Reversal of Dense Signs Predicts Recovery in Acute Ischemic Stroke

Pitchaiah Mandava, MD, PhD; Thomas A. Kent, MD

Background and Purpose—The presence of computed tomography dense signs in acute ischemic stroke indicates thrombosis. We sought to ascertain whether reversibility of these signs provides additional prognostic information.

Methods—Baseline and follow-up imaging was obtained from 18 patients who had received intravenous abciximab and heparin as part of an ongoing safety study in acute ischemic stroke. Presence of signs and their reversal were assessed and correlated with mortality and 90-day outcome.

Results—Fourteen of the 18 patients had dense dot signs in the middle cerebral or dense signals in the basilar artery on baseline computed tomography. The signs reversed in 7 (group 1) and persisted in 7 (group 2). Mean baseline National Institutes of Health Stroke Scale did not differ. All 7 in group 1 were alive at 90 days, with 3 of 7 alive in group 2. Ninety-day modified Rankin Scale was lower in group 1 (1.9±1.57) compared with group 2 (4.6±1.9; P=0.01).

Conclusions—The reversal of dense signs predicts a much better outcome than its persistence. These signs should receive additional attention for both their diagnostic and prognostic importance. (Stroke. 2005;36:e2490-e2492.)

Key Words: antithrombotic agents • computed tomography • platelet glycoprotein GpIIb-IIIa complex • stroke, acute • thrombolysis

A dense dot sign in the distal branches of middle cerebral artery (MCA) in the Sylvian fissure on head computed tomography (CT) in acute ischemic stroke is highly suggestive of thrombosis of these branch vessels.1 Cerebral angiographic studies indicate that the presence of this sign on CT had a high specificity and positive predictive value for an acute occlusion of M2/M3 branches of MCA.2 Although less widely reported, a hyperdense basilar artery (BA) also reflects thrombosis, as well as poor prognosis if untreated.3

The frequency of resolution of the dense signs and its clinical importance has not been reported. We followed the progression of these dense signs in patients who received abciximab (ReoPro) and heparin4 for acute ischemic stroke.

Methods

Patients with moderate to severe strokes who were postinvasive procedure or anticoagulated have been treated with abciximab and heparin after informed consent at our institutions as part of an ongoing assessment of its safety in patients ineligible for intravenous recombinant tissue plasminogen activator. Details and outcomes from the first 14 patients in this series have been reported with no treatment-associated serious adverse events.4 Mean time to treatment was 5.5±3.01 hours.

Brain CT scans were performed for clinical use before and after treatment. The majority of CT scans were performed with 2.5- to 3.0-mm slice thickness of the ventral 20 to 25 slices for better visualization of the posterior-fossa and dorsal slices either 5- or 7.5-mm thick. Patients received intravenous abciximab (0.20 mg/kg bolus and infusion of 0.05 μg/kg per minute over 12 hours) plus heparin as clinically indicated. National Institutes of Health Stroke Scale (NIHSS) before initiation of treatment and up to 90 days were recorded as modified Rankin Scale.

Dense dot signs in branches of MCA and hyperdense signals in the BA were assessed by investigators blind to outcome. Any discrepancies were resolved by joint review and resulted in a decision in all of the cases. Hyperdense MCA signs5 were also noted, but there was less agreement (data included in Table I, available online only at http://www.strokeaha.org). Hounsfield units (HU) in ovoid regions of interest of the dense signs and in comparable regions at follow up were obtained by the method of Koo et al.6 Multiplanar reformattting and postprocessing of CT images were performed on an eFilm workstation (version 1.9). Student t tests were performed using SigmaPlot 8.0. Institutional review board permission was obtained to report these findings.

Results

Reversal of Dense Sign

Fourteen of 18 patients (78%) had dense signs. Four dense signs were in the BA, and the remainder of dense dot signs was in the MCA. On repeat CT, 7 of 14 patients had resolution of the dense sign as determined by visual inspection (group 1), whereas it did not resolve in 7 (group 2). HU was lower between pretreatment and posttreatment CT scans in group 1 than in group 2. The Table lists baseline characteristics and outcomes. An example of a dense sign in the BA and its reversal are seen in Figure 1 compared with a persistent dense sign in Figure 2. Figure 3 shows an example...
of a persistent Sylvian fissure dot sign and associated large infarction.

