Primary granulomatous angiitis of the central nervous system: findings of magnetic resonance spectroscopy and fractional anisotropy in diffusion tensor imaging prior to surgery

Case report

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Primary granulomatous angiitis of the central nervous system (CNS) is extremely rare. Its preoperative diagnosis is difficult as the condition displays nonspecific features on routine neuroimaging investigations. In this paper, the authors report findings of magnetic resonance (MR) spectroscopy and fractional anisotropy (FA) with diffusion tensor MR imaging in a case of granulomatous angiitis of the CNS.

A 30-year-old man presented with morning headaches and grand mal seizures. An MR image revealed a mass resembling glioblastoma in the right temporal lobe. Magnetic resonance spectroscopy showed a high choline/creatine (Cho/Cr) ratio indicative of a malignant neoplasm, accompanied by a slight elevation of glutamate and glutamine. The FA value was very low, which is inconsistent with malignant glioma. The mass was totally removed surgically. Histologically, the peripheral lesion of the mass consisted of a rough accumulation of fat granule cells, infiltration of inflammatory cells, and distribution of capillary vessels. Some vessels within the lesion were replaced by granulomas. The histological diagnosis was granulomatous angiitis of the CNS. The MIB-1–positive rate of the granuloma was approximately 5%. Both MR spectroscopy and FA were unable to accurately diagnose granulomatous angiitis of the CNS prior to surgery; however, elevated Cho/Cr and glutamate and glutamine shown by MR spectroscopy may indicate the moderate proliferation potential of the granuloma and the inflammatory process, respectively, in this condition. Although the low FA value in the present case enabled the authors to rule out a diagnosis of glioblastoma, FA values in inflammatory lesions require careful interpretation. (DOI: 10.3171/JNS-07/10/0873)

KEY WORDS • diffusion tensor imaging • fractional anisotropy • magnetic resonance spectroscopy • MIB-1 • primary granulomatous angiitis • proliferation

Abbreviations used in this paper: Cho = choline; CNS = central nervous system; Cr = creatine; DT = diffusion tensor; FA = fractional anisotropy; MR = magnetic resonance; NAA = N-acetylaspartate; ROI = region of interest; VOI = voxel of interest.

CNS is extremely rare; between its first mention in 1959 and 1997 only 136 cases had been reported in the literature.²³ The origin, diagnosis, and natural course of granulomatous angiitis of the CNS remains unclear, even though it has been nearly 50 years since the first report. The diagnosis of granulomatous angiitis of the CNS is commonly made based on specimens obtained at surgery, and the disease responds effectively to corticosteroid and/or cyclophosphamide treatment;²³ however, the outcome is fatal if patients are untreated because of delayed diagnosis.²³²⁴ A preoperative diagnosis of granulomatous angiitis of the CNS is essential for treatment; however, diagnosis is difficult because neuroimaging findings, such as those on computed tomography scanning, MR imaging, and cerebral angiography are not specific.²³ Magnetic resonance imaging and angiography findings are not always in agreement.²⁰
The MR images commonly reveal nonspecific abnormal foci in the white matter, meningeal enhancement, and mass lesions that are commonly misinterpreted as malignant neoplasms. Cerebral angiography reveals abnormal findings in 60% of patients, whereas “classic” findings of arteritis (alternating areas of stenosis and ectasia in multiple vascular distributions) are observed in less than 40% of patients. Findings of other noninvasive neuroimaging examinations such as MR angiography, positron emission tomography, and single-photon emission computed tomography are also not specific; consequently, an additional examination is required that enables preoperative differential diagnosis for granulomatous angiitis of the CNS. In the current study, we report findings of using single-voxel MR spectroscopy and FA in DT imaging prior to surgery in a case of granulomatous angiitis of the CNS.

Case Report

History and Examination. This 30-year-old man presented with morning headaches and grand mal seizures. On admission, neurological examination revealed no deficit other than left homonymous upper quadrantanopia. His history included no episode suggestive of systemic autoimmune disease, intracranial infection, or head injury, and he had not undergone previous surgery or radiation therapy. Physical examination revealed no skin abnormality. Results of serum examinations, including a white blood cell count and C-reactive protein test, were within the normal ranges. The patient did not have temporal arteritis on admission. Computed tomography scanning and echography of the chest failed to reveal any aortic arteritis, including Takayasu arteritis.

