Proton Magnetic Resonance Spectroscopy and Diffusion-Weighted Imaging of Tumefactive Demyelinating Plaque
—Case Report—

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Abstract

Proton magnetic resonance spectroscopy, diffusion-weighted axonography, and diffusion tensor tractography in a patient with tumefactive demyelination plaque (TDP) were evaluated for differential diagnosis from glioblastoma. The findings of glutamate and glutamine elevations on magnetic resonance spectroscopy and apparent tracts within the lesion on axonography and tractography were unlikely to represent glioblastoma, and were thus useful for the preoperative diagnosis of TDP.

Key words: glioblastoma, tumefactive demyelination plaque, diffusion-weighted magnetic resonance imaging, magnetic resonance spectroscopy, diagnosis

Introduction

Tumefactive demyelinating plaque (TDP) is a rare demyelinating disorder manifesting with different clinical characteristics from multiple sclerosis (MS), such as solitary lesion greater than 2 cm on neuroimaging, and focal neurological deficits due to mass lesions. Two series of brain biopsies for various diseases have shown that the incidence of TDP was 14/15,394 cases (0.09%) over 22 years and 4/1,220 cases (0.3%) over 5 years.1,9) Preoperative diagnosis of TDP is occasionally difficult for neuro-oncologists, given the rarity of the disorder and the similarities to malignant neoplasm on routine neuroimaging.7,15) For example, 5 patients with TDP mimicking brain tumor underwent biopsy among 1,119 cases with MS or other inflammatory diseases.16)

We report a case of TDP, in which preoperative proton magnetic resonance (MR) spectroscopy, diffusion-weighted axonography, and diffusion tensor tractography were useful for the differential diagnosis of TDP from glioblastoma.

Case Report

A 64-year-old man presented with rapidly progressive hemiparesis (stage 1 in the arm and stage 4 in the foot, according to Brunnstrom's grading system9). His history did not include any episodes of relapsing or remitting symptoms suggestive of MS. Cerebrospinal fluid analysis showed that cell count, and protein and glucose levels were within the normal ranges, and no oligoclonal band was detected.

Routine MR imaging, proton MR spectroscopy, diffusion-weighted MR imaging for axonography, and diffusion tensor imaging for tractography and fractional anisotropy were performed using a 3.0-T system (Signa VH/I; GE Medical Systems, Milwaukee, Wis., U.S.A.). T1-weighted MR imaging with gadolinium revealed a peripheral enhanced mass with a maximal diameter of 3.7 cm resembling glioblastoma in the right basal ganglia (Fig. 1). Single-voxel MR spectroscopy with an echo time of 25 msec revealed marked elevations of choline-containing compounds (Cho), lactate, and lipid, and attenuation of N-acetyl aspartate (NAA). Furthermore, the glutamate and glutamine peak at 2.2 ppm was considered to be slightly elevated (Fig. 2).

Axonography using diffusion-weighted imaging (repetition time [TR] 5000 msec, echo time [TE] 66.6 msec, matrix 256 × 256, field of view [FOV] 240 mm × 240 mm, 4 mm thickness, b value 1000 sec/mm²) was performed as previously described.10) The axonography images showed some colored structures within the lesion. In particular, the lesion encased structures localized symmetrically to the pyramidal tract and the putamen on the non-pathological side (Fig. 3). Tractography and measurement of fractional anisotropy, as a parameter of neuronal fiber integrity, was
Fig. 1  T-weighted magnetic resonance image revealing a space-occupying lesion with mass effect and thick peripheral enhancement.

Fig. 2  A: T-weighted magnetic resonance (MR) image showing the voxel of interest placed over the mass. B: MR spectroscopy scan showing marked elevations of choline-containing compounds (Cho) at 3.2 ppm, lactate (Lac) at 1.3 ppm, and lipid (Lip) at 1.0 ppm, and attenuation of N-acetyl aspartate (NAA) at 2.1 ppm. Slight elevations of glutamate and glutamine (Glx) are also seen at 2.2 ppm.

Fig. 3  Diffusion-weighted axonography image showing dark orange-colored structures suggesting an apparent pyramidal tract (arrowhead) and the putamen (arrow) within the lesion.

Fig. 4  A: Diffusion tensor tractography image demonstrating thinner fibers (arrow) ascending from the region corresponding to the apparent pyramidal tract within the lesion on axonography, compared to fibers on the contralateral, non-pathological side. B: Fractional anisotropy map showing regions of interest (circles on the figure) placed over the pyramidal tract on the non-pathological side (No. 1), apparent pyramidal tract (No. 2), and the other region (No. 3) within the lesion.

Based on diffusion tensor imaging (TR 10000 msec, TE 62 msec, matrix 128 × 128, FOV 240 mm × 240 mm, 4 mm thickness with 1.5 mm gap, 6 motion-probing gradient directions, b value 1000 sec/mm²). Tractography images were processed using a free software package, VOLUME-ONE/dTV provided by the Department of Radiology, University of Tokyo, Tokyo (http://www.volume-one.org), and fractional anisotropy was measured using a subprogram of the Functool™ image analysis software (General Electric Medical Systems, Buc, France). Tractography demonstrated thin fibers representing an apparent pyramidal tract within the lesion (Fig. 4A). Fractional anisotropy values for the pyramidal tract on the non-pathological side, the apparent pyramidal tract, and the other region within the lesion were 0.51, 0.31, and 0.14, respectively (Fig. 4B).

