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CASE REPORT

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Two cases of steroid dementia showing partial recovery during 2-year follow-up

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Abstract

Background: Steroid dementia has been reported since the 1970s. In the current super-aged society, it increasingly receives attention because of the growing number of elderly people that are medicated with steroids for systemic rheumatic disease.

Case Presentation: We report two cases of steroid dementia that were diagnosed as a result of careful observation of clinical symptoms and biological examination, including nuclear medicine tests. Cognitive and daily living functions were partially recovered in both cases after decrease or discontinuance of steroid medication in 2-year follow-up, but their daily living function could not be totally restored to premorbid level.

Conclusion: Cognitive dysfunction caused by steroids is suggested by these cases, although definitive diagnosis in these cases is not possible. It was partially reversible over the course of a few years, but some functional loss remains. Cognitive function should be assessed appropriately before, during, and after steroid treatment. Detailed differential diagnosis of neurodegenerative disorders and longitudinal follow-up is required when cognitive dysfunction is observed after initiation of steroid therapy.

KEYWORDS
cognition, dementia, elderly, recovery, steroid

BACKGROUND

Glucocorticoid medications were first reported to cause cognitive deficit in patients with steroid psychosis in a review of 13 patients in 1979 by Hall et al.; intermittent memory impairment was seen in 71% of patients and persistent memory impairment in 7%.[1,2] The term "steroid dementia" was coined by Varney et al. in 1984,[3] although today it is regarded as cognitive impairment induced by steroid medication and which may persist beyond their discontinuation.[4,5] While the incidence rate of sever neuropsychiatric outcomes was estimated to be 15.7 per 100 person-years at risk for glucocorticoid exposure,[6,7] prevalence of steroid dementia is estimated to be seen in no more than 0.4%–1.25% of individuals who have taken steroid medication, which is a relatively low prevalence but not negligible.[4,5] The mechanism of steroid dementia may reflect steroid neuro-endangerment or neurotoxicity.[4,5] Meanwhile, substantial recovery from steroid-induced cognitive dysfunction has been shown in a limited number of cases after interruption of steroid administration.[8,9]

In the current super-aged society, the number of elderly people who receive steroid medication for systemic disease is continuously

increasing. Appearance of steroid dementia thus requires urgent attention. Further, the use of biological tests, including cerebral blood flow single-photon emission computed tomography (SPECT), metaiodobenzylguanidine (MIBG) myocardia scintigraphy, or dopamine transporter (DAT) scans, has improved the differential diagnosis of dementia. Importantly, detailed exclusion diagnosis of neurodegenerative disease is now more achievable in patients with steroid dementia compared with at the time of earlier case reports that were published between the 1970s and early 2000s.[2,4,10–12] Here, we present two cases of steroid dementia that were diagnosed as a result of careful observation of clinical symptoms and biological examination, including nuclear medicine tests. Both patients developed acute cognitive dysfunction after steroid administration, which was reduced or discontinued during 2-year follow-up, and this resulted in mild residual cognitive impairment. Written informed consent for publication of the case report was obtained from the patient in Case 1 and from the patient's daughter in Case 2.