Neuroimaging. All image analyses including MR spectroscopy, FA for DT imaging, and routine MR imaging, were performed using a 3.0-tesla MR imaging system (Signa VH/i, General Electric Medical Systems). Gadolinium-enhanced T1-weighted MR images revealed a mass with peripheral enhancement resembling glioblastoma (Fig. 1). In contrast, right carotid artery angiography revealed an avascular area in the right temporal lobe and demonstrated narrowing of the posterior temporal artery with poor filling (Fig. 2). There was a contradiction between the MR imaging findings, which suggested a malignant neoplasm, and those of angiography, which suggested a benign tumor or any ischemic disease.

We performed single-voxel MR spectroscopy (TE 144 msec). The VOI was placed over the central and peripheral regions of the mass lesion on T2-weighted MR images. Magnetic resonance spectroscopy revealed remarkable elevations of Cho-containing compounds, Cr, and NAA in the VOI at the peripheral region (Fig. 3), whereas the lipid peak was observed in the central region (not shown in the figure). When we evaluated the MR spectroscopy findings following the final histological diagnosis, we considered that the glutamate and glutamine peak was slightly elevated on a spectroscopic pattern of the peripheral region (Fig. 3). We interpreted the findings of MR spectroscopy for both regions prior to surgery and concluded that they were consistent with the pattern typical of an aggressive neoplasm such as glioblastoma.

We also measured the FA value on DT imaging with a b-factor of 800 sec/mm². We placed the ROI at the peripheral enhancing and central necrotic regions of the lesion as well as at the genu of the callosum on Gd-enhanced T1-weighted images (Fig. 4). The FA value was highest in the genu of the callosum (0.76); in contrast, FA values in the lesion were very low in both the peripheral enhancing region (0.09) and in the central necrotic region (0.08). A marked

Fig. 1. Axial Gd-enhanced T1-weighted MR image revealing a peripheral enhancing mass resembling glioblastoma in the right temporal lobe.

Fig. 2. Right cerebral angiogram revealing upward displacement of the main trunks of the middle cerebral artery due to a space-occupying lesion, in the absence of tumor blush vessels. Findings of narrowing and poor filling of the posterior temporal artery were also observed (arrow).
ly low FA value at the peripheral region enabled us to eliminate a diagnosis of a glioblastoma and speculate on the possibility of an edematosus and hypocellular lesion.

Operation. We performed a gross-total removal of the lesion because the lesion was causing considerable mass effect and widespread peripheral edema. When we opened the dura mater, the cortical arachnoid and vessels appeared almost normal. The mass was very hard but not demarcated from the surrounding xanthochromic edematous white matter. Postoperative MR imaging confirmed that the lesion had been completely debulked.

Histologically, the structure of the removed mass was revealed to consist of widespread necrotic tissue in the central region with an inflammatory lesion in the peripheral region. The inflammatory lesion consisted of a rough accumulation of abundant fat granule cells and inflammatory cells such as normal lymphocytes, astrocytes, and microglia, and included small hemorrhages, vessels infiltrated by lymphocytes, and vessels replaced by granuloma that consisted predominantly of proliferated epithelioid cells (Fig. 5A–C). The histological diagnosis was granulomatous angiitis of the CNS. The MIB-1 index within the granulomas was approximately 5% (Fig. 5D).

Postoperative Course. After surgery, treatment with low-dose (2 mg/day) bolus dexamethasone was initiated and continued for 1 month, and the patient made a full recovery. Three months after completion of the therapy, Gd-enhanced T1-weighted images revealed multiple enhancing lesions in the cerebral white matter bilaterally. The specimen obtained from a stereotactic biopsy targeted to one of these lesions showed similar histological features to those of the previous lesion. The patient was treated initially with intravenous high-dose dexamethasone (16 mg/day), which was tapered gradually to 2 mg/day within 2 weeks; additionally, cyclophosphamide was administered as a bolus (100 mg/day). A low-dose bolus of dexamethasone (2 mg/day) and bolus of cyclophosphamide (100 mg/day) were continued for 3 months. The MR images obtained after the completion of these therapies revealed the disappearance of all lesions. The patient underwent rehabilitation therapy and currently exhibits mild dementia.

Discussion

In the present case, we performed MR spectroscopy and calculated the FA value by using DT imaging. In MR spectroscopy Cho and Cr were significantly elevated, suggesting increased cell turnover and an energy-dependent system, respectively. A high Cho/Cr ratio was also observed at the periphery of the lesion. In the central region, the lipid peak that indicates necrosis was remarkably elevated. We interpreted the findings of MR spectroscopy to represent the high proliferation potential of a malignant neoplasm such as glioblastoma. When observed retrospectively following his-
tological diagnosis, we found a slightly elevated level of glutamate and glutamine.

