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LETTER TO THE EDITOR

A case of tauopathy with auditory agnosia and dysprosody diagnosed by [^{18}F]PM-PBB3 tau PET scan

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Dear Editor,

[^{18}F]PM-pyridinyl-butadienyl-benzothiazole 3 (PBB3), a propanol variant of the first tau positron emission tomography (PET) tracer, [^{11}C]PBB3, is reportedly a reliable tool for detecting tau fibrils in non-Alzheimer's disease (AD) tauopathies [1]. Here, we report an antemortem tauopathy diagnosis by [^{18}F]PM-PBB3 imaging in a rare case with auditory agnosia and dysprosody.

A 73-year-old right-handed woman, a former teacher, was referred to our hospital because she developed a gradual difficulty in hearing and unusual change in speech over the past 2 years. She had no significant medical history besides stomach cancer surgery at the age of 65 and no family history of similar diseases. Neurological examination, including tests for extrapyramidal symptoms, ataxia, cortical signs, or autonomic dysfunctions, revealed no abnormalities, except that she spoke like a foreigner who had just learned Japanese.

Head magnetic resonance imaging (MRI) revealed mild right anterior temporal lobe atrophy (Fig. 1a), and single-photon emission computed tomography showed hypoperfusion in the same area (Fig. 1b). Dopamine transporter scintigraphy indicated slightly reduced tracer uptake at the posterior right striatum (Fig. 1c). The patient did not provide consent for a spinal tap, but the plasma concentration of neurofilament light chain (14.25 pg/mL) measured by single-molecule array was high (normal range at our facility: less than 6 pg/mL).

Neuropsychological evaluations revealed normal intelligence and no cognitive disturbance, based on standard assessment scores (Mini-Mental State Examination: 27; Wechsler Adult Intelligence Scale-III–V IQ 96; PIQ 112; Raven's Colored Progressive Matrices: 28/36; Rey-Osterrieth Complex Figure Test-copy: 36/36; Rey-Osterrieth Complex Figure Test — 3-min delayed: 16.5/36; Wechsler Memory Scale-Revised Logical Memory Story A: immediate recall: 16/25; delayed recall: 13/25; Trail Making test A: 126 s, B:141 s, Word Fluency Category: 41/3 min, Initial letter: 21/3 min). She had no apraxia including bucco-facial apraxia. Her spontaneous speech was slow and dysprosodic, but her articulation was intact, indicating no dysarthria or apraxia of speech (AOS). We observed occasional phonemic paraphasia. Per the Japanese Standard Language of Aphasia test (Supplementary figure), she exhibited normal naming and word fluency. In auditory comprehension, she had difficulty recognizing spoken words, resulting in partially impaired repetition. Conversely, her written language comprehension was completely preserved. She could write sentences in both Kana and Kanji characters.

Pure-tone audiometry and otoacoustic emissions were intact, but speech audiometry was impaired. Her auditory temporal resolution was reduced, and she had verbal auditory agnosia. In the auditory brainstem response, the auditory steady-state response and pure-tone threshold were normal; therefore, the auditory conduction pathway was not impaired. Moreover, environmental sound agnosia and amusia were observed. Consequently, we classified her symptoms as generalized auditory agnosia [2].

