Aortic Dissection as a Possible Underlying Cause of Acute Ischemic Stroke

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Ischemic stroke is caused by various pathological conditions. The etiology can be categorized into 3 major mechanisms: cardioembolism, large-artery atherosclerosis and small-vessel occlusion, and others (uncommon or undefined etiology). Aortic dissection is not a major, but possible cause of ischemic stroke. If patients do not present with typical symptoms of aortic dissection, physicians may not take such a hidden disorder into consideration as a possible underlying cause of ischemic stroke. Although aortic dissection is an uncommon cause of ischemic stroke, neurologic manifestations are not rare in patients with aortic dissection. Neurologic deficits involving the brain, spinal cord, or peripheral nerves have been reported to occur in 13–42% of patients with aortic dissection. Among them, ischemic stroke is the most frequent complication, which affects 6–32% of patients with aortic dissection.

Aortic dissection can cause abrupt occlusion or narrowing of proximal lesions of the extracranial carotid or vertebral arteries branching from the aorta. The prevalence of involvement of supra-aortic branches in aortic dissection was reported as 29% by postmortem investigation or 43% by imaging or intraoperative visualization. In particular, carotid circulation (81%) and right-sided arteries (69%) are often affected. There are 2 possible mechanisms for ischemic stroke secondary to aortic dissection. First, dissection obstructs blood flow through the true lumen of branching arteries, thus reducing cerebral perfusion and eventually causing brain tissue damage. Second, in the case of reentry into the true lumen, thrombus is transferred to the distal portion of the arteries and causes thromboembolism. Gaul et al reported that in stroke patients with aortic dissection, supra-aortic arteries were involved in 62.5%, whereas others suffered from ischemic stroke without extension of the dissection toward the supra-aortic vessels, indicating that stroke is caused by an embolic mechanism.

Most patients with aortic dissection present with sudden onset of chest pain and this typical or distinctive pain is indicative of aortic dissection. However, dissection without pain may occur. The frequency of painless aortic dissection is 6–15%, whereas others suffered from ischemic stroke without extension of the dissection toward the supra-aortic vessels, indicating that stroke is caused by an embolic mechanism. In the case of aortic dissection complicated by ischemic stroke, the presentation of pain may be less frequent. A previous study showed that only two-thirds of patients had chest pain, although most patients without initial neurologic symptoms experienced pain. Chest pain at onset may be missed in patients with acute ischemic stroke.

### Table

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Sex</th>
<th>SBP/DBP, mmHg</th>
<th>NIHSS</th>
<th>Affected site</th>
<th>Chest symptoms</th>
<th>Chest X-ray</th>
<th>Carotid ultrasonography</th>
<th>Outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>54</td>
<td>M</td>
<td>106/55</td>
<td>–</td>
<td>L</td>
<td>No pain</td>
<td>No MW</td>
<td>–</td>
<td>Death</td>
<td>8</td>
</tr>
<tr>
<td>44</td>
<td>M</td>
<td>–</td>
<td>18</td>
<td>R</td>
<td>Left flank and back pain after rt-PA therapy</td>
<td>–</td>
<td>CCA dissection</td>
<td>Independent walking at 1 m</td>
<td>9</td>
</tr>
<tr>
<td>56</td>
<td>F</td>
<td>108/56</td>
<td>16</td>
<td>R</td>
<td>Midsternal pain</td>
<td>No MW</td>
<td>CCA occlusion</td>
<td>mRS 4 at 3 m</td>
<td>10</td>
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<tr>
<td>76</td>
<td>F</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>No pain</td>
<td>–</td>
<td>–</td>
<td>Death</td>
<td>5</td>
</tr>
<tr>
<td>69</td>
<td>F</td>
<td>140/90</td>
<td>8</td>
<td>R</td>
<td>Chest discomfort*</td>
<td>MW</td>
<td>–</td>
<td>NIHSS 0 at 3 m</td>
<td>11</td>
</tr>
<tr>
<td>72</td>
<td>F</td>
<td>160/110</td>
<td>16</td>
<td>R</td>
<td>No pain</td>
<td>No MW</td>
<td>–</td>
<td>Death</td>
<td>12</td>
</tr>
<tr>
<td>81</td>
<td>F</td>
<td>174/122</td>
<td>22</td>
<td>R</td>
<td>No pain</td>
<td>MW</td>
<td>CCA dissection</td>
<td>mRS 3 at 3 m</td>
<td>13</td>
</tr>
<tr>
<td>55</td>
<td>M</td>
<td>82/41</td>
<td>6</td>
<td>R, L</td>
<td>Retrosternal discomfort*</td>
<td>MW</td>
<td>CCA dissection</td>
<td>No symptom at 18 m</td>
<td>14</td>
</tr>
<tr>
<td>70</td>
<td>M</td>
<td>137/92</td>
<td>9</td>
<td>R</td>
<td>Dorsal discomfort after rt-PA therapy</td>
<td>No MW</td>
<td>CCA dissection</td>
<td>NIHSS 2 at 12 m</td>
<td>15</td>
</tr>
</tbody>
</table>