These findings suggested that the lesion did not represent aggressive neoplasm such as glioblastoma but rather demyelinating disease. Stereotactic biopsy was performed targeting the peripheral region. The biopsy specimen demonstrated typical histological features of acute demyelinating plaque (Fig. 5). The clinical diagnosis was TDP. Steroid-pulse therapy was initiated immediately after the diagnosis. Lesion size and symptoms were observed for 2 months. Lesion size was slightly reduced, and the hemiparesis improved to stage 2 in the arm and stage 5 in the foot, but did not fully resolve.

Discussion

Generally, TDP appears on routine MR imaging as a circumscribed lesion with a diameter of more than 2 cm with little mass effect, absence of vasogenic edema, and open...
ring sign with incomplete enhancement on the gray matter side.\(^{6,7,14}\) Neuroimaging of 168 cases of TDP requiring biopsy suggested various enhancement patterns and a strong statistical association between lesion size and presence of mass effects and peripheral edema.\(^{13}\) Therefore, no neuroradiological indications for TDP can be defined as specific findings. MR imaging showed discernible lesion size from 2.1 to 5 cm in 44\% of all cases.\(^{13}\)

In the present case, the 3.7-cm lesion was associated with slight mass effect, absence of edema, and open ring sign, consistent with the reported findings, but we could not confidently diagnose TDP based only on routine MR imaging. Indeed, TDP is often not correctly diagnosed until after surgical biopsy or resection. Therefore, preoperative examinations for TDP, including MR spectroscopy, positron emission tomography, and single photon emission computed tomography have been the object of many studies.\(^{3,5,12,17–20}\)

In this case, MR spectroscopy detected elevated Cho, lactate, and lipid peaks, and reduced NAA peak. Patients with demyelinating diseases including TDP show such changes of these four metabolites, which have been interpreted as follows: elevation of Cho indicates increased membrane turnover associated with reactive astrogliosis; attenuation of NAA reflects a decrease in relative volume of neuronal tissue; elevation of lactate indicates lactate production associated with ischemia and/or increased glycolysis caused by macrophage activation; and elevation of lipid reflects increased mobility of lipid protons during myelin breakdown.\(^{3,5,12,18,20}\) However, spectral abnormalities of these metabolites are also associated with various malignant neoplasms. Therefore, MR spectroscopy may be unsuitable for differential diagnosis of TDP from malignant neoplasms.\(^{3,12,18}\)

In the present case, MR spectroscopy using a 3.0-T system detected slight elevations of glutamate and glutamine, along with the classical metabolites described above. Detection of glutamate and glutamine elevations on MR spectroscopy using a 1.5-T system may facilitate the diagnosis of TDP, because the cell breakdown of both neural and glial elements leads to high concentrations of glutamate and glutamine, which are not seen in aggressive malignancy.\(^{3}\) However, this was a retrospective study affected by bias and lack of statistical power caused by few objective cases and absence of control cases.\(^{11}\) The present MR spectroscopy findings may provide some support.

Myelin breakdown within demyelinating plaque generally occurs in the acute phase, whereas the axon is preserved even in the late phase.\(^{9}\) In the present case, findings from axonography and tractography suggested that even if the myelin of the pyramidal tract had been severely disrupted, the axons were at least somewhat preserved. Fractional anisotropy values of the apparent pyramidal tract within the lesion were between the values of the contralateral normal pyramidal tract and the other regions within the lesion, so supported the contention that apparent pyramidal tract fibers within the lesion were demyelinated but not completely disrupted. Slight improvement of hemiparesis following steroid-pulse therapy might support this suggestion.

We believe that the characteristics of malignant neoplasm differ entirely from the findings in this case. The initial growth pattern of malignancies in the white matter involves clusters of neoplastic cells extending into the white matter, with the tumor mass separating or splitting fiber tracts. In the late phase, when symptoms appear, almost all normal fiber and cell structures have been destroyed by the tumor nidus or displaced to surround the tumor nidus.\(^{22}\) The mass size and symptoms in the present case represent progression to the late phase if malignancy was present. Major tracts such as the pyramidal tract on the pathological side should have been destroyed or displaced to surround the lesion. The pyramidal tract adjacent to glioblastoma was destroyed or displaced to surround the tumor, and disappeared within the tumor on axonography.\(^{2}\) Diffusion tensor tractography showed the fiber bundles involved in the glioblastoma disappeared due to severe disruption.\(^{21}\) However, no reports have described visualization of fiber tracts within TDP.

The present case supports the possibility that glutamate and glutamine elevations on MR spectroscopy provide a useful indicator of TDP, and suggests that visualization of fiber tracts within the lesion using diffusion-weighted imaging or diffusion tensor imaging are valuable if the TDP encases major fiber tracts such as the pyramidal tract. Further studies comparing the lesions of TDP with malignant neoplasm are needed to confirm the utility of MR spectroscopy and visualization of fiber tracts within the lesion for the diagnosis of TDP.

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