosin stain, $\times 40$.

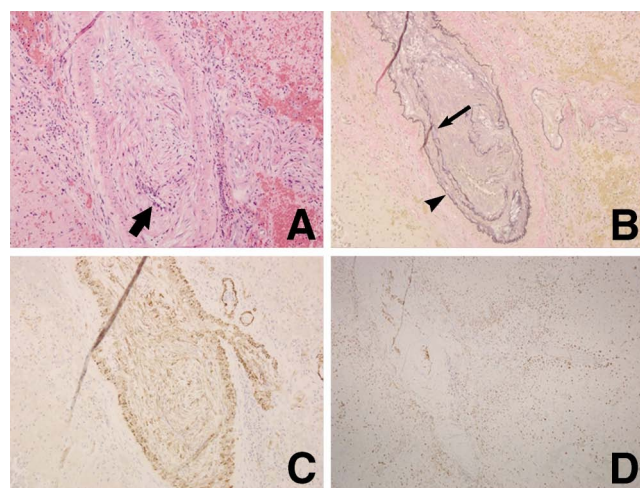


Fig. 4 Photomicrographs of a small artery in hemorrhagic infarction showing proliferations of endothelial cells which caused narrowing of intravascular lumen (thick arrow) (A: hematoxylin-eosin stain, $\times 200$), and internal lamina (arrow) and external elastic lamina (arrowhead) (B: Van Gieson's elastic stain, $\times 200$), and positive immunostaining for smooth muscle actin in endothelial cells (C: $\times 200$) and for CD68 in perivascular space (D: $\times 200$). These findings indicate proliferation of fibroblast cells in endothelium and infiltration of macrophages in the perivascular space.

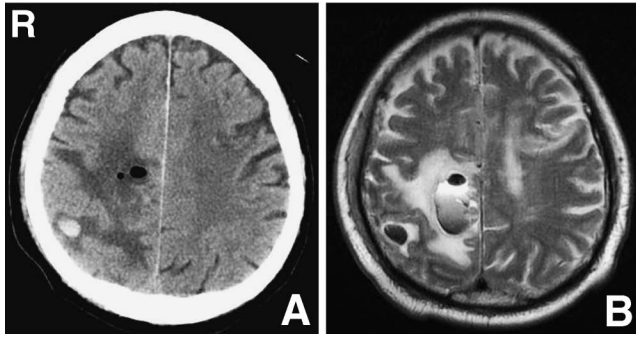


Fig. 5 Computed tomography scan (A) showing a small hemorrhage in the right parietal lobe. T₂-weighted magnetic resonance image (B) showing the hematoma distant from the tumor removal cavity.

Three days after the operation, the patient's consciousness slightly deteriorated. CT and MR imaging revealed a small intracerebral hemorrhage in the right parietal lobe, an area which was not contacted during surgery (Fig. 5). His consciousness gradually improved with medical treatment, and no new hemorrhagic or ischemic lesions appeared. He had sequelae of mild motor aphasia, although left hemiparesis was improved, and he was transferred to another rehabilitation hospital. He did not receive any steroid or immunosuppressive therapy because the histological diagnosis of PACNS was established after his transfer. Six months after surgery, follow-up MR imaging did not show any new lesions.

Discussion

The clinical features of PACNS are various, so a clear diagnosis is difficult. The diagnosis of PACNS is still reached by a process of exclusion. The most common frequent clinical manifestations at presentation are headache, altered cognition, hemiparesis, or persistent neurological deficit or stroke.^{15,17,19} MR imaging is commonly performed in the majority of patients with PACNS, and usually reveals abnormal findings.^{15,17,19} The MR imaging findings of PACNS are multiple bilateral asymmetrical supratentorial lesions representing infarctions, which predominantly occur in the subcortical and deep white matter.^{5,8,15} Single or multiple mass lesions are also known in PACNS.^{8,11,12,19} Approximately 5% of cases with PACNS present as a tumor-like mass lesion.¹¹ One of the mechanisms of formation of mass lesion is breakdown of the blood-brain barrier of the small vessels by infiltration of inflammatory cells in the perivascular and parenchymal regions, resulting in the mass mimicking enhanced lesion.⁸ Cerebral angiography is useful in making the presumptive diagnosis of cerebral vasculitis, but abnormal angiographic findings were reported in only 25% of patients with PACNS.⁴ Nine of 14 patients who were diagnosed with PACNS by biopsy had normal angiography findings.¹ Therefore, the diagnosis is difficult based on only angiographic findings. Histological examination allows the definite diagnosis of PACNS.^{1,15,17,19}

