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Intracranial and extracranial arterial dissection presenting with ischemic stroke: Lesion location and stroke mechanism

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ABSTRACT

Background and purpose
Although cervicocranial artery dissections (CADs) are common causes of ischemic stroke in young individuals, anatomical locations and mechanisms of ischemic strokes are still unclear.
We evaluate the prevalence, location, and pathogenic mechanisms of ischemic stroke caused by CADs.
Methods: We reviewed CAD patients who presented with acute (<7 days) ischemic events and who had undergone diffusion weighted magnetic resonance imaging (MRI) and appropriate vascular imagings (MR angiography, computed tomography angiography, digital subtraction angiography, and high-resolution MRI). Stroke mechanisms were categorized as artery-to-artery (AA) embolism, local branch occlusion, in situ thrombotic occlusion and hemodynamic impairment.
Results: One hundred and thirty-five patients with cerebral infarcts (n = 125) or transient ischemic attacks (n = 10) were included. The locations of 159 dissected vessels were: 77 vertebral, 29 internal carotid, 24 middle cerebral, 12 basilar, eight posterior inferior cerebellar, five anterior cerebral, and four posterior cerebral arteries. Among stroke mechanisms, A–A embolism (n = 70, 55.5%) was the most common followed by local branch occlusions (n = 40, 31.7%) and in situ thrombotic occlusions (n = 8, 6.3%). Intracranial CADs were more common (89 vs. 44), less often associated with trauma (21.3% vs. 40.9%, p = 0.018) and A–A embolism (32.9% vs. 97.6%, p < 0.001), and more often treated with intravenous thrombolysis (15.7% vs. 2.3%. p = 0.021) than extracranial CADs.
Conclusions: In our cohort, intracranial CADs are more common than extracranial CADs, and the vertebral artery is the most frequently involved site. Although A–A embolism is the main stroke mechanism, local branch occlusion is another important stroke mechanism.

1. Introduction

Although cervicocranial artery dissections (CADs) are a common cause of ischemic stroke in young adults, [1] the locations of the CADs are disputed. While internal carotid artery dissections (ICA-D) are recognized as being the most common, [2,3] some reported that the vertebral artery dissection (VA-D) is equal to or more common than ICA-D [4–6]. Moreover, while extracranial CADs are considered the most common, [5,7] recent studies showed a higher frequency of intracranial CADs than extracranial CADs [4]·[8]. These previous studies used a relatively small number of patients or focused only on particular vessels. In addition, although artery-to-artery (A-A) embolism [9–11] was identified as an important stroke mechanism for ICA-D, the stroke mechanisms of CADs occurring in other locations have not been investigated. The aim of the present study was to elucidate the anatomical locations of CADs that cause ischemic stroke and transient ischemic attack (TIA) and the relevant pathogenic mechanisms using modern imaging methods.

2. Methods

2.1. Subjects

We retrospectively reviewed prospectively registered, consecutive patients with CADs admitted to the Department of Neurology, Asan Medical Center, from January 2005 to June 2014. All patients underwent appropriate etiological workups including various vascular imaging and heart evaluations. Included were the patients; 1) with CADs identified by appropriate imaging methods (for definition, see below); 2) with ischemic stroke identified by diffusion-weighted imaging (DWI) or TIA within 7 days after symptom onset. TIA was defined as a brief (<24 h) episode of focal neurological symptoms of cerebral origin without DWI lesions. Because the purpose of our study was to assess the stroke mechanism, patients presenting with headache, neck pain, cranial nerve

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palsy, brainstem compression symptoms or hemorrhages were excluded.

2.2. Imaging assessment of CADs and stroke mechanisms

CAD diagnoses were based on combinations of the findings of various imaging methods, including magnetic resonance imaging (MRI), MR angiography (MRA), computed tomography angiography (CTA), Digital subtraction angiography (DSA), and high-resolution vessel-wall MRI (HR-MRI). Duplex sonography was additionally performed, especially on proximal ICA-D or VA-D patients.

HR-MRI was performed in patients with vascular stenosis but with uncertain diagnosis, e.g., young patients without vascular risk factors, with the use of the Achieva 3.0-T HR-MRI scanner (Philips Healthcare, Eindhoven, Netherlands). Three-dimensional time-of-flight MRA, T1-weighted, T2-weighted, proton density-weighted, and contrast-enhanced proton density images were obtained. The parameters of the imaging sequences were as follows: T1W (repetition time/echo time, 600/12 ms; slice thickness, 1.5 mm; 512 × 512 matrix); T2W (repetition time/echo time, 3000/80 ms; slice thickness, 1.5 mm; 512 × 512 matrix); and proton density (repetition time/echo time, 1000/20 ms; field of view, 200 × 200 mm; matrix size, 720 × 720 matrix; slice thickness, 1 mm; inter-slice gap, 0.5 mm; average, 1). Sagittal images were obtained perpendicular to the dissected vessel. Post-enhanced T1-weighted enhanced image were taken using gadolinium unless contraindicated.

CAD diagnosis was made with a modification of previous criteria [12]. We defined CADs when at least one of the following findings was revealed by any of the vascular imaging techniques: double lumen (the presence of a false lumen or an intimal flap), dissecting aneurysm (pseudoaneurysm) at a non-branching site, intramural hematoma, flame-shaped non-atherosclerotic occlusion, pearl-and-string sign, and non-atherosclerotic tapered stenosis or occlusion.