There has been only one report of MR spectroscopy performed in a patient with primary angiitis of the CNS in which the authors described remarkable elevation of glutamate and glutamine in addition to the spectroscopic pattern consistent with a neoplastic process. The authors proposed that a marked elevation of glutamate and glutamine is associated with an inflammatory process of the CNS, and that the observed elevation of glutamate and glutamine in primary angiitis of the CNS reflects the cell breakdown of neural and glial elements, as well as the adjacent astrocytic response, leading to the high concentration of glutamate and glutamine in inflammatory conditions.

A remarkable elevation of glutamate and glutamine may lead to preoperative diagnosis of any inflammatory disorder, including granulomatous angiitis of the CNS; however, MR spectroscopy in the present case revealed a slight elevation of glucose and glutamine but marked elevations of Cho and Cr. These findings possibly result from granulomas retaining a moderate proliferation potential (MIB-1, ~ 5%). To determine whether the granuloma in granulomatous angiitis of the CNS generally retains a higher proliferation potential, further reports of cumulatively increased MR spectroscopy of granulomatous angiitis of the CNS are warranted.

The peripheral enhancing lesion on Gd-enhanced T1-weighted images showed a low FA value of 0.09, whereas the genu of the callosum displayed a high value of 0.76. The callosum shows strong directionality of water diffusion and consequently a high FA value. Previous reports of the FA value of the callosum, 0.77 and 0.61, were similar to that of the genu in the present case. This similarity confirms the reliability of the FA values obtained in the present study. The FA in the astrocytic tumor tissue is affected by a balance between the extent of nerve fiber destruction and an increasing number of cells that represent spindle-shaped neoplastic cells and elongated nuclei, and/or alignment of cells in a preferred direction such as pseudopalisading. There is a tendency for tumors classified as high-grade gliomas to present with higher FA values. In previous studies, the mean FA values have been reported as 0.24 in glioblastoma, and 0.23 in anaplastic astrocytomas. In the present case, the FA value for the peripheral enhancing region was significantly lower than those for glioblastoma and anaplastic astrocytoma. A very low FA value enabled us to confidently propose prior to surgery that the peripheral lesion was different from glioblastoma. Surgical specimens showed rough accumulations of fat granule cells and normal inflammatory cells in most of the peripheral region, as shown in Fig. 5A to C. Extracellular edema and small hemorrhages were also observed. These histological characteristics may lead to a decrease in the degree of water diffusion directionality, and

Fig. 5. Photomicrographs showing histological features of the inflammatory region of the mass. A: Low-power image demonstrating that the lesion consists of a rough accumulation of inflammatory cells and includes small hemorrhages (H), vessels infiltrated by lymphocytes (V), and vessels replaced by granuloma (G). B: A capillary vessel infiltrated by lymphocytes. C: A vessel partly occluded and replaced by granuloma consisting predominantly of proliferated epithelioid cells. (Rough accumulations of fat granule cells and inflammatory cells are seen surrounding vessels in panels B and C.) D: Demonstration of MIB-1–positive cells within the granuloma. H & E (A–C), original magnification × 40 (A) and × 200 (B–D).
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dtherby to a largely reduced FA value; however, FA values in inflammatory lesions are probably largely influenced by the different degrees of inflammation among patients and by the different histological characteristics among inflammatory disorders. For example, the FA values for multiple sclerosis are different along the inflammatory process (acute, subacute, and chronic plaques, and among regions of the plaques). Although in the present case the FA was helpful in the exclusive diagnosis of glioblastoma, FA values for inflammatory disorders require careful interpretation. Further study of FA in a limited group of patients with angiitis of the CNS is required to confirm the suitability of FA for diagnosis of angiitis, including granulomatous angiitis, of the CNS.

Conclusions

To our knowledge, there are no other reports of MR spectroscopy or calculations of the FA value for granulomatous angiitis of the CNS. We emphasize that brain and meningeal biopsy is the gold standard for the diagnosis of granulomatous angiitis of the CNS. Magnetic resonance spectroscopy proved less useful for preoperative diagnosis for granulomatous angiitis of the CNS because it displayed a nonspecific spectroscopic pattern similar to that for malignant neoplasm, although a slight elevation of glucose and glutamine indicative of inflammatory character was observed. However, these findings suggest the possibilities that: 1) granulomatous angiitis of the CNS retains moderate proliferation potential; and 2) the elevation of the glucose and glutamate peak is an indicator of any inflammatory disorder of the CNS. In contrast, the low FA value in the present case was sufficient to enable us to presume that the lesion was inconsistent with malignant gliomas; however, the use of FA to interpret inflammatory disorders of the CNS should be predominantly influenced by differences in the histological behavior of inflammation among patients.

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References


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