Transient phonemic paraphasia by bilateral hippocampus lesion in a case of limbic encephalitis

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Abstract

Although the hippocampus has not typically been identified as part of the language and aphasia circuit, recent evidence suggests that the hippocampus is closely related to naming, word priming, and anomic aphasia. A 59-year old woman with limbic encephalitis of possible autoimmune etiology, after recovery of consciousness, presented with severe memory impairment in both anterograde and retrograde modalities, episodes of fear, hallucination and convulsion, and transient fluent, phonemic paraphasia, together with small sharp waves diffusely by EEG. Brain MRI revealed bilateral symmetric, discrete lesions in the body to the infundibulum of the hippocampus.

The transient phonemic paraphasia noted in our patient may have been a result of primary damage in the hippocampus and its fiber connection to the Wernicke's area or secondary partial status epilepticus that might have originated in the hippocampus.

Introduction

Although the hippocampus has not typically been identified as part of the neuronal circuit for language and aphasia, recent evidence suggests that the hippocampus is closely related to naming, word priming, and anomic aphasia.[1,2] We present herein a case that presented with limbic encephalitis (LE),[3] bilateral symmetric, discrete lesions within the hippocampus, as well as transient phonemic paraphasia, a combination that has not been reported previously.

Case Report

A 59-year old, previously healthy, right-handed woman developed high fever (39°C) and vomiting. Five days later, she became somnolent and began to have generalized convulsions that brought her to our hospital. On the day of admission to our hospital, she was status epilepticus and in a deep coma. She had nuchal rigidity and a positive Kernig's sign bilaterally. Blood tests showed only a mild inflammatory change. The cerebrospinal fluid (CSF) examination carried out on the first day from admission showed an increased cell count (40/mm^3, mononuclear: polymorphonuclear = 35:5, no malignant cells), increased total protein of 84 mg/dL, and normal glucose levels. The brain magnetic resonance imaging (MRI) from the first day showed no apparent lesions; and no contrast enhancement by gadolinium injection was seen. Electroencephalogram (EEG) showed high amplitude slow delta waves (2-3Hz) diffusely. At that time, herpetic encephalitis was first suspected and the patient was started on intravenous 1500 mg/day acicrovir. On the 3rd day after admission she returned to normal consciousness. She had no muscle weakness or sensory disturbances, while she had mildly increased deep tendon reflexes in the lower extremities and a positive Babinski sign bilaterally. In addition, we asked the patient to recall 10 small episodes (by our observations [antegrade, recent memory] or by interviewed histories taken from the families [retrograde]), in order to quantify amnesia. As a result, she was revealed to have extreme retrograde (unable to tell 100% of life histories that happened in the past 30 years) and anterograde memory impairment (unable to tell 100% of events that had happened in the last three minutes). On the 6th day after admission, the CSF examination revealed a cell count of 41/mm^3 (all mononuclear cells) and total protein of 23 mg/dL. At that time, antibodies against herpes simplex, herpes zoster viruses in the CSF and the serum were negative. A survey of paraneoplastic antibodies showed the following results. Antibodies for anti-neuronal nuclear antibody (ANNA)-1 (anti-Hu), ANNA-2 (anti-Ri), ANNA-3, anti-glial nuclear antibody-1, Purkinje cell cytoplasmic antibody (PCA)-1 (anti-Yo), PCA-2, PCA-Tr, amphiphysin, collapsin response mediator protein-5, neuronal voltage-gated K^+ channel, striated muscle, muscle acetylcholine (ACh) receptor, neuronal ganglionic ACh receptor, P/Q-type and N-type voltage-gated Ca^+ channel, and glutamate receptor $\varepsilon 2$ and $\delta 2$ subunits were all negative. A whole-body CT scan including the ovary revealed no malignancy. She had repeated attacks of fear, hallucination (both lasting hours), and short-duration seizures (lasting minutes), but meanwhile she remained almost normal and was started on 5 mg intramuscular haloperidol, 300 mg/day oral phenytoin, and 90 mg/day phenobarbital. She was anorexic. Cognitive test results were as follows: Mini-Mental State Examination (MSME) score 16/30; Wechsler Memory Scale Revised Version (WMSR) general score under 50, verbal score 56, visual score under 50, attention score not performed; Frontal Assessment Battery (FAB) score 14/18. She had no speech difficulty or aphasia at all at that time.

On the 18th day after admission, brain MRI results revealed bilateral, symmetrical high signal lesions localized at the body to the infundibulum of the hippocampus, which slightly extended to the parahippocampal gyrus and the amygdala on diffusion-weighted images and fluid attenuated inversion recovery (FLAIR) images. Therefore, non-herpetic, autoimmune limbic encephalitis (LE) became the tentative diagnosis. The patient was then started on 3 courses of 1,000 mg/day intravenous methylprednisolone for three days. After these treatments, her hallucination and seizures disappeared gradually, and she became able to eat meals, although her memory disturbances persisted. On the 31^{s}t day after admission, EEG showed 6Hz theta waves in the frontal lobe bilaterally, and no spikes were observed. On the 39th day, brain MRI still revealed bilateral, symmetrical high signal lesions at the body to the infundibulum of the hippocampus, which slightly extended to the parahippocampal gyrus and the amygdala only by FLAIR images (Figure 1). The CSF findings returned to normal. On the 41st day, she began to show signs of transient fluent, phonemic paraphasia; e.g., omotai (heavy) > amatai, saba (mackerel) > sabako, jinja (shrine) > chinja, nebusoku (sleepless) > nobusoku, tsukatte morau (let someone to use it) > takette morau, passport > kasport. Her speech was fluent, and word/sentence recognition was preserved. This phenomenon lasted for half a day and then disappeared, but was repeatedly observed by the co-medical staff for a week. We were not able to perform a detailed aphasia battery during a period of a week because of non-availability of a clinical psychologist. On the 44th day, EEG showed small sharp waves in

