Total Mismatch
Negative Diffusion-Weighted Imaging but Extensive Perfusion Defect in Acute Stroke

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Background and Purpose—The perfusion-weighted imaging (PWI)/diffusion-weighted imaging (DWI) mismatch may identify patients who benefit from thrombolysis. However, some patients exhibit a “total mismatch,” ie, negative DWI but extensive PWI defect. We aimed to assess clinical and MRI data of these patients.

Methods—From June 2007 to December 2008, patients with anterior circulation ischemic stroke were evaluated for a “total mismatch” profile. MRI was performed at admission and at day 1. The score was assessed at baseline and the modified Rankin scale score was assessed at day 30.

Results—Among 52 patients, 3 showed a total mismatch with arterial occlusion confirmed on magnetic resonance angiography. All had fluctuating symptoms (National Institutes of Health Stroke Scale scores, 0 to 10) and received intravenous tissue plasminogen activator. Day 1 DWI disclosed minimal changes in all patients. Outcome was favorable in all patients (day 30 modified Rankin scale, 0–1).

Conclusion—PWI may be helpful for treatment decisions in patients without DWI damage and fluctuating clinical course. (Stroke. 2009;40:3400-3402.)

Key Words: mismatch ■ MRI ■ stroke ■ thrombolysis

The use of perfusion-weighted imaging (PWI)—diffusion-weighted imaging (DWI) mismatch in acute ischemic stroke was suggested in the 1990s.1 Multiparametric MRI can identify patients who may benefit from thrombolysis within and beyond 3 to 4.5 hours after symptoms onset.2 However, recent studies demonstrated that the PWI/DWI mismatch only approximates the ischemic penumbra.3 The complexities associated with PWI have prompted other imaging paradigms. The clinical diffusion and magnetic resonance angiography (MRA) diffusion mismatch were suggested as surrogates for penumbra.4,5

In patients without DWI damage, diagnosis of ischemic stroke relies on clinical features, MRA and PWI. Symptoms of acute stroke can be confusing and distal branch occlusions may be missed by MRA. Thus, PWI may provide relevant information in this setting. We aimed to assess the clinical and MRI characteristics of patients with “total mismatch”: negative DWI and extensive perfusion defect.

Table. Clinical and MRI Features

<table>
<thead>
<tr>
<th>Patient</th>
<th>N/Gender/Age</th>
<th>Day 0 NIHSS Fluctuations*</th>
<th>Occlusion Level</th>
<th>Mean TTP Delay</th>
<th>Mean CBF Ratio</th>
<th>tPA Treatment Delay</th>
<th>Day 1 NIHSS</th>
<th>Recanalization</th>
<th>Day 1 DWI/PWI</th>
<th>mRS, Day 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/77</td>
<td>6/1/6</td>
<td>Left MCA M2</td>
<td>5.6 sec</td>
<td>0.54</td>
<td>215 min</td>
<td>2 Complete</td>
<td>Minimal</td>
<td>lesions/normal</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2/M/29</td>
<td>8/2/8</td>
<td>Left MCA M2</td>
<td>8.0 sec</td>
<td>0.51</td>
<td>135 min</td>
<td>3 Complete</td>
<td>Minimal</td>
<td>lesions/normal</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>3/F/60</td>
<td>10/0/10</td>
<td>Right MCA M2</td>
<td>7.0 sec</td>
<td>0.43</td>
<td>200 min</td>
<td>2 Partial</td>
<td>Minimal</td>
<td>lesions/abnormal</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

*NHISS scores during each episode of symptoms fluctuations.

CBF indicates cerebral blood flow; F, female; M, male; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; tPA, tissue plasminogen activator; TTP, time-to-peak; MCA, middle cerebral artery occlusion, M2 level.