The location of the dissection was dichotomized as “intracranial” when the dissection occurred in the petrous, cavernous, or clinoid segments of the internal carotid artery, the intradural segment of the vertebral artery, the middle cerebral (MCA-D), anterior cerebral (ACA-D), posterior cerebral (PCA-D), basilar (BA-D), and posterior inferior cerebellar (PICA-D) arteries, and “extracranial” when the dissection developed in the remaining portions of the internal carotid or vertebral arteries. A dissection involving both the extracranial and intracranial vessels was classified as “extracranial” partly because an intimal laceration usually occurs in the proximal part and partly because the mural hematoma usually extends in the direction of the bloodstream [7].

Trauma, that may be associated with CAD, was considered significant when it occurred <1 month before the onset of symptoms; it included 1) any direct mechanical impact to the neck/head region; or 2) any impact to the head with indirect involvement of the neck region; 3) mechanical activity causing extraordinarily increased intrathoracic pressure. Examples are whiplash injury, cervical manipulation therapy, heavy lifting, and extreme head movements [13].

After analyzing the DWI, angiographic, and clinical data, we classified stroke mechanisms as follows (Fig. 1): [14–16].

Artery-to-artery embolism: DWI shows small infarcts distal to the dissected vessel in the territory of the relevant artery. The infarct lesions are usually small, multiple, and scattered, and are often associated with perfusion deficits in the territory of the dissected vessel.

Local branch occlusion: The infarct is localized to the area adjacent to the dissected vessel, presumably because the orifice of one or more of the small perforators supplying the regions is occluded by local thrombus formation.

In situ thrombotic occlusion: The territorial infarction is caused by a relatively large artery occlusion or severe stenosis resulting from thrombus formation adjacent to the dissected vessel. Usually the lesions are confluent and large, but some portions may be preserved due to the development of collateral vessels.

Hemodynamic impairment: The DWI-identified infarcts are located in border zone areas, usually linear in shape, and are associated with perfusion deficits distal to the severely stenosed or occluded vessel. Symptoms are closely associated with a clinical history of hemodynamically disturbing conditions, such as recent bleeding, severe anemia, dehydration, or exhaustion. Because border zone areas are still argued in the posterior circulation, [17]. DWI findings were not considered in patients with posterior circulation dissection.

The radiological findings and CAD mechanisms were interpreted and determined by consensus among an experienced neuroradiologist and two stroke neurologists.

2.3. Statistical analysis

We compared demographics, imaging characteristics, and outcomes of patients with intracranial artery dissection to those with extracranial artery dissection using Pearson's chi-squared and Fisher's exact test for categorical variables and Student's *t* test for continuous variables. The threshold of significance was set at $p < 0.05$. All statistical analyses were performed using SPSS version 21.0 software (SPSS, Chicago, IL).

3. Results

3.1. Patient characteristics

We identified 135 consecutive patients with CAD (cerebral infarcts 125, TIAs 10), representing 1.49% of the ischemic stroke/TIA patients and 10.4% of the young (age < 45) patients (75 out of 721). There were 45 men and the ages ranged from 17 to 82 years (mean ± SD: 42.7 ± 13.7). Seventy-eight (57.8%) patients had preceding or concomitant head/neck pain. In patients with stroke, the median NIHSS score at admission was 2 (IQR of 0–7). A history of trauma, found in 37 (27.8%) patients, was more frequent in extracranial CAD patients (40.9%) than intracranial CAD patients (21.3%). HR-MRI was more often used in patients with intracranial CAD (44.9%) than extracranial CAD (11.4%). For vascular imaging, MRA was most often performed (93.3%) followed by DSA (65.9%), HR-MRI (34.1%), CTA (17.8%) and Duplex sonographies (16.3%) (Table 1). HR-MRI has been used since May 2008, after which the proportion of CAD patients increased from 1.22% to 1.63%.

3.2. Location of CADs and imaging characteristics

Overall, there were 159 dissected vessels including 77 VA-D, 29 ICA-D, 24 MCA-D, 12 BA-D, seven PICA-D, five ACA-D, and four PCA-D (Table 2). Among the 135 CAD patients, 89 (65.9%) had intracranial dissection, 44 (32.6%) extracranial dissection, and two (1.5%) had both (one patient with left extracranial VA-D and PICA-D, and another with left extracranial VA-D and right intracranial VA-D). Twenty-two (16.3%) patients had multiple dissections, involving two vessels in 20 patients, and three vessels in two patients. The most frequent pathognomonic imaging findings were an intimal flap (22.8%) followed by a double lumen (16.9%) and a dissecting aneurysm (15.6%). Extracranial CADs were more frequently associated with flame-shaped occlusion (15.9% vs. 1.1%, $p = 0.001$) and string sign (13.6% vs. 2.2%, $p = 0.009$) than intracranial CADs (Table 3).

3.3. Stroke mechanisms

Among the patients who showed DWI ischemic lesions, stroke mechanisms included 70 A-A embolisms (55.5%), 40 local branch

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