Outcome
There were no differences in baseline NIHSS between groups (Table). Four patients in group 2 (57%) died before completion of day 90. Ninety-day NIHSS was significantly lower in group 1 than group 2, as was modified Rankin Scale. Baseline serum glucose values, an important prognostic indicator, trended lower in group 1 than group 2 but was not significantly different.

Discussion
In our series, resolution of a dense sign on follow-up CT scan in BA and MCA predicted good functional recovery and poor

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1, mean±SD</th>
<th>Group 2, mean±SD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline NIHSS</td>
<td>22.3±9.0</td>
<td>24.7±2.4</td>
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<tr>
<td>Baseline serum glucose, mg/dL</td>
<td>128±29.7</td>
<td>172±73.6</td>
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<tr>
<td>Initial HU of dense sign</td>
<td>51.8±8.66</td>
<td>47.73±6.78</td>
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<tr>
<td>Follow-up HU of dense sign</td>
<td>35.7±6.98</td>
<td>50.6±10.46</td>
<td>0.008</td>
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<td>Change in HU</td>
<td>-16.2±6.33</td>
<td>2.8±5.96</td>
<td>&lt;0.001</td>
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<td>90-day or last NIHSS</td>
<td>5.3±3.63</td>
<td>15.9±7.63</td>
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<tr>
<td>90-day modified Rankin Scale</td>
<td>1.9±1.57</td>
<td>4.6±1.9</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Figure 1. A, Noncontrast head CT. Note high intensity signal (HU 60) in the BA (notched arrow and left inset). The right inset is a coronal multiplanar reformatted image. Note the intense signal in the distal BA (arrow). Baseline NIHSS was 37. B, Follow-up head CT. Note the BA signal is now isointense (HU 38; arrow). An early right pontine hypodensity is also visible (arrowhead). The right inset is a coronal multiplanar reformatted image illustrating lack of intense signal (arrow). Follow-up NIHSS was 12.

Figure 2. A, Noncontrast CT of the head with an intense signal (notched arrow; HU:58) in the BA. Baseline NIHSS was 26. The right inset is a coronal multiplanar reformatted image showing an intense signal in the BA (straight arrow). B, Follow-up CT shows persistent dense signal in the BA (notched arrow; HU:71). The right inset multiplanar reformatted image shows increase in the length of the intense signal suggesting thrombus extension (straight arrow). This patient died 4 days after stroke.

Figure 3. A, CT of the head with an intense signal (notched arrow; HU:42) in the Sylvian fissure of a patient with baseline NIHSS of 26. B, Follow-up CT shows persistent dense signal in the Sylvian fissure (notched arrow; HU:49). This patient died after 12 days.
outcome for those in whom the sign did not reverse. Small sample size and lack of randomization precludes us from determining whether this resolution represents spontaneous or treatment-augmented recanalization; nor do we know whether rethrombosis was a factor in group 2.

Our series had a higher incidence (78%) of dense signs than reported previously.1,2 This could represent selection bias, because our treatment protocol addresses moderate to severe stroke and emphasized large vessel or cardioembolic etiology given that many of our patients had previous cardiac or vascular procedures. We also paid particular attention to dense signals in the BA, signs not usually addressed in other reports.

Although reversal of dense signs has not been correlated with recovery, the presence of dense signs appears to have prognostic value.2,3 Leary et al2 did show that the dense dot sign could disappear with intraarterial thrombolytic treatment, but the frequency of reversal was not stated. Other factors, such as dose and longer treatment intervals after intraarterial therapy, may make reversibility of the dense sign less predictive of outcome than as seen here after intravenous therapy. The high incidence of the sign in both the MCA and the BA in this moderate to severe stroke population suggests that more attention should be paid to this potential prognostic indicator.

References
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