A Case of Anoxic Brain Injury Presenting with Agraphia of kanji in the Foreground

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Abstract
A 63-year-old woman was hospitalized for rehabilitation from the aftereffects of an anoxic brain injury. In addition to a general cognitive decline, agraphia of kana and kanji was noted at the time of admission, which had advanced to agraphia which is dominant in kanji at the time of hospital discharge. Brain magnetic resonance imaging revealed no stroke lesions, and brain perfusion scintigraphy found a decreased blood flow in the bilateral parietal lobes. We hereby report on this case because case reports on agraphia caused by anoxic brain injury are extremely rare.

Introduction
The resuscitation rate following cardiopulmonary arrest has improved as a result of advances in critical care, but there are many cases in which severe aftereffects persist. These aftereffects are diverse and include motor disorders (e.g., paralysis and ataxia) and cognitive dysfunction, mainly involving impaired memory.

On the other hand, a language disorder is a local symptom commonly associated with stroke and brain trauma that is observed to complicate 71% of anoxic brain injury cases [1]...
and is thus by no means a rare aftereffect in these cases. However, alexia and agraphia are 2 serious language disorders and have been reported to occur in only approximately 1% of anoxic brain injury cases [1], most of which are due to strokes.

Here we report on a case of agraphia of kana and kanji that occurred due to anoxic brain injury following resuscitation from cardiopulmonary arrest and progressed to agraphia which is dominant in kanji throughout the course of the illness.

Case Presentation

A 63-year-old, right-handed female was admitted to our hospital with the chief complaint of inability to write. She had been admitted to a different hospital for ventricular fibrillation and cardiopulmonary arrest due to an acute myocardial infarction in January 2014. Although she had been successfully resuscitated within 23 min, a higher brain dysfunction due to anoxic brain injury persisted, and she was transferred to our hospital for rehabilitation on day 47 of the illness. Her past medical history showed that she was taking insulin medication for diabetes and had been administered oral drugs for hypertension and dyslipidemia since the age of 42 years. She was a housewife and her final education was high school. She was able to perform activities of daily living independently and there were no symptoms of dementia. No significant issues were noted with regard to her family history.

The patient’s status at the time of admission was as follows: height, 156 cm; weight, 45 kg; blood pressure, 118/66 mm Hg; pulse, 89 bpm; and body temperature, 35.7°C. In addition, there were no physical abnormalities in the thoracoabdominal region. The patient was lucid and displayed good manners, with no reported problems in everyday conversation. In addition, the patient did not experience any defects in her visual field or eye movements, abnormal facial sensations, paralysis of the facial muscles, hearing loss, dysarthria, dysphagia, paralysis or ataxia of the limbs or trunk, limb-kinetic apraxia, ideomotor apraxia, ideational apraxia, constructional apraxia, or unilateral spatial neglect. Her deep tendon reflex was normal, with no observed asymmetry. There was no sensory impairment of the limbs or trunk. However, she was “unable to write” when asked to write her name and address.

The laboratory findings at the time of admission showed that blood count, liver and kidney function, and electrolytes were within the respective normal ranges. Her blood sugar and HbA1c (National Glycohemoglobin Standardization Program) were elevated to 165 mg/dL and 7.8%, respectively. Electrocardiography and a plain chest X-ray revealed no abnormalities.

Neuropsychological tests on days 47–54 of the illness revealed that the Wechsler Adult Intelligence Scale, 3rd edition (WAIS-III) [2] scores were generally decreased, including a verbal IQ of 64, a performance IQ of 54, a full-scale IQ of 57, verbal comprehension of 76, perceptual organization of 55, working memory of 54, and a processing speed of 52. In addition, the Wechsler Memory Scale-Revised (WMS-R) [3] scores were generally decreased, with verbal, visual, and general memory as well as attention/concentration and delayed recall scoring below 50. The standardized profile score of the Rivermead Behavioural Memory Test (RBMT) [4] was 2/24, indicating severe memory impairment, and the Clinical Assessment for Attention (CAT) [5] scores were below the cutoff values for all tasks, except the visual cancelation task. In the Visual Perception Test for Agnosia (VPTA) [6], decreased scores were observed for shape discrimination, overlapping figures, graphic replication, picture classification, context pictures, familiar faces, unknown faces, symbol replication, and spontaneous drawing. In the Standard Language Test of Aphasia (SLTA) [7], the patient’s
scores were low for sentence repetition and word fluency in II (speaking) and all subcategories of IV (writing). The scores for written kanji words, narrative writing, and dictated kanji words were particularly low (Fig. 1, Fig. 2).

Based on the test results, the patient was diagnosed with decreased intellectual function, memory impairment, attention disorder, apperceptive visual agnosia, prosopagnosia, and agraphia of kana/kanji due to an anoxic brain injury. For rehabilitation, the patient underwent (1) physical and occupational therapy as stimulation for her overall cognition, (2) speech-hearing therapy for attention and memory training, and (3) transcription and key-word training for dysgraphia. She was discharged on day 226 of the illness.

Neuropsychological testing during days 210–225 of the illness yielded the following results. We could not administer the WAIS-III because of the patient’s refusal. In the WMS-R, the verbal, visual, and general memory, attention/concentration, and delayed recall scores were 52, 55, <50, 54, and <50, respectively, indicating that mild improvements had occurred but the scores remained low. In the RBMT, the standardized profile score improved mildly to 6/24 but still indicated a severe memory impairment. Moreover, the CAT score was slightly improved overall but remained below the cutoff values for nearly all items. In the VPTA, the scores remained low for familiar faces and unknown faces, whereas improvements were observed in shape discrimination, overlapping figures, graphic replication, picture classification, context pictures, symbol replication, and spontaneous drawing. In the SLTA, the sentence repetition and word fluency scores in II (speaking) remained unchanged; the IV (writing) scores tended to improve for kana-related items, but those for kanji-related items did not improve (Fig. 1). These test results suggest that the patient still had kanji-specific agraphia as well as memory impairment, attention disorder, and prosopagnosia on day 225 of the illness.

