Brain atrophy occurs at a faster rate than normal in patients with multiple sclerosis (MS) and may be accelerated in the year after initiation of immunomodulatory therapy—a phenomenon that is often attributed to the resolution of edema.

To explore the nature of the changes in brain volume after anti-inflammatory therapy, we measured global brain volume changes on MRI scans of patients with active disease who were participating in a tricenter phase II trial of immunomodulation followed by AHSCT.2

Methods. We studied nine secondary progressive (SP) MS patients with aggressive MS being treated with immunomodulation and autologous hematopoietic stem cell transplantation (AHSCT). We also measured brain volume changes on MRI scans of a patient with lymphoma that did not involve the CNS and who was undergoing a similar treatment.

Results. The patient demographics and rates of atrophy at baseline and 1 month after AHSCT are shown in the table. Atrophy (brain volume loss) is reported as a positive percentage change. The entire therapy (stem cell mobilization, immunomodulation, and AHSCT), resulted in a decrease of brain volume by a median value of 3.2% (interquartile range [IQR] = 2.6 to 3.4%/year, n = 5) during a median time interval of 2.4 months, which represents a median annualized rate of atrophy of 15.1%/year (IQR = 12.9 to 16.4%/year, n = 5) which is higher than baseline (p < 0.001). During the same interval, on average there was either no significant change or slight increases in the simplified estimated T2-relaxation times. The rates of atrophy after the acute period were slightly slower than but not significantly different from baseline (figure).

Relation of atrophy to inflammation. Brain atrophy after treatment exceeded concurrent decreases in T2LV by 2- to 20-fold, suggesting that resolution of edema in lesions was not solely responsible for the acute brain atrophy.

To assess a possible direct toxic effect of the immunomodulation on the brain, we measured brain volume change in a patient with lymphoma without CNS involvement who underwent analogous treatment. Baseline measurements in this patient were stable. During the treatment interval (baseline to 3 months after immunomodulation and transplantation), the patient showed an annualized rate of atrophy of 6.0%/year, which was within the range of atrophy measurements in the MS patients during a similar treatment interval. This patient continued to show a high rate of brain atrophy during the subsequent 3 to 6 months, which again was similar to atrophy measured in the MS patients during a similar interval.

Discussion. We found that substantial brain atrophy (median 3.2% over median 2.4 months) occurred acutely after immunomodulation and AHSCT in patients with MS and BMT in a patient with lymphoma without preexisting CNS disease.

Decreases in brain volume can be associated with a decrease in the volume of cellular components or a loss of water without tissue loss, often called “pseudoatrophy.” Dehydration associated with acute
illness or medication could cause acute reversible brain volume change. We do not believe that atrophy in our patients was secondary to water shifts, because patients were in dedicated transplant centers that carefully maintained nutritional and hydration status during the acute phase of their treatment, and changes in body weight during the acute period were not consistently associated with the magnitude of acute changes in brain volume. In addition, simplified estimates of T2-relaxation times did not show the decreases that would be expected with loss of tissue water. To explore whether the resolution of edema in lesions might be the explanation for the brain volume changes observed, we compared the change in T2LV during the acute interval with the change in brain volume. Brain volume loss exceeded the change in T2LV by 2- to 20-fold. Therefore, resolution of focal edema associated with lesions is not likely to explain the acute atrophy observed. We also considered the possibility that resolution of diffuse inflammatory edema involving normal-appearing brain tissue could result in pseudoatrophy. The average change in simplified estimates of T2-relaxation times in normal-appearing brain tissue during the acute interval did not show the decreases that would be expected with resolution of diffuse inflammatory edema. In addition, we obtained MRI scans from a patient with lymphoma without CNS involvement, before and after immunoablation and allogeneic bone marrow transplantation. This patient showed acute brain atrophy comparable to that in the transplanted MS patients. This suggests that the brain volume change observed in the MS patients also may not be simply related to the resolution of edema; toxicity of the therapy, which included cyclophosphamide and busulfan (as well as steroids and other concomitant medications), likely contributed. Cerebral toxicity of chemotherapy is a known complication of such therapy.

The observation of rapid brain atrophy from baseline to 1 month after immunoablation suggests that yearly measurement of brain atrophy may not be optimal for assessing brain volume changes after therapeutic intervention. Measurements early after therapeutic intervention can distinguish treatment-related changes and establish a new baseline for ongoing atrophy.

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**Table Subject demographics**

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range), y</td>
<td>32 (26–40)</td>
</tr>
<tr>
<td>Sex, F:M</td>
<td>5:4</td>
</tr>
<tr>
<td>EDSS, median (range)</td>
<td>6 (4–6)</td>
</tr>
<tr>
<td>Disease duration, mean (range), y</td>
<td>6 (2–10)</td>
</tr>
</tbody>
</table>

**MRI at baseline**

| Volume of T2-weighted lesions, mean (range), cc | 36.87 (13.84–84.40) |
| Number of patients with Gd⁺ lesions | 4 |
| Number of Gd⁺ lesions, median (range) | 10 (0–23) |
| Volume of Gd⁺ lesions, cc, mean (range) | 0.76 (0–5.72) |
| Rate of atrophy, annualized median (interquartile range), (%)y | 1.4 (−1.3 to 1.6) |

**MRI after treatment**

| Number of patients with Gd⁺ lesions | 0 |
| Rate of atrophy from pretreatment to 1 mo after AHSCT, annualized median (interquartile range), (%)y | 15.1 (12.9–16.4) |

AH SCT = autologous hematopoietic stem cell transplantation; EDSS = Expanded Disability Status Scale; Gd⁺ = gadolinium-enhancing.
References


Intracranial dermoid cyst rupture with subarachnoid and intraventricular fat dissemination

Gerard Plans, MD; Alberto Aparicio, MD; and Carles Majós, PhD, Barcelona. Spain

A 53-year-old man presented with an abrupt onset of depressive syndrome with atypical features (depersonalization, derealization, and occasional disorientation). Neurologic examination revealed mild sensory loss in the first left trigeminal division and diminished swallowing reflex. Cranial MRI showed a ruptured left cerebello-pontine angle dermoid cyst extending to the middle cranial fossa (figure).

A retrosigmoid craniotomy allowed resection of the posterior fossa cyst, and pathologic analysis confirmed the diagnosis. Despite initial treatment with an external ventricular drainage, the patient developed hydrocephalus and finally needed a ventriculoperitoneal shunt. Six months after initial treatment, the patient has no psychotic symptoms and follows treatment with antidepressant drugs and valproate due to left temporal irritative activity. CT images of fat dissemination still persist.

Dermoid cysts account for 0.04 to 0.25% of all intracranial tumors. Their rupture is relatively rare.1

Disclosure: The authors report no conflicts of interest.

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Figure. (A) Sagittal and (B) axial T1-weighted imaging (WI) demonstrate the mass to be heterogeneously hyperintense. Multiple focal areas of T1 shortening are present within the subarachnoid space. Note the presence of a fluid-fluid level into the ventricles (arrow). (C) Axial T2-WI shows a prominent chemical shift artifact (arrowhead) that confirms lipid content.

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