The Impact of Diagnosing Branch Atheromatous Disease for Predicting Prognosis

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Background: We had reported that, in the acute phase of the brain penetrating artery infarction, patients with branch atheromatous disease (BAD) tended to be worsened compared with the lacunar infarction (LI). Because no prospective study has been reported, we composed a multicenter study (Japan Branch Atheromatous Disease [J-BAD] Registry) in which patients of penetrating artery infarction were prospectively enrolled for exploring the clinical features of BAD. *Methods:* From the associated 9 hospitals, acute ischemic stroke patients were asked to be enrolled in the J-BAD Registry and classified into the lenticulostriate arterial (LSA) infarction (n = 124) and the pontine penetrating arterial (PPA) infarction (n = 42) groups. The clinical courses and the repeated magnetic resonance imaging findings were investigated. *Results:* Neurologic worsening was observed at a significantly higher rate in BAD compared with the LI patients in both the LSA and PPA groups ($P < .01$, 45.1% versus 22.6% and 46.7% versus 0%, respectively). In the LSA group, the enlargement of the ischemic lesion was significantly more frequent in BAD compared with the LI patients ($P < .01$, 66.2% and 34.0%, respectively). There was a significant relation between the enlargement of the lesion and the worsening of neurologic deficits ($P < .001$). Moreover, the clinical features, which predict the lesion enlargement, were BAD and older age. *Conclusions:* LSA infarction of BAD diagnosis or older age patients might show an increase of lesion size and a tendency of neurologic worsening. It could be important to discriminate BAD from other ischemic stroke subtypes, in regard to the prediction of prognosis. **Key Words:** Acute stroke—diagnosis—prognosis—MRI.

Introduction

In the acute phase of the brain penetrating artery infarction, some patients may have a worsening of neurologic deficits and/or an increase of the ischemic lesion regardless of intensive treatments. We had reported that branch atheromatous disease (BAD) patients tended to show the worsening more often than lacunar infarction (LI) patients.[1] However, the clinical entity of BAD has not been standardized. Some studies reported that the prognosis of BAD patients depends on the findings of imaging studies performed on admission.[1,2] Other reports compared the outcome of BAD and the size of ischemic lesion observed by repeatedly performed magnetic resonance imaging (MRI) T2-weighted images.[3-5] Because the lesion on the diffusion-weighted MR images (DWIs) may include not only the ischemic core but also

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Author contributions: T.N. analyzed all data and performed the statistical analysis; Y.Y. and M.T. equally participated in setting up and conducted this study. All J-BAD members contributed in collecting patients' data. The members of the J-BAD Steering Committee are listed in the Appendix.

All authors declare no conflict of interest.

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cytotoxic edema, the DWI–positive area will change in size over the course of time.[6,7] It is, therefore, necessary to investigate chronologic changes of the ischemic lesion in the MRI findings.

Here, there has been no report in which the clinical features of BAD were prospectively explored in a large-scale study. Therefore, we composed a multicenter study (Japan Branch Atheromatous Disease [J-BAD] Registry) in which patients of penetrating artery infarction were prospectively enrolled.[8] It has been explored whether diagnosing BAD based on an imaging study on admission and follow-up studies is appropriate for clinical diagnosis and whether it is meaningful for predicting patient outcome by assessing the relation between the original size of the lesion and the enlargement of the lesion in regard to clinical outcome.

Methods

This study was originally approved by the committee of medical ethics in the Saiseikai Central Hospital, Tokyo, and then independently approved by the ethical committee in each associated hospital.

For the J-BAD Registry, consented patients were prospectively enrolled from the associated hospitals from April 2011 to March 2012. The inclusion criteria were (1) the admission within 48 hours after onset, (2) an ischemic lesion, which was confirmed by the DWI on admission, localized in the cerebral lenticulostriate arterial (LSA) region or in the pontine penetrating arterial (PPA) region, (3) no evidence of cardioembolism, and (4) no evidence of critical vessel stenosis (>50% stenosis) of the responsible parent artery assessed by magnetic resonance angiography.

The diagnosis of BAD and LI was based on the previously reported criteria.[1,9] Briefly, the definition of BAD in the LSA region was that the lesion size was 15 mm or more in diameter on the axial picture showing its largest size and/or the lesion was observed in more than 3 axial pictures (at a slice thickness of 5 mm). Lesions, which were too small to meet the BAD criteria were defined as LI. The definition of BAD used in the PPA region was that the lesion extended from the ventral pontine surface to the deep pons. Lesions, which were localized in the deep pons, were defined as LI. The enlargement of ischemic lesion was defined as cases where the lesion size, which was assessed by MRI at the time of neurologic worsening or on the seventh day after onset, was horizontally and/or vertically larger compared with the size of the lesion on admission. The definition used for neurologic worsening was that the patient's score on the National Institutes of Health Stroke Scale increased more than 1 point within 7 days after the onset of medical treatments. The acute medical treatments in each hospital were adopted following the guideline.[10]

The following factors were defined as the clinical risks at onset: hypertension, diabetes mellitus, hyperlipidemia, smoking, and obesity. The severity of the periventricular hyperintensity lesion (PVH) was assessed following previously reported criteria.[11] The existence of atherosclerosis was defined as cases where arterial stenosis was observed in the responsible parent artery assessed by magnetic resonance angiography.

Statistical Analyses

Data are presented as mean ± standard deviation or as a number and percentage. The clinical characteristics were compared between LSA and PPA by the *t* test for mean variable and by the χ^2 test for percentage variable. The frequency of each risk was compared between the enlargement group and the stable group in both LSA and PPA by the χ^2 test. The severity of PVH was compared between the enlargement group and the stable group in both LSA and PPA by the Mann–Whitney *U* test. All statistical analyses were performed by JMP9 software (SAS Institute Inc, Cary, NC).

Results

Baseline Characteristics

A total of 180 patients were enrolled in this study. Because 14 cases had incomplete data, 166 cases were finally adopted for the analysis. One hundred twenty-four cases were classified into the LSA group and 42 cases were classified into the PPA group. Clinical characteristics are listed in Table 1. There was no significant difference in the distribution of risk factors between the 2 groups. The total numbers of LI and BAD patients were 65 and 101, respectively.

Lesion Size and Clinical Course

Our data showed that the enlargement of the lesion was observed in nearly half of all cases, but it was observed in a significantly higher percentage among BAD compared

Table 1. *Clinical characteristics of all patients*

	Total	LSA	PPA
n	166	124	42
Male/female	102/64	75/49	27/15
Age, y (mean ± SD)	71.7 ± 10.9	71.4 ± 11.6	71.8 ± 8.5
Hypertension (%)	139 (83.7)	102 (82.3)	36 (85.7)
Diabetes (%)	45 (27.1)	30 (24.2)	15 (35.7)
Dyslipidemia (%)	74 (44.6)	49 (39.5)	25 (59.5)
Obesity (%)	38 (22.9)	29 (23.4)	9 (21.4)
Smoking (%)	38 (22.9)	31 (25.0)	7 (16.7)

Abbreviations: LSA, lenticulostriate artery; PPA, pontine penetrating artery.