*Symptoms were retrospectively confirmed after thrombolytic therapy. CCA, common carotid artery; L/R, left/right; mRS, modified Rankin scale; MW, mediastinal widening; NIHSS, National Institute of Health Stroke Scale; rt-PA, recombinant tissue plasminogen activator; SBP/DBP, systolic/diastolic blood pressure.

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impaired consciousness or aphasia, because of difficulty in inquiring about onset symptoms. Moreover, syncope occurs in 6–19% of patients with aortic dissection,\(^2\)\(^–\)\(^5\)\(^7\) and this may also contribute to unawareness of aortic dissection.

If ischemic stroke develops secondary to aortic dissection, thrombolytic therapy is deleterious. Table 1 shows previous case reports of ischemic stroke treated by thrombolytic therapy,\(^5\)\(^–\)\(^15\) despite aortic dissection. Thrombolytic potential causes critical adverse effects, such as cardiac tamponade or hemothorax. In Japan, a nationwide post-marketing survey was performed after approval of alteplase as a treatment for acute ischemic stroke. From October 2005 to September 2006, data sheets obtained from 2,069 ischemic stroke patients who were treated with intravenous alteplase disclosed that 10 patients died of exacerbation of thoracic aortic dissection or rupture of thoracic aortic aneurysm. Currently, intravenous thrombolytic therapy with alteplase is contraindicated for patients with aortic dissection.

To diagnose underlying aortic dissection in patients with ischemic stroke at an early stage, chest or back pain at onset needs to be confirmed with the possibility of this disease in mind. A cautious physical examination is also required regarding pulse or blood pressure differentials and a murmur of aortic regurgitation. A chest X-ray should be routinely performed to evaluate mediastinal or aortic widening. Further, carotid ultrasonography is indispensable for identifying arterial dissection because the non-invasive test can be performed at the bedside without wasting time. Previous case reports (Table 1) implicate the importance of these procedures before starting thrombolytic therapy.

The diagnosis of aortic dissection is confirmed by computed tomography (CT), magnetic resonance imaging, transthoracic and transesophageal echocardiography, or aortography. Sensitivity of these diagnostic tests is 65–100% and specificity is 85–100%.\(^16\) Although each diagnostic test has advantages and limitations,\(^16\) tests are performed considering their availability, as well as urgency and acceptability of ischemic stroke patients. Definitely ruling in and out acute aortic syndrome is important. Unenhanced CT can rule in acute aortic syndrome but does not have good properties regarding ruling out acute aortic syndrome.\(^17\) Therefore, contrast-enhanced CT may be required to definitely rule out aortic dissection. However, use of contrast medium is often avoided to reduce the time to administer recombinant tissue plasminogen activator in patients with ischemic stroke.

In this issue of the Journal, Yoshimuta et al\(^18\) suggest the usefulness of D-Dimer in the early diagnosis of aortic arch dissection causing ischemic stroke. They retrospectively investigated the D-Dimer values within 24 h of onset in 1,236 consecutive patients with ischemic stroke, among whom 9 patients suffered concomitant Stanford type A aortic arch dissection. They concluded that a cut-off value of 6.9 \(\mu \text{g/ml}\) of D-Dimer discriminated aortic dissection with a sensitivity of 100%, specificity of 94.8%, positive predictive value of 14.7%, and negative predictive value of 100% in patients with acute ischemic stroke. Because the prevalence of underlying aortic dissection is low overall in ischemic stroke patients, the positive predictive value is low. Therefore, D-Dimer above the cut-off value does not necessarily indicate the presence of aortic dissection, although a high D-Dimer value may indicate a possibility. In contrast, when D-Dimer is below the cut-off value, involvement of aortic dissection may be less likely, although a definite rule out is still required. Recently, a new clinical policy for thoracic aortic dissection was published by the American College of Emergency Physicians.\(^19\) According to this policy, the use of D-Dimer to rule out aortic dissection was assigned a Level C recommendation. The prognosis of patients with ischemic stroke secondary to aortic dissection is often catastrophic. Further study is required to validate the usefulness of D-Dimer in the early diagnosis of underlying aortic dissection in patients with acute ischemic stroke.

References