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Subjects and Methods

Patients
From June 2007 to December 2008, patients with symptoms of acute ischemic stroke were prospectively collected in our MRI database. Inclusion criteria were as follows: (1) intravenous tissue plasminogen activator-treated patients with MRI performed within 6 hours of symptoms onset or conservatively treated patients undergoing imaging within 12 hours of symptoms onset; (2) acute MRI completed before initiation of tissue plasminogen activator; and (3) DWI or PWI consistent with acute anterior circulation ischemic stroke. Exclusion criteria were: (1) unknown time of onset; (2) intracranial hemorrhage on MRI; (3) lacunar stroke; and (4) posterior circulation stroke. The National Institutes of Health Stroke Scale score was assessed at baseline and at days 1 and 30, and the modified Rankin scale at day 30. All patients had routine diagnostic work-up. The study was approved by our local ethical committee and all patients gave informed consent.

MRI
MRI was performed at admission and day 1 with a 1.5-T imager (Siemens Avanto), including the following sequences: (1) time-of-flight MRA; (2) T2*; (3) echoplanar DWI (b-values=0 and 1.000 sec/mm²); and (4) echoplanar PWI, using bolus passage-of-contrast with 0.1 mmol/kg of gadopentetate dimeglumine. Perfusion maps were calculated from the concentration-time curve. Time-to-peak refers to the time between the first T2*-weighted measurement and bolus peak. Mean time-to-peak delays were assessed within the time-to-peak lesion outline and normal contralateral hemisphere. Mean cerebral blood flow within time-to-peak lesion was evaluated as a ratio to contralateral hemisphere. Recanalization was classified as absent, partial, or complete on day 1 MRA.

Results
One hundred nine patients underwent MRI because of suspicion of acute anterior ischemic stroke during the study period. After exclusion of patients with intracranial hemorrhage, stroke mimics, or posterior circulation stroke (n=57), 52 patients were included in the MRI database. Among these, 3 exhibited an isolated perfusion defect without DWI damage. All 3 patients presented with fluctuating symptoms related to middle cerebral artery M2 branch occlusion and were treated by intravenous tissue plasminogen activator. Outcome was favorable in all patients (day 30 modified Rankin scale, 0–1). Clinical and MRI features are summarized in the Table and Figure.

Discussion
We report a rare MRI profile in which no DWI lesion is seen, whereas MCA branch occlusion and PWI defect are demonstrated early after stroke onset. Recurrent, fluctuating symptoms were characteristic of all patients.

Negative DWI has been reported in 2% to 7% of patients with a final diagnosis of stroke. Two scenarios may explain negative DWI in these patients: (1) moderate hypoperfusion not severe enough to produce a diffusion lesion; and (2) DWI lesion reversal attributable to recanalization; however, this explanation is inadequate in our cases, because arterial occlusion and hypoperfusion were still present. The former scenario therefore likely underlies early “total mismatch.” In total mismatch, perfusion may lie just below the penumbra threshold, delaying the development of the DWI lesion while still causing symptoms; the clinical fluctuations may be attributable to parts of the hypoperfused tissue going in and out of penumbra because of fluctuating local pressure from leptomeningeal collaterals and possibly metabolic factors such as depolarization waves.
while exhibiting a dramatic perfusion defect. Patients with unstable or regressing deficits have an uncertain fate if left untreated, with some being at risk for secondary deterioration. Sustained hemodynamic exposure may contribute to early neurological deterioration, possibly through recruitment of oligemic tissue into the penumbra. Moreover, in patients with fluctuating symptoms, PWI may be used to confirm persistent arterial occlusion, notably for distal clots that may be missed on MRA. A scoring system such as the National Institutes of Health Stroke Scale may fail to reflect the full severity of underlying hemodynamic and tissular abnormalities. Thus, with a more accurate depiction of tissue at risk, PWI can be of particular benefit in unstable cases with negative DWI.

The lack of truly quantitative cerebral blood flow assessment inherent to PWI techniques precluded a definite identification of penumbral and oligemic tissue. However, the time-to-peak delays and cerebral blood flow ratios measured in our patients would appear to be within the penumbral range.

In conclusion, we report patients with total mismatch who had a favorable outcome after intravenous thrombolysis. Additional prospective data are required to delineate the prognostic and therapeutic implications of this MRI profile.

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Disclosures

None.

References

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