Clinical Implications of Splenium Magnetic Resonance Imaging Signal Changes

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Background: Magnetic resonance imaging (MRI) may show discrete splenium abnormalities; however, the implications of this radiologic finding are unclear.

Objective: To describe causes, clinical presentations, and prognoses of midline splenium changes evident on MRI.

Design: Retrospective case series.

Setting: Teaching hospital.

Patients: Medical records of 9 patients with MRI-noted splenium changes were studied; 60 additional published cases were accessed.

Interventions: Sixty-nine cases were reviewed.

Main Outcome Measures: Clinical and imaging findings, causes, and prognosis.

Results: Confusion (35 patients), ataxia (25 patients), and recent seizure (23 patients) were common. Causes included alcohol use, infections, hypoglycemia, trauma, salt abnormalities, and seizure. Twenty-eight patients had complete resolution, 23 improved, and 1 died. Diffusion-weighted imaging showed splenium abnormalities the best. Eleven of 12 patients showed decrease in apparent diffusion coefficient. Most improved clinically, as did their subsequent MRI studies.

Conclusions: Midline splenium changes are commonly seen on MRI diffusion-weighted imaging sequences. Multiple causes can result in splenium changes. Physicians should evaluate for glucose and electrolyte abnormalities, seizure risk, ongoing infectious or parainfectious process, and traumatic causes.

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METHODS

Magnetic resonance imaging (MRI) studies suggest splenium injury is common, reversible, and associated with multiple origins and presentations (Table 1); however, the implications of this radiologic finding are unclear. In this series of MRI-evident splenium injuries, causes are recorded with clinical findings and outcomes. We evaluate records of patients with midline splenium changes incidentally noted on brain MRI to determine if they share a characteristic presentation or common cause. The results are discussed and evaluation strategies proposed.

RESULTS

Medical records of 9 patients along with 60 published cases with MRI splenium changes were studied. Of 69 patients evaluated, 52 had clinical outcomes recorded: 28 had complete resolution, 23 improved, and 1 died. Causes are given in Table 1. The vignettes and imaging of unique patients evaluated by the authors appear in the Figure. Clinical findings of 58 patients are given in Table 2. The most consistent splenium changes evident from MRI were reduced T1 signal intensities, increased T2 and fluid-attenuated inversion recovery signals, and, if performed,
increased diffusion-weighted imaging (DWI) (Figure). Splenium abnormalities were easiest to see with DWI in 8 of 9 original cases. Seven of our 9 patients had DWI changes in posterior limbs of the internal capsules. No splenium abnormalities were evident in computed tomograms of the 9 patients reviewed from our institution. Of those same patients, 3 had elevations of creatine kinase levels, necessitating directed treatment and surveillance.

The DWI was reported with apparent diffusion coefficient (ADC) values in 12 patients; all but 1 was reduced.3,15,19,21,26-28 Of those with reductions, 8 of 11 had complete clinical recovery. In 16 of 18 patients, splenium abnormalities resolved on follow-up MRI. The DWI changes and ADC values related to convulsions showed no residual MRI or clinical abnormalities. The patient with increased ADC values had complete resolution of MRI and clinical findings.28

Table 1. Causes Associated With Splenium Damage

<table>
<thead>
<tr>
<th>Possible Causes</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol, alcohol and malnutrition</td>
<td>1-14, PS</td>
</tr>
<tr>
<td>Trauma</td>
<td>15-16, PS</td>
</tr>
<tr>
<td>Human herpesvirus 6</td>
<td>17</td>
</tr>
<tr>
<td>Malaria</td>
<td>18</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>19</td>
</tr>
<tr>
<td>Measles</td>
<td>20</td>
</tr>
<tr>
<td>Salmonella</td>
<td>21</td>
</tr>
<tr>
<td><em>Escherichia coli</em> 0157</td>
<td>22, 23</td>
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<tr>
<td>Human immunodeficiency virus</td>
<td>24</td>
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<tr>
<td>Acute disseminating encephalomyelitis</td>
<td>25, PS</td>
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<tr>
<td>Seizure</td>
<td>6, 17, 23, 26-33, PS</td>
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<tr>
<td>Altitude sickness</td>
<td>27, 32</td>
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<tr>
<td>Neoplasia</td>
<td>34</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td>35</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td></td>
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<tr>
<td>Fluorouracil</td>
<td>36</td>
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<tr>
<td>Cyclosporine</td>
<td>37</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>22, PS</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>23</td>
</tr>
<tr>
<td>Hypernatremia</td>
<td>PS</td>
</tr>
<tr>
<td>Leukodystrophy</td>
<td>25, 38</td>
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<tr>
<td>Renal failure</td>
<td>23</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>39</td>
</tr>
<tr>
<td>Hypertension or preclampsia</td>
<td>40, 41</td>
</tr>
</tbody>
</table>

Abbreviation: PS, present study.