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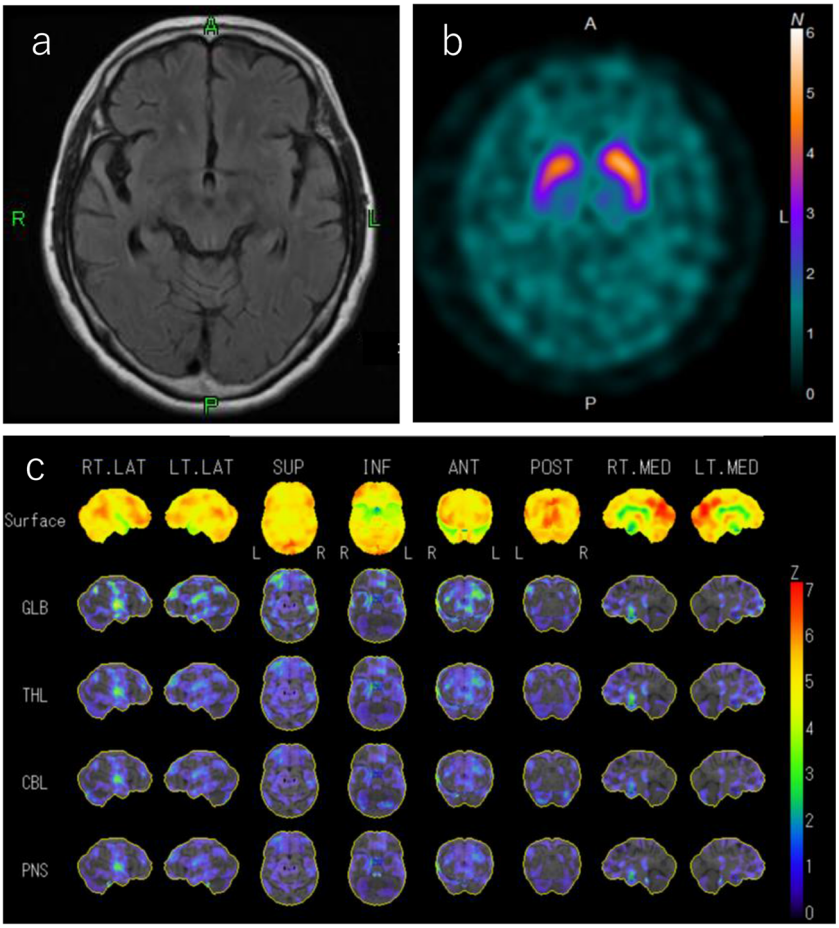

Fig. 1 Head MRI and scintigraphic images. **a** T2 fluid-attenuated inversion recovery (FLAIR) imaging. **b** Single-photon emission computed tomography (SPECT) with ^{123}I-ioflupane (DaTSCAN). **c** Three-dimensional stereotactic surface projections (3D-SSP) of ^{123}I-IMP SPECT

This patient neither met the criteria for the clinical diagnosis of corticobasal degeneration (CBD) [3], primary progressive aphasia, nor behavioral variant of frontotemporal dementia [4]. One year later, she developed mild left upper limb rigidity, and PET scans with [^{18}F]Florbetaben and [^{18}F]PM-PBB3 were performed to evaluate tau deposits after written informed consent was obtained (ethics committee authorization number: #N20170237). No amyloid deposition was observed, but tau PET showed accumulation in the right occipital cortex, basal ganglia, thalamus, and midbrain (Fig. 2). Collectively, we diagnosed her with non-AD tauopathy and suggested the presence of CBD pathology, because of the [^{18}F]PM-PBB3 accumulations in the subcortical region and asymmetrical neocortex, mimicking the topologies of [^{18}F]PM-PBB3 radio signals described in a subtype of frontotemporal lobar degeneration by Tagai et al. [1].

To our knowledge, this is the first report of a patient with auditory agnosia and dysprosody whose neuroimaging findings confirmed tauopathy. Auditory agnosia typically results from cerebrovascular diseases [2]. Although auditory agnosia in primary progressive aphasia has been reported [5], this patient's speech impairment was only dysprosodic, and she did not show agrammatism and AOS, which are crucial components of progressive nonfluent aphasia.

Environmental sound agnosia and amusia occur with right temporal lobe lesions involving the right superior temporal gyrus and auditory cortex [5], which were atrophic in this case. Contrarily, auditory agnosia is generally caused by bilateral primary auditory cortical lesions. Unilateral left-lateralized lesions are generally associated with unilateral disturbance [2]. In the present case, left-sided lesions were not evident in structural MRIs, but the left auditory cortex, medial geniculate body, or acoustic radiation projecting to the left auditory cortex may be functionally disturbed by tau deposition [2].

The clinical symptoms of non-AD tauopathies, especially CBD, are diverse, and antemortem diagnosis is often difficult. Our findings indicate that [^{18}F]PM-PBB3 could be a powerful tool for the diagnosis of early-stage non-AD tauopathy.

