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Case report

# A decade with anomic primary progressive aphasia

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ABSTRACT

Some patients with primary progressive aphasia (PPA) demonstrate only anomia. The lack of longitudinal observations of anomic PPA precluded us from determining whether progressive anomic aphasia was simply an early stage of semantic or logopenic variants, or a relatively independent variant. Herein, we report the 10-year clinical course of a patient with PPA who presented with pure anomic aphasia for 9 years. He is a right-handed man with anomia, who noticed word-finding difficulty at age 73. He was admitted to the hospital at age 77. On admission, the patient showed pure anomic aphasia with preserved other language function. Episodic memory and visuospatial function were preserved. Magnetic resonance imaging (MRI) revealed left temporal lobe atrophy. At 82 years of age, the patient presented with pure anomic aphasia. At 83 years old, he showed mild impairment in word comprehension and semantic memory, in addition to anomia. MRI demonstrated further atrophy in the bilateral anterior temporal lobes, predominantly on the left side. This case suggests the possibility of slowly progressive, late-onset anomic PPA, which could be differentiated from the early stage of semantic or logopenic variants.

## 1. Introduction

Primary progressive aphasia (PPA) is a clinical syndrome characterized by an isolated decline in language function. The current classification criteria for PPA have identified three variants: nonfluent/agrammatic variant (nfvPPA), semantic variant (svPPA), and logopenic variant (lvPPA) [1]. However, one third of PPA patients are not classified under these variants [2]. Some patients with unclassified PPA have anomia as a prominent symptom [3–6]. Some of these patients may be in the early stage of svPPA or lvPPA, but the long-term course has not been reported. Here, we discuss a patient who presented with progressive anomic aphasia for 9 years after onset and consider that some patients with anomic PPA may not be classified as early svPPA or lvPPA.

## 2. Case presentation

A 77-year-old right-handed man with 16 years of education was admitted to our hospital with a 4-year history of anomia. The patient had no remarkable medical or family history. At age 73, he noticed word-finding difficulty, and one year later, he visited a local hospital. He scored 30/30 on the Mini-Mental State Examination (MMSE). Brain magnetic resonance imaging (MRI) showed atrophy of the left medial temporal lobe. A primary care physician diagnosed the patient with Alzheimer's disease and put him on donepezil. Subsequently, he presented irritability and agitation and had trouble with his neighbours. At age 77, he consulted a registered neurologist who discontinued donepezil treatment, and his irritability and agitation improved.

*Abbreviations:* PPA, Primary Progressive Aphasia; MMSE, Mini-Mental State Examination; MRI, Magnetic Resonance Imaging; TLPA, Test of Lexical Processing in Aphasia; WAB, Western Aphasia Battery Japanese version; WAIS-III, Wechsler Adult Intelligence Scale-Third Edition; WMS-R, Wechsler Memory Scale-Revised.

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### 2.1. The first assessment at age 77

His chief complaint was word-finding difficulty without any other problems in his daily life. Neurological examination revealed only slight right-dominant paratonia. He exhibited mild anomic aphasia with fluent speech and spared repetition. The Aphasia Quotient (AQ) of the Western Aphasia Battery Japanese version (WAB) was 98. However, he scored 164/200 on the naming task of the Test of Lexical Processing in Aphasia (TLPA)-the standard test for naming and word comprehension in Japanese. The most common naming errors were circumlocution and semantic paraphasia; no phonological paraphasia was detected. Auditory comprehension was preserved. Episodic memory and visuospatial function were preserved. He scored 26/30 on the MMSE. He performed normally on the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) and the Wechsler Memory Scale-Revised (WMS-R). No semantic memory impairment was observed in these tests. The neuropsychological test results are summarized in Table 1. Brain MRI demonstrated mild atrophy of the left temporal lobe (Fig. 1a), which was confirmed by *Z*-score maps of voxel-based morphometry (VBM)-MRI (Fig. 1b). Z-score maps of VBM-MRI were created using a voxel-based specific regional analysis system for Alzheimer's disease (VSRAD®) software (Eisai, Tokyo, Japan) [7]. $^{123}$I-iodoamphetamine single-photon emission computed tomography ($^{123}$I-IMP SPECT) showed mild bilateral frontotemporal hypoperfusion (Fig. 1c). Laboratory testing of the cerebrospinal fluid revealed slightly elevated phosphorylated tau protein (p-tau: 59.2 pg/ml, cut-off value: <50 pg/ml), but the beta-amyloid 1–42/1–40 ratio was not decreased (Aβ1–42/1–40: 0.082, cut-off value: ≥0.067).