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the frontal, temporal, and parietal lobes bilaterally. On the 47th day after admission, the patient had two seizures. After that, no seizures or phonemic paraphasia were observed, and her memory impairment was gradually ameliorated. On the 65th day, EEG showed a small amount of 6 Hz theta waves, but no sharp waves were seen. We performed single-photon emission computed tomography (SPECT) scans one month and three months after admission, both of which showed normal findings (on the 10th day, motion artifacts alone). Six months after admission, she was discharged from hospital. At that time, she had moderate retrograde (unable to tell 80% of life histories that happened in the past 20 years) and anterograde memory (unable to tell 10% of events that happened in the recent 60 minutes) impairment. The cognitive test results were as follows: MSME score 23/30; WMSR general score 66, verbal score 70, visual score 70, attention score 82; FAB score 17/18. FLAIR images of MRI revealed amelioration of the bilateral high signal foci at the hippocampus, parahippocampal gyrus and the amygdala.

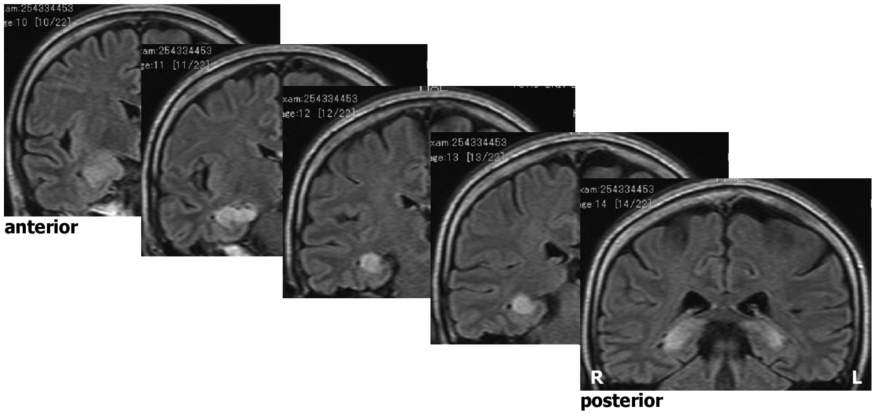

Figure 1. Brain magnetic resonance imaging of the patient. Bilateral, symmetrical high signal lesions localized in the body to the infundibulum of the hippocampus, which slightly extended to the parahippocampal gyrus and the amygdala on fluid attenuated inversion recovery (FLAIR) images. Coronal images are shown. Pre-existing mild malformation in the temporal neocortex was also noted.

Discussion

The diagnosis of LE in this case was based on: clinical features of acute onset of high fever, disturbance of consciousness, and epilepsy; and after recovery of consciousness, severe memory impairment, fear, and hallucination; the CSF finding of pleocytosis and increased protein content; bilateral symmetrical lesions in the hippocampus by an MRI scan.

Our patient was unique in that she developed, during a course of LE, transient phonemic paraphasia. The paraphasias appeared to be very transient, lasting for approximately half a day, observed for one week. The hippocampus has not typically been identified as part of the language and aphasia circuit. However, recent evidence suggests that the hippocampus is closely related to naming, word priming, and anomic aphasia.[1,2,4] Among these, Urbach *et al.* have described the results of the Wada test, in which sodium amytal and SPECT tracer ^{99m}Tc- hexamethylpropyleneamine oxime (HMPAO) were injected into the posterior cerebral artery, with 4 of the 14 injected subjects revealing transient (lasting 1-3 min.) fluent anomic aphasia, together with contralateral hemianopia.[1] Paralyzed brain areas as shown by HMPAO were the parahippocampal gyrus, the hippocampus, and the occipital lobe. Similarly, Jernigan *et al.* performed MRI volumetry in normal volunteers and found that the hippocampal volume contributed independently to increased naming latency and decreased word priming by a speech test.[2] These findings might be a reflection of anatomical evidence that the hippocampus has fiber connections with the Wernicke's area.[5]

Another factor related to the transient phonemic paraphasia in our patient was the focal epilepsy. This is because our patient had seizures twice at the end of a one-week episode of phonemic paraphasia. EEG in our patient at the times of transient paraphasia also showed small sharp waves in the frontal, temporal, and parietal lobes bilaterally. Although partial status epilepticus can present with multiple, discrete MRI lesions in the brain,[6] MRI lesions in our patient were localized at the body to the infundibulum of the hippocampus. Previously, aphasic status epilepticus has been recognized in complex partial seizures (temporal lobe epilepsy).[7] Dong *et al.* reported 4 aphasic patients in whom this condition lasted from two days to three months. In those patients, MRI findings were normal; but focal slow waves by an electroencephalography and focal hypermetabolism by ^{18}F-fluorodeoxyglucose (FDG)- positron emission tomography (PET) were shown in the temporal lobe. Taken these findings into account, the transient phonemic paraphasia noted in our patient may have been a result of primary damage in the hippocampus and its fiber connection to the Wernicke's area or secondary partial status epilepticus that might have originated in the hippocampus and the temporal lateral cortex.

In conclusion, we have reported a 59-year old woman with limbic encephalitis of possible autoimmune etiology and bilateral symmetric, discrete lesions in the hippocampus based on an MRI scan. The transient phonemic paraphasia noted in our patient may have been a result of primary damage in the hippocampus and its fiber connection to the Wernicke's area or secondary partial status epilepticus that might have originated in the hippocampus and the temporal lateral cortex.

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