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RESEARCH LETTER

Indicative biomarkers of Lewy body disease with oral sensory hallucinations in the older people

Oral sensory hallucinations (OSHs), referred to as oral cenesthopathy, are psychiatric symptoms predominantly observed in older individuals.[1] Nonvisual hallucinations, including OSHs, have been identified as clinical features that have potential to support the diagnosis of Parkinson's disease (PD) and dementia with Lewy bodies (DLB).[2,3] Since individuals with PD/DLB have alterations in the dopaminergic system due to alpha-synucleinopathy,[3,4] research suggests that OSHs may also be linked to these alterations.[3–5] However, the underlying pathophysiology of OSHs remains unclear.

Functional imaging modalities, such as dopamine transporter single photon emission computed tomography (DaT-SPECT) with ^{123}I-ioflupane as well as ^{123}I-metaiodobenzylguanidine (MIBG) cardiac scintigraphy, have shown promise in the early diagnosis of PD/DLB due to their ability to detect monoaminergic abnormalities caused by alpha-synucleinopathy even before the manifestation of overt clinical symptoms.[4,6–8] Although monoaminergic abnormalities, including dopaminergic dysfunction, have been linked to OSHs, no studies have explored the findings of DaT-SPECT and MIBG cardiac scintigraphy in individuals with OSHs. We conducted a retrospective case series to assess the results of these functional imaging modalities in patients presenting with OSHs.

We reviewed the medical records of patients who admitted to a specialized geriatric psychiatry unit between August 2018 and July 2022. Patients who exhibited OSHs were included in the study. DaT-SPECT and MIBG cardiac scintigraphy were conducted based on clinical decision to rule out prodromal PD/DLB, which can cause various psychiatric symptoms. DaT-SPECT was prioritized in the examinations in our hospital. The collected patient data included patient demographics, functional imaging outcomes, and diagnosis at the time of discharge. DaT-SPECT images were evaluated using the specific binding ratio (SBR). If patients' *Z*-scores were −2.00 or higher, compared to the average SBR of individuals of the same age and sex, they were considered normal. MIBG cardiac scintigraphy results were assessed based on the heart-to-mediastinum uptake ratio (H/M) from early and delayed images, and cardiac washout rate (WR). If both early and late H/M were higher than 2.2 and WR was 34% or lower, they were considered normal. Diagnosis at discharge was made per the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition. Ethical approval was granted by the Ethics Committee of the Tokyo Metropolitan Institute for Geriatrics and Gerontology (R22-072). Opt-out consent was offered to the patients.

Twenty patients (19 female) with OSHs were identified, with a median age of 81.5 years (range: 67–91 years). The discharge diagnoses were as follows: mood disorders in 12 (two bipolar disorder [BD] and 10 major depressive disorder [MDD]), DLB in three, PD in two, delusional disorder (DD) in one, adjustment disorder in one, and Alzheimer's disease in one.

Among the patients without PD/DLB, 12 of 15 underwent DaT-SPECT imaging. In 11 patients, the *Z*-scores of SBR decreased (nine MDD, one BD, one DD, median: −2.78 [range: −4.38 to −2.27]). Furthermore, eight of these patients also underwent MIBG cardiac scintigraphy, and six of them exhibited abnormal accumulations (four with MDD, one with BD, and one with DD; early H/M: median: 2.11 [range: 1.58–2.88], late H/M: median: 1.78 [range: 1.06–2.32], WR: median: 50.1 [range: 36.3–91.0], two cases with only elevated WR). Figure 1 presents the study's workflow.

The results of this case series demonstrated that 92% (11 out of 12) of the patients with OSHs had reduced accumulation on DaT-SPECT imaging, even in the absence of major symptoms associated with PD/DLB. These findings suggest a potential association between dopamine dysfunction and the pathophysiology of OSHs in older inpatients. Furthermore, among individuals with reduced dopamine transporter density, 75% (six out of eight) showed abnormal accumulations on MIBG cardiac scintigraphy. Considering the high specificity of MIBG cardiac scintigraphy,[8] these findings suggest that older patients with OSHs might have a potential risk for the development of PD/DLB.