**Table 1**
Results of the neuropsychological tests.

| Duration from onset | 4 years | 8–9 years | 10 years |
|---|---|---|---|
| MMSE (/30) | 26 | 26 | 24 |
| RCPM (/36) | 35 | 27 | 30 |
| WAIS-III | | | |
| VIQ | 107 | – | 89 |
| PIQ | 122 | – | 101 |
| WMS-R | | | |
| Verbal memory index | 98 | – | 61 |
| Visual memory index | 110 | – | 71 |
| Attention/Concentration index | 92 | – | 89 |
| Delayed memory index | 97 | – | 50 |
| WAB | | | |
| Aphasia Quotient (/100) | 98 | 92 | 90.6 |
| Spontaneous speech (/20) | 20 | 18 | 18 |
| Auditory comprehension (/10) | 9.8 | 9.7 | 9.7 |
| Repetition (/10) | 10 | 10 | 10 |
| Naming (/10) | 9.3 | 8.3 | 7.6 |
| Reading (/10) | 9.8 | 8.4 | 8.8 |
| Writing (/10) | 9.9 | 10 | 10 |
| TLPA[a] | | | |
| Naming (/200) | 164 (HF92, LF72) | 126 (HF88, LF38) | 112 (HF80, LF32) |
| Auditory comprehension (/200) | 198 (HF99, LF99) | 190 (HF96, LF94) | 170 (HF92, LF78) |
| 2-way anomia | 0 | 5 | 23 |
| Verbal fluency | | | |
| Animal (/minute) | 17 | 11 | 10 |
| Initial /ka/ (/minute) | 18 | – | 8 |
| STRAW 6th grade[b] | | | |
| Kanji dictation (/20) | 19 | 12 | 14 |
| Kana dictation (/20) | 20 | 19 | 20 |
| FAB (/18) | 13 | 11 | – |

Abbreviations: FAB, Frontal Assessment Battery; HF, High Familiarity; LF, Low Familiarity; MMSE, Mini-Mental State Examination; PIQ, Performance Intelligence Quotient; RCPM, Raven's Coloured Progressive Matrices test; STRAW, Screening Test of Reading and Writing for Japanese Primary School Children; TLPA, Test of Lexical Processing in Aphasia; VIQ, Verbal Intelligence Quotient; WAB, Western Aphasia Battery Japanese version; WAIS-III, Wechsler Adult Intelligence Scale-Third Edition; WMS-R, Wechsler Memory Scale-Revised.

[a] Normal score of naming is 193.35 ± 5.43 (1 standard deviation) and that of auditory comprehension is 199.40 ± 0.95.

[b] Japanese orthography utilizes two types of characters: morphograms (kanji) and phonograms (kana). Each kanji character has a meaning and more than one pronunciation, while each kana character has one pronunciation and no meaning.

### 2.2. The second assessment at age 81–82

Mild amnesia appeared at the age of 79, and he visited our hospital again at the age of 81. Neurological examination revealed a postural tremor in the right upper limb; no other motor symptoms were observed. The patient exhibited progressive anomic aphasia with spared repetition. The AQ on the WAB was 92, and the naming and reading scores were slightly lower than those at the first evaluation (Table 1). The naming score of the TLPA also decreased, especially for low-frequency words (38 out of 100). He scored 26/30 on the MMSE. Brain MRI revealed greater atrophy of the left temporal lobe (Fig. 1d and e). $^{123}$I-IMP SPECT revealed bilateral frontotemporal and parietal hypoperfusion (Fig. 1f).