Diagnostic biopsy shows transmural mononuclear inflammatory cells involving small vessels of the leptomeninges and/or parenchyma.^{14,17} Three main histological patterns are reported, granulomatous, lymphocytic, and necrotizing vasculitis patterns.^{10,14} Granulomatous vasculitis is the most common pattern and is characterized by mononuclear infiltration associated with granulomas. The granulomas are located in the vascular wall from the intima to the adventitia. Lymphocytic vasculitis is characterized by predominantly lymphocytic inflammation through the vascular wall with distortion and destruction, devoid of granulomas. Necrotizing vasculitis is characterized by transmural fibrinoid necrosis. No statistically significant differences in outcome were noted between the three histological patterns,¹⁰ although deposition of amyloid protein is related to poorer outcomes in PACNS.¹¹ Eight of 31 patients with PACNS diagnosed by biopsy specimens were positive for amyloid protein.¹⁴ The histological features in our case were consistent with a granulomatous inflammatory pattern and staining for amyloid was negative.

The etiology in our case was angiitis-related damage to vessel walls and proliferation of endothelial cells in the intracranial small and medium arteries, which induced narrowing of the intravascular lumen, artery occlusion, and multiple small infarctions.⁹ The right parietal infarction did not initially manifest as obvious clinical symptoms. Then inflammatory cells, which mainly consisted of macrophages, infiltrated the perivascular space and the elastic capsule was formed several days later. These changes caused the lesion to mimic a tumor and induced surrounding edema, which caused slight left hemiparesis. When a new left frontal infarction occurred, the patient presented with motor aphasia and was transferred to our hospital. Postoperative presentation of a small intracerebral hemorrhage was distant from the tumor removal cavity, so the hemorrhage was caused by PACNS. Intracerebral hemorrhages may accompany the ischemic lesions in PACNS.^{2,3,6,13,18} The rate of hemorrhages associated with lesions in observed cases of PACNS was 4%.⁴ The hemorrhages often involved cortical and subcortical regions and no risk factors predisposing to hemorrhages were identified.

No consensus on the most advantageous therapy for PACNS has been established, but only steroid therapy or combination with immunosuppressive, cyclophosphamide, methotrexate, and azathioprine therapies improved the condition.^{3,7,11,14-17,19} Our patient did not receive steroid or immunosuppressive therapies, yet he did not present with any new clinical symptoms or new lesions on MR imaging in the 6 months after surgery. We did not administer steroid therapy even after the small intracerebral hemorrhage occurred, because the diagnosis of PACNS had not been established at that time. However, we think steroid or immunosuppressive therapies should be used if the lesion is identified as PACNS and new lesions occur, such as intracerebral hemorrhage or cerebral infarction. One of the reasons we did not choose a more aggressive clinical course was the absence of deposition of amyloid protein.¹¹

The presentations of PACNS are various such as multiple infarctions, encephalopathy, and intracranial mass lesion like in our case. PACNS should be considered in the differential diagnosis of any atypical mass lesion.

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Address reprint requests to: Takafumi Tanei, MD, Department of Neurosurgery, Nagoya Central Hospital, 3-7-7 Taiko, Nakamura-ku, Nagoya 453-0801, Japan.
e-mail: nsgtakasyun@msn.com