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Short Commentary

Clinical Course of Diabetes-Related Dementia

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Type 2 diabetes mellitus (DM) is a risk factor for dementia. However, a variety of mechanisms and underlying brain pathologies are involved in DM [1]. Most cases of dementia associated with DM are considered to be Alzheimer disease (AD) and vascular dementia (VaD). Recently, we proposed a dementia subgroup associated with specific DM-related metabolic abnormalities rather than AD pathology or cerebrovascular disease (CVD), referred to as diabetes-related Dementia (DrD) [2-4]. This type of dementia, showing neither CVD on magnetic resonance imaging (MRI) nor parietotemporal hypoperfusion on single photon emission computed tomography (SPECT), was clinically characterized by high hemoglobin A1c (HbA1c), long duration of diabetes, high frequency of insulin therapy, low frequency of apolipoprotein E4 carriers, less severe medial temporal lobe atrophy, more impaired attention and executive functions, and less impaired memory. These features are apparently different from those in AD and VaD. In our amyloid positron emission tomography (PET) studies, approximately 30% of patients with Diabetes-related dementia displayed amyloid positivity, indicating AD pathology, whereas the remaining patients displayed amyloid negativity, indicating non-AD pathology [5]. As many of the patients with clinically diagnosed Diabetes-related dementia are thought to have different neuropathologies from patients with AD, Diabetes-related dementia is expected to show different clinical courses from AD. In this study, we hence investigated differences in the clinical courses and cognitive progression between patients with Diabetes-related dementia and those with AD.

A total of 24 patients with AD associated with DM (AD+DM) and 29 with Diabetes-related dementia were enrolled in this study. Most of the patients were from our 2019 PET study [6]. After amyloid PET, the patients were followed longitudinally from 1 to 6 years (mean: 2.5 ± 1.4 years) in our memory clinic. All patients with AD met the criteria of probable AD based on the National Institute on Aging and Alzheimer's Association criteria [7], and displayed amyloid positivity on PET. The diagnosis of Diabetes-related dementia was based on the guidelines for the clinical diagnosis of Diabetes-related dementia [3]. Diabetes-related dementia patients displayed amyloid negativity. All patients displayed no definite CVD lesions on MRI that were causative of their cognitive impairment or dementia. The Ethics Committee of Tokyo Medical University approved the study protocol. All subjects gave written informed consent before participating in this study.

At first, among the patients who continued to visit the clinic, we compared annual Mini-Mental State Examination (MMSE) score changes [(last MMSE-baseline MMSE)/year] between the AD+DM group and the Diabetes-related dementia group. According to the annual MMSE score change (cut-off value=−2.0 points), they were divided into the fast progression group and the slow progression group. Next, regarding the patients who could not continue to visit the clinic, we investigated the reason of each patient. We compared the numbers of patients with admission to hospital (or death) owing to each medical complication (e.g., fall-associated injuries, bronchopneumonia, or other medical diseases) or institutionalization to nursing homes and others (e.g., owing to the relocation, health problems of the caregiver, or unknown reasons). Values were expressed as the mean ± S.D. Statistical analysis was performed using the Student t-test, χ^2 test, and Mann-Whitney U-test. A p-value of less than 0.05 was considered to indicate a statistically significant difference between the 2 groups.

Table 1 shows differences in demographics and clinical courses. There were no significant differences in age, sex, duration of dementia, education, baseline MMSE score, frequency of insulin therapy, and follow-up time from the PET study between the AD+DM group and the Diabetes-related dementia group. The Diabetes-related dementia group showed a significantly lower frequency of ApoE4 carriers, higher hemoglobin A1c level, and longer duration of diabetes than the AD+DM group. Rates of discontinuation of visits were similar (38% in the AD+DM group and 41% in the Diabetes-related dementia group). There were significantly fewer patients showing fast progression in the Diabetes-related dementia group than in the AD+DM group. On the other hand, significantly more patients were admitted to hospital or died in the Diabetes-related dementia group than in the AD+DM group.