### 2.3. The third assessment at age 83

He showed very mild frontal symptoms, including disinhibition and perseveration, which did not interfere with his daily activities and were not present at the time of admission. Neurological examination revealed grasp reflexes in both hands and soles. In addition to anomia, he showed mild impairment in word comprehension, with spared repetition. The AQ on the WAB was 90.6, and the naming and auditory comprehension scores on the TLPA were worse than those on the second assessment (Table 1). The TLPA revealed 2-way anomia for 23 out of 200 words. He also presented mild surface dyslexia (独楽 a top /koma/→/doku-raku/) and loss of semantic knowledge (The Pyramids and Palm Trees Test picture version: 39/52). Kanji writing scores on the Screening Test of Reading and Writing for Japanese Primary School Children declined slightly from the first assessment, but kana writing was preserved. He scored 24/30 on the MMSE. His amnesia progressed as indicated by the WMS-R. The WAIS-III showed a declining function compared with the first assessment. Brain MRI revealed significant bilateral atrophy of the anterior temporal lobes, predominantly on the left side (Fig. 1g and h). $^{123}$I-IMP SPECT revealed right-dominant bilateral temporal and frontoparietal hypoperfusion (Fig. 1i). Results of the cerebrospinal fluid were same as the previous one, slightly elevated p-tau (66.8 pg/ml) and no decrease in the Aβ1–42/1–40 ratio (0.088).

## 3. Discussion

In this case report, we present a patient with unclassified PPA who showed only anomia for at least 9 years, the longest observation period for anomic PPA. Very mild impairments in word comprehension and semantic knowledge appeared 10 years after the onset. Although amnesia and frontal symptoms appeared later in the course of the disease, the predominant symptom was anomia throughout the course, which fulfilled the criteria for PPA. The prominent features of this patient included long-standing, slowly progressive anomic aphasia with an older onset at over 65 years of age.

Previous studies have reported several patients with progressive anomic aphasia and preserved object knowledge, grammar, and motor speech. These cases are referred to as anomic variant of PPA [3], progressive fluent aphasia [4,5], or unclassified fluent variant of PPA [6] (Table 2). The duration of follow-up from disease onset in these patients ranged from 2 to 7 years. Mesulam et al. [3] reported the case of a 75-year-old patient with anomic variant of PPA who demonstrated only anomic aphasia 4 years after onset. Josephs et al. [4] and Botha et al. [5] described 10 patients with progressive fluent aphasia, marked anomia, and no impairment in object knowledge or repetition. One of the 10