One of the limitations of this study was its retrospective design and single-center evaluation of inpatient clinical data. Furthermore, long-term follow-up data were unavailable. In addition, the results of DaT-SPECT imaging can be affected by depression and treatments, such as electroconvulsive therapy and medication in our sample.[9,10]

In conclusion, this retrospective case series suggests that OSHs in older individuals, even in the absence of primary PD/DLB symptoms, may be associated with dopamine dysfunction. Abnormal findings on DaT-SPECT and MIBG cardiac scintigraphy imply the possibility of future development of PD/DLB in these individuals. Further prospective studies with long-term follow-up are warranted to validate and extend these findings.

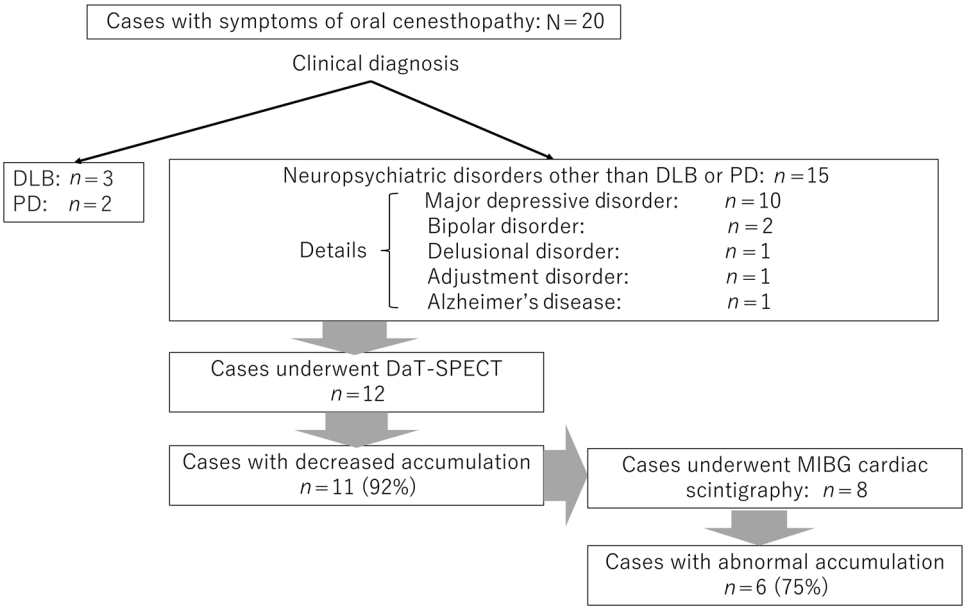

FIGURE 1 Cases with symptoms of oral cenesthopathy: *N* = 20. DAT-SPECT, ^{123}I-ioflupan dopamine transporter single photon emission computed tomography; DLB, Dementia with Lewy bodies; MIBG, ^{123}I-metaiodobenzylguanidine; PD, Parkinson's disease.

AUTHOR CONTRIBUTIONS

Hitomi Matsui and Tsuyoshi Okamura contributed to designing this study and initial manuscript preparation. Yuki Omori and Ko Furuta assisted with literature review and analyzed results. Masashi Kameyama gave some expert advice on nuclear medicine. Shuichi Awata gave advice on future direction. Takehiro Tamura, Takashi Takeuchi, Genichi Sugihara, Hidehiko Takahashi revised the manuscript of this paper. All authors read and approved the final manuscript.

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CONFLICT OF INTERESTS STATEMENT

Genichi Sugihara and Takashi Takeuchi are the Editorial Board members of *Psychiatry and Clinical Neurosciences Reports* and co-authors of this article. To minimize the bias, they were excluded from all editorial decision-making. The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS APPROVAL STATEMENT

This study was approved by the ethics committee of the Tokyo Metropolitan Institute for Geriatrics and Gerontology (R22-072).

PATIENT CONSENT STATEMENT

Opt-out consent was offered to the patients.

CLINICAL TRIAL REGISTRATION

N/A.

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