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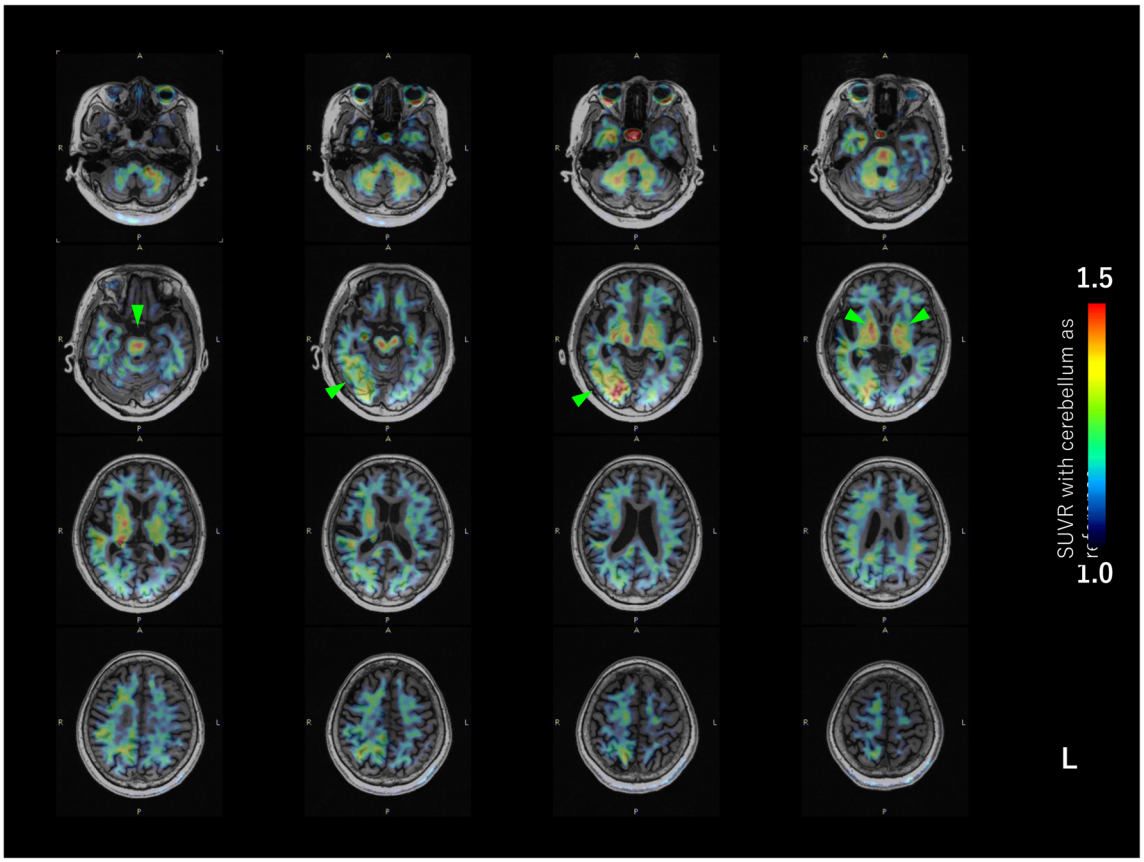

Fig. 2 [^{18}F]PM-PBB3 tau PET imaging in this patient reveals the range of tracer binding. Transaxial [^{18}F]PM-PBB3 images are shown. Cerebellar gray matter was used as the reference region for quantification. Accumulation of [^{18}F]PM-PBB3 was detected in the right occipital cortex, basal ganglia, thalamus, and midbrain (green arrowheads). SUVR = standardized uptake value ratio

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Code availability Not applicable

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Declarations

Ethics approval The study was approved by the Ethics Committee for Human Research of the Keio University School of Medicine, and informed consent (#N20170237) was provided by this participant.

Consent to participate The patient gave informed consent prior to inclusion in the study.

Consent for publication All authors approved the manuscript.

Conflict of interest The authors declare no competing interests.

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