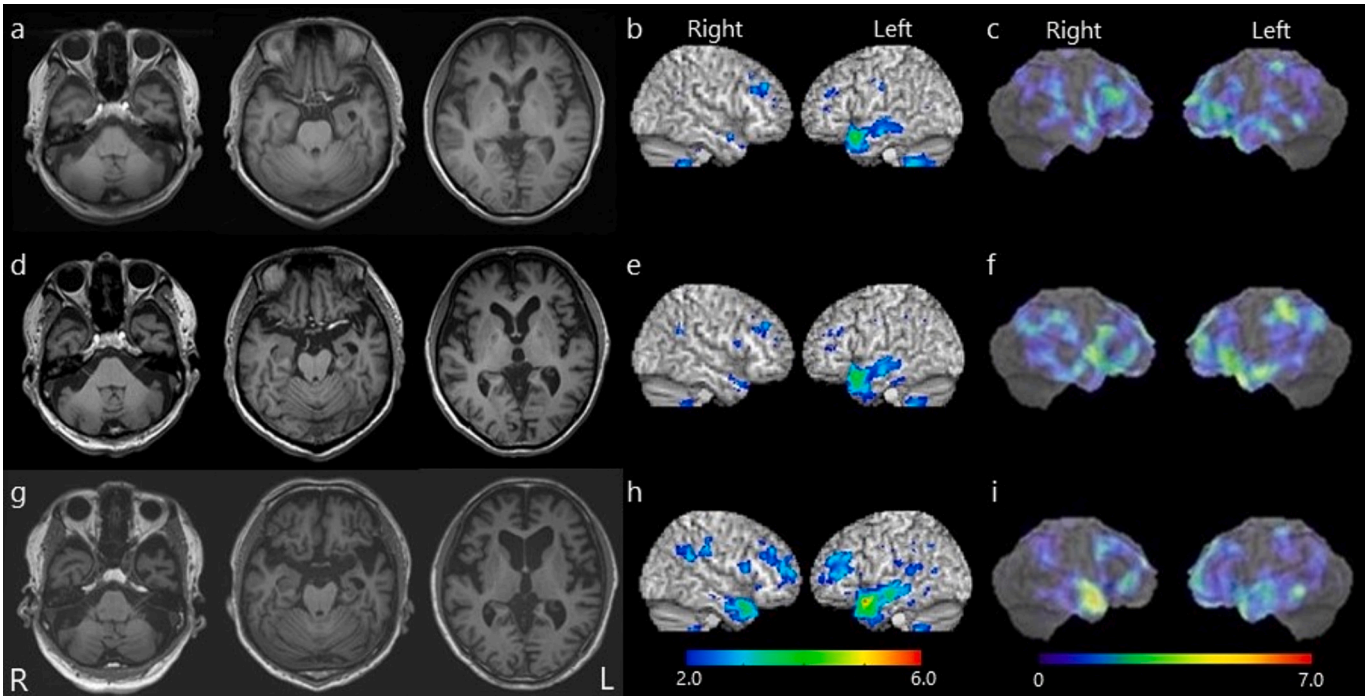


**Fig. 1.** Magnetic resonance imaging data (T1-weighted), *Z*-score maps of voxel-based morphometry-magnetic resonance imaging, and results of three-dimensional stereotactic surface projections on $^{123}$I-iodoamphetamine single-photon emission computed tomography. (a) The images at age 77 showed mild atrophy of the left temporal lobe. (b) *Z*-score maps at age 77 revealed mild atrophy of the left temporal lobe. (c) The cluster in which regional cerebral blood flow (rCBF) at age 77 was decreased in the bilateral frontotemporal lobes. (d) The images at age 81 showed progressive atrophy of the left temporal lobe. (e) *Z*-score maps at age 81 revealed progressive atrophy of the left temporal lobe. (f) The cluster in which rCBF at age 81 was decreased in the bilateral frontotemporal and parietal lobes. (g) The images at age 83 showed significant atrophy of the left-dominant bilateral temporal lobes. (h) *Z*-score maps at age 83 revealed bilateral atrophy of the temporal lobes. (i) The cluster in which rCBF at age 83 was decreased in the right-dominant bilateral temporal lobes and the bilateral frontoparietal lobes.
Abbreviations: R, Right; L, Left. The coloured bars indicate the *Z*-values

**Table 2**
Cases of primary progressive aphasia with anomic aphasia.

| Author | Case number | Sex | Age at onset, y | The 1st visit | | | | The last visit | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Age at the 1st visit, y | WAB AQ | Hypometabolism/ hypoperfusion | MRI atrophy | Age at the last visit, y | Onset to the last visit, y | Aphasia type at the last visit |
| Mesulam et al. [3] | 25 | F | 75 | 78 | 92 | NA | Negative | 79 | 4 | anomic |
| Josephs et al. [4] | 16 | M | 63 | 65 | NA | L anteromedial T | NA | 65 | 2 | fluent |
| | 17 | M | 78 | 80 | NA | L > R T; L P | NA | 80 | 2 | fluent |
| | 18 | M | 69 | 74 | NA | mild B Front; L > R T, B P | NA | 74 | 5 | fluent |
| | 19 | M | 68 | 70 | NA | L > R P, O, posterior T | NA | 70 | 2 | fluent |
| | 20 | F | 71 | 72 | NA | L > R T, P, medial P | NA | 73 | 2 | fluent |
| | 21 | M | 67 | 72 | NA | L anteromedial T | NA | 74 | 7 | fluent |
| Botha et al. [5] | 4 cases | F3/ M1 | 67.3 ± 6.8 | 70.0 ± 7.3 | 92.5 ± 5.2 (85.9–98.4) | NA | L T | 71.3[a] | 4.0 ± 2.1[a] (2.5-5.5) | fluent |
| Watanabe et al. [6] | 1 | F | 82 | 84 | 91.8 | B T, P | R > L Front, T | 84 | 2 | anomic |
| | 2 | F | 69 | 74 | 88.8 | L Front, P | B Front, T, P | 74 | 5 | anomic |
| | 3 | F | 75 | 77 | 84.4 | L anterior T; R P | B Front, T; R P | 77 | 2 | anomic |
| | 4 | M | 74 | 79 | 83.8 | B posterior T, O | B Front, T, P, O | 79 | 5 | anomic |
| | 5 | F | 68 | 70 | 86.2 | L > R anterior T, P | L > R Front, T, P | 70 | 2 | anomic |
| | 6 [b] | M | 77 | 81 | 85 | R > L Front, anterior T, P | R > L Front, T, P | 82 | 5 | anomic to mild TCSA |
| | 7 | F | 83 | 85 | 80.2 | L anterior T | B Front, T | 85 | 2 | anomic |
| | 8 | F | 82 | 84 | 85.2 | L > R anterior T, P | L > R Front, T | 84 | 2 | anomic |
| Present case | | M | 73 | 77 | 98 | B Front, T | L > R Front, anterior T | 83 | 10 | anomic to mild TCSA |