The MRI-documented splenium changes may be associated with confusion, ataxia, seizure, hemispheric disconnection findings, and dysarthria. The most common clinical finding was altered mental status. The triad of tremor, dementia, and death as described in patients with Marchiafava-Bignami disease was not seen.42 Diagnoses associated with splenium abnormalities varied markedly (Table 1). More important, DWI often showed other areas of involvement, particularly the posterior limbs of the internal capsules. The DWI demonstrated splenium changes markedly better than other MRI sequences or computed tomograms.

Reporting bias limits the usefulness of the study. Descriptions of patient symptoms, particularly of hemispheric disconnection or psychiatric findings, were sparse. In a literature-based case series, reported causes or clinical findings may not parallel what is most common. Follow-up MRI was rare, and few reports documented ADC values.

**POSSIBLE INJURY MECHANISMS**

The DWI signal changes suggest restricted movement of free water. The ADC values help clarify this restriction: reduced ADC values, as seen in 11 patients, suggest cytotoxic edema; ADC value increases (1 patient) suggest vasogenic edema.26,43,44 Patients with increased and decreased splenium ADC values may normalize with additional imaging, perhaps implying an absence of cytotoxic edema. Both ADC reduction and subsequent reversal are uncommon; associated diagnoses include hemiplegic migraine, venous sinus occlusion, and seizure.26,44 Splenium injuries should be added to this list.

In healthy patients who underwent MRI T2 relaxation studies, the splenium and posterior limb of the internal capsule displayed heterogeneity in water content; however, comparison tissue myelin water content was higher.45 The splenium may have easily perturbed cellular fluid mechanics when compared with surrounding tissues. Origins associated with splenium injury, including renal failure, hyponatremia, hypernatremia, hypoglycemia, infection, altitude sickness, and thiamine deficiency and alcoholism, can compromise cellular fluid regulation. How generalized convulsions might contribute to splenium DWI and ADC changes is harder to explain.

Convulsions might transiently impair available glucose, leading to brief, reversible failures of cellular fluid regulation. A similar mechanism could explain why hypoglycemic patients develop reversible splenium changes. Alternatively, antiepileptic drug toxicity or level fluctuations combined with changes in salt homeostasis and resultant myelin edema are other suggested mechanisms.26-28

Not all MRI findings reversed. Persisting changes included cystic lesions within the splenium, although pathologic correlation was limited.58 Magnetic resonance spectroscopy suggests that lactate levels can be abnormal and may resolve over time; in patient 5, however, no spectroscopic changes were seen.7

**CONFUSION, MUTISM, AND HALLUCINATIONS: WHAT IS THE ROLE OF THE SPLENIUM?**

Thirty-five of the patients had confusion and delirium, and hallucinations occurred in at least 4 patients. Patient 2 is unique, because the presentation included catatonia, increased muscle tone, waxy posturing, and an amobarbital response, features similar to catatonic schizophrenia. Splenium pathologic findings from patients with schizophrenia may show increased fiber thickness and preservation of axonal fiber density.46-48 Neuroimaging of new-onset schizophrenia demonstrates differing splenium size and diffusion tensor imaging anisotropy.49 Both agenesis of the corpus callosum and
schizophrenia in patients suggest that disrupted interhemispheric communication predisposes to behavioral change and psychosis. 50

Mutism, hallucinations, psychosis, and hemispheric disconnection are potentially more specific findings of splenium compromise. Still unclear is if and how the splenium regulates mutism or hallucinations. Perhaps the right and left hemispheres generate independent nonsense, the censure of which is necessary and normal and requires an intact splenium.

IS THERE A SPLENIUM SYNDROME?

From this series, nonspecific common findings, such as ataxia, dysarthria, increased tone, and delirium, do not easily localize. More important, splenium injuries in 7 of 9 patients occurred, with subtle changes evident in the posterior limbs of the internal capsule. Damage to these corticospinal pathways could result in marked dysarthria, ataxia, and increased tone. What surprised us was that findings of hemispheric disconnection were not common, potentially illustrating reporting bias. Prospective, descriptive studies that used DWI inclusion criteria might clarify this concession.

PROPOSED EVALUATION

Splenium changes evident on MRI are not incidental. Although infrequently associated with death, the finding can suggest treatable causes. A detailed history with re-
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