We found that the Diabetes-related dementia group showed significantly slower progression of dementia and higher risk of admission to hospital or death than the AD+DM group. As patients in the Diabetes-related dementia showed less-well controlled glycemia, they have a higher risk of medical complications. Our previous study showed that patients with Diabetes-related dementia had a higher frequency of frailty [8] and dynapenia [9], such as muscle weakness and low gait speed, than AD patients with and without DM. These findings suggest that Diabetes-related dementia is likely to show

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adverse health outcomes, including falls, disability, admission, and death. Diabetes-related dementia is characterized by less severe brain damage with the absence of amyloid deposition and more severe physical disability, supporting our present results. Therefore, geriatric interventions are necessary for providing the appropriate therapy and care for patients with Diabetes-related dementia.

	AD+DM (n=24)	Diabetes-related dementia (n=29)
Age (years; mean ± S.D.)	79.3 ± 5.2	80.7 ± 5.9
Sex (men/women)	10/14	12/17
Duration of dementia (years; mean ± S.D.)	2.9 ± 0.8	3.1 ± 1.2
Education (years; mean ± S.D.)	12.3 ± 2.5	11.9 ± 2.6
Mini-mental state examination	22.4 ± 2.1	21.3 ± 2.4
ApoE4 carrier, n(%)	12 (50%)	3 (12%)**
HbA1c (%; mean ± S.D.)	7.3 ± 1.2	8.5 ± 1.4**
Duration of diabetes (years; mean ± S.D.)	13.3 ± 9.7	20.1 ± 10.9*
Insulin therapy, n(%)	5 (21%)	11 (38%)
Follow-up time after PET study (years; mean ± S.D)	2.6 ± 1.7	2.5 ± 1.2
Number of patients who continued their visits	15	17
Fast progression	9	2
Slow progression	6	15**
Number of patients who discontinued their visits	9	12
Hospital admission or death	2	9*
Institutionalization or others	7	3

Table 1: Differences in demographics and clinical courses of the patients.

HbA1c: hemoglobinA1c, PET: positron emission tomography, $p<0.05$,**$p<0.01$, compared with the AD+DM group.

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References

1. Biessels GJ, Staekenborg S, Brunner E, Brayne C, Scheltens P (2006) Risk of dementia in diabetes mellitus: A systemic review. Lancet Neurol 5: 64-74.

2. Fukazawa R, Hanyu H, Sato T, Shimizu S, Koyama S, et al. (2013) Subgroups of Alzheimer's disease associated with diabetes mellitus based on brain imaging. Dement Geriatr Cogn Disord 35: 280-290.

3. Hanyu H, Hirose D, Fukasawa R, Hatanaka H, Namioka N, et al. (2015) Guidelines for the clinical diagnosis of diabetes-related dementia. J Am Geriatr Soc 63: 1721-1722.

4. Fukasawa R, Hanyu H, Shimizu S, Kanetaka H, Sakurai H, et al. (2015) Identification of diabetes-related dementia: Longitudinal perfusion SPECT and amyloid PET studies. J Neurol Sci 349: 45-51.

5. Takenoshita N, Fukasawa R, Ogawa Y, Shimizu S, Umahara T, et al. (2018) Amyloid and tau positron emission tomography in suggested diabetes-related dementia. Curr Alzheimer Res 15: 1062-1069.

6. Takenoshita N, Shimizu S, Kanetaka H, Sakurai H, Suzuki R, et al. (2019) Clasification of clinically diagnosed Alzheimer's disease associated with diabetes based on amyloid and tau PET results. J Alzheimers Dis 71: 261-271.

7. McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack CR Jr, et al. (2011) The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 7: 263-269.

8. Hirose D, Hanyu H, Fukasawa R, Hatanaka H, Namioka N, et al. (2016) Frailty in diabetes-related dementia. Geriatr Gerontol Int 16: 653-655.

9. Tsugawa A, Ogawa Y, Takenoshita N, Kaneko Y, Hatanaka H, et al. (2017) Decreased muscle strength and quality in diabetes-related dementia. Dement Geriatr Cogn Dis Extra 7: 454-462.

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