Abbreviations: AQ, Aphasia Quotient; B, Bilateral; F, Female; Front, Frontal; L, Left; M, Male; MRI, Magnetic Resonance Imaging; NA, Not Available; O, Occipital; P, Parietal; R, Right; T, Temporal; TCSA, Transcortical Sensory Aphasia; y, years.
[a] Follow-up cases with fluent aphasia were two of four patients, and we calculated them according to the supplementary data. [b] Left-handed.

patients, a 72-year-old man, was assessed 7 years after onset and showed fluent aphasia. Watanabe et al. [6] reported that 8 of 12 patients with unclassified fluent PPA were classified into anomic aphasia, whose duration from onset was ≤5 years. Only one of the 8 patients, a 77-year-old man, was assessed again one year after the first visit, 5 years after onset, and showed slight impairment of word comprehension in the TLPA (174 out of 200). These cases suggest that some patients with PPA may present with only anomia for at least several years after onset. We confirmed that our patient presented with pure anomic aphasia for the longest period, 9 years after onset.

The neuropathological bases of anomic PPA have not yet been proven. Clinical course and neuroimaging studies have indicated that some patients with svPPA and lvPPA may present with anomic aphasia during the early stages [3,8]. Patients with svPPA show relatively preserved word comprehension at the early stage and present with anomic aphasia. Semantic memory impairment progresses over the next 2–8 years to develop semantic dementia, fulfilling the diagnostic criteria of svPPA [9]. Frontal symptoms, such as disinhibition or behavioral changes, may occur at this stage. According to Kashibayashi et al. [10], a decline in daily activities at an average of 5.4 years was seen in typical semantic dementia. Another clinical feature of svPPA is that its onset occurs at relatively young age, most often under 65 years of age. In contrast, with a few exceptions, the onset of most anomic PPA was in patients aged >65 years (Table 2). The onset of the present case was at 73 years of age and progressed without object knowledge impairment or frontal symptoms for at least 9 years, which suggests the least possibility of svPPA. Patients with lvPPA demonstrate anomia and impaired repetition of short sentences. When the impairment of repetition is very mild at the early stage of lvPPA, it appears to be anomic aphasia [8]. However, in the present case, the repetition score was not worse through the long course. Therefore, this case study suggests that progressive anomic aphasia is not an early stage of these two variants. The cerebrospinal fluid data did not confirm Alzheimer pathology, although its possibility could not be excluded. Further pathological studies are necessary to clarify this patient's background.

## 4. Conclusions

The present case, along with several previous ones, displayed only anomic aphasia for several years without any other significant cognitive dysfunction, which indicates anomic variant of PPA. It could be a type of PPA characterized by late-onset and slow progression, rather than the prodromal state of the three known subtypes. Further research is necessary to clarify the features of unclassified PPA to recognise PPA classification and associate it with background diseases.

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## Informed consent

Written informed consent was obtained from the patient and his family after a detailed description of the study.

## CRediT authorship contribution statement

**Shoko Ota:** Writing – original draft, Visualization, Investigation, Formal analysis, Conceptualization. **Kazuo Kakinuma:** Writing – review & editing, Investigation. **Wataru Narita:** Investigation. **Yoshiyuki Nishio:** Investigation. **Nobuko Kawakami:** Investigation. **Ayane Tamagake:** Investigation. **Shigenori Kanno:** Writing – review & editing, Visualization, Supervision, Formal analysis. **Minoru Matsuda:** Supervision. **Kyoko Suzuki:** Writing – review & editing, Supervision.

## Declaration of Competing Interest

None declared.

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