On day 329 of the illness, brain magnetic resonance imaging indicated slightly high signal intensities in the periventricular white matter, centrum semiovale, subcortical white matter of the left supramarginal gyrus, and corpus callosum in addition to mild but global atrophy of the brain on axial fluid-attenuated inversion recovery imaging (Fig. 3a). Brain perfusion scintigraphy using single-photon emission computed tomography (SPECT) revealed a decreased blood flow in the bilateral parietal lobes (Fig. 3b).

**Discussion**

In the present case there was agraphia of kana/kanji in addition to general cognitive functional decline, apperceptive visual agnosia, and prosopagnosia on the 47th day according to neuropsychological testing. On the 225th day, the agraphia dominant in kanji remained, whereas there was a tendency for improvement in agraphia of kana.

In his neurological classification, Roeltgen [8] classified agraphia into (1) pure agraphia, (2) alexia with agraphia, (3) aphasia with agraphia, (4) apraxic agraphia, and (5) spatial agraphia. We could not diagnose pure agraphia in this case, because of the presence of a general cognitive functional decline. In addition, there seemed to be no aphasia and alexia from the results of the SLTA, but it cannot completely be denied that aphasia with agraphia occurred, due to the decreased performance in word fluency on the SLTA and the lower WAIS verbal IQ scores. There was the possibility of apraxic agraphia, since the patient’s ability in copying was better than that in dictation, and she could produce the form of the letter orally. Also, we thought that there was no spatial agraphia, because she did not have unilateral spatial neglect.
Lesions responsible for agraphia are located in multiple sites. The first site is the posteroinferior temporal gyrus. Iwata [9] reported that damage to this site results in kanji-selective alexia with agraphia and proposed a dual neural circuit hypothesis for Japanese reading and writing. This hypothesis states that kanji and kana are related to left occipitotemporal and occipitoparietal association areas, respectively. The second site is the angular gyrus. Lesions localized to this site result in pure agraphia of kanji [10], whereas those located in the vicinity of the angular gyrus lead to lexical agraphia (which corresponds to agraphia of kanji) [11]. The third site is the supramarginal gyrus. Lesions localized to this site are reportedly associated with kanji-dominant pure agraphia [10]. In addition, lesions in the angular, lateral occipital, and supramarginal gyri have been associated with errors of order in kana character reading, whereas those in the supramarginal gyrus have been associated with errors of order in kana character writing [10]. The fourth site involves the superior parietal lobule. Apraxic agraphia develops when damage occurs in this region [12] or around the intraparietal sulcus [13]. Difficulties in recalling characters are often associated and become prominent when the damage reaches the supramarginal gyrus, superior occipital gyrus, and precuneus [14]. The fifth and final site is the posterior middle frontal gyrus. Sakurai et al. [15] reported a case of agraphia with impairment, predominantly of kanji, due to a lesion in this region.

In the present case, a decreased blood flow in the bilateral parietal lobes was found via SPECT, although no obvious stroke lesions were noted on magnetic resonance imaging in the abovementioned regions. It was difficult to point out a lesion responsible for the agraphia from imaging in this case. However, if this case is apraxic agraphia or aphasia with agraphia, we can connect it with the decreased blood flow observed on SPECT, because it was said that apraxic agraphia has also been attributed to damage to the superior parietal lobule [12] and the neighborhood of the intraparietal sulcus [13]; also damage to the left inferior parietal lobule can result in aphasia. Furthermore, we cannot deny the involvement of ischemic lesions in the subcortical white matter of the left supramarginal gyrus, which are lesions known to be responsible for pure agraphia [10].

Conclusion

Reported cases of agraphia primarily include vascular disorders, and there have been virtually no reports of agraphia in cases of anoxic brain injury. The symptoms of anoxic brain injury often improve within a short time, which is why detailed assessments are required with particular attention to higher brain dysfunctions found during the course of illness.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors declare that they have no conflicts of interest to disclose.
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**Fig. 1.** Standard Language Test of Aphasia (SLTA) [13]. The scores on day 47 were low for sentence repetition and word fluency in II (speaking) and all items of IV (writing). On day 225, sentence repetition and word fluency in II (speaking) remained unchanged. Moreover, *kana*-related items in IV (writing) improved, whereas scores for *kanji*-related items remained low.
Fig. 2. 1a Writing kanji words. 1b Writing kana words. IIa Dictation of kanji words. IIb Dictation of kana words (selected SLTA results). In both writing (writing while observing a picture of an object) and dictation (writing the name of an object that was heard), the answers in kana were correct, but those in kanji were incorrect. There is paragraphia in kanji.
Fig. 3. a Brain magnetic resonance images (fluid-attenuated inversion recovery) on day 329. Slightly high signal intensities are to be seen in the periventricular white matter, centrum semiovale, subcortical white matter of the left supramarginal gyrus, and corpus callosum, in addition to mild but global atrophy of the brain. b $^{99}$Tc-ethyl cysteinate dimer-single-photon emission computed tomography on day 329 (Z score map). Reduced blood flow was observed in the bilateral parietal lobes.