CASE PRESENTATION

Case 1

A 68-year-old female lived with her husband with full independence in activity of daily living. She was able to perform general household chores and work with her husband at their barbershop. She underwent stent surgery with angina pectoris and was doing well with no sequelae. The patient had been treated with thyroid hormone medication for Hashimoto's disease since 60 years of age. She was admitted to the Department of Rheumatology and Clinical Immunology for anti-aminoacyl t-RNA synthetase antibody-positive interstitial lung disease in April. There was no hypoxemia because the patient was appropriately oxygenated. She was immediately prescribed 60 mg/day (1 mg/kg/day) of prednisolone (PSL). There were no problems for the first month of hospital care, but 45 days after admission she became confused about procedures such as bathing and operating the television. The Hasegawa's Dementia Scale-Revised (HDS-R) score was 24 (cutoff point for dementia = 20/21[13,14]). Electroencephalogram (EEG) revealed no slow-wave activity and no obvious brain atrophy or abnormal signals shown by 3T magnetic resonance imaging (MRI). The interstitial pneumonia began to improve, so PSL was gradually reduced to 30 mg/day in late May. After discharge in mid-June, the patient showed signs of behavioral disturbance, such as wearing too many clothes for the season and eating all the food in the refrigerator at home. There were no obvious steroid-induced psychiatric symptoms. She was admitted to the Department of Neuropsychiatry of our hospital. A very slight decrease in FT3 was noted on admission, but subsequent blood tests showed no significant thyroid hormone abnormalities. No slow waves in EEG and no abnormal findings in brain MRI ruled out Hashimoto's encephalopathy. The HDS-R score was 17. Disorientation, short-term and long-term memory disturbance, and loss of episodic memory were observed during her hospital stay. Her consciousness was not altered, and repeated EEG showed no abnormal waves in line with a previous report of steroid dementia,[4] suggesting no existence of delirium. Cognitive function tended to have partial improvement with steroid tapering during the treatment of pneumonia. In June, the HDS-R score was 19 at PSL 20 mg/day. In August, the HSD-R score was 22 and the Alzheimer Disease Assessment Scale-Cognitive Subscale Japanese version (ADAS-J Cog) (cutoff point for dementia = 9/10[15]) was 21.6 at PSL 10 mg/day. MRI showed no obvious brain atrophy or abnormal signals (Figure 1a). Cerebral blood flow on SPECT showed decreased blood flow in the bilateral medial prefrontal cortex and occipital lobes (Figure 1b). She continued to attend our department as an outpatient after discharge in September. In January the following year, PSL was decreased to 5 mg/day. In December that year, the HDS-R score was 24 and ADAS-J Cog score was 18. At follow up two years later, HDS-R score was 27, showing impairment in reciting numbers backwards, delayed recall, and naming of objects and ADAS-J cog score was 15.6. The patient continues to receive medical treatment with steroids for pneumonia. Daily living function remains slightly impaired; she is able to do simple cooking but requires support in shopping for daily necessities.

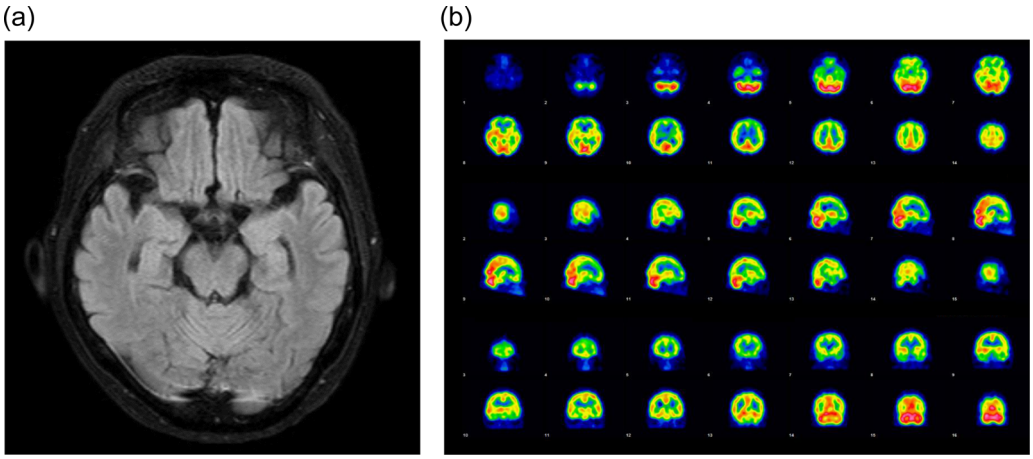

FIGURE 1 Case 1: (a) 3T magnetic resonance imaging (MRI) and (b) single-photon emission computed tomography (SPECT). In the MRI, the patient's left is shown on the right of the images. In the SPECT, axial view is shown from the feet to head, sagittal view is displayed from right to left, and coronal view is lined up from anterior to posterior.

Case 2

An 80-year-old woman lived fully independently by herself. A cerebral aneurysm of a pre-existing condition had been discovered during her 70 s. She was able to cook by herself, and she used to go out on the bicycle. Her eldest daughter had noticed no memory loss in her. In February, she started taking 20 mg/day of PSL for polymyalgia rheumatica with general pain. Three weeks later, symptoms such as depression, thoughts of death, and psychomotor agitation appeared. She was admitted to our Department of Neuropsychiatry owing to behavioral disturbance with delusion of theft, spatial cognitive impairment, and marked anxiety and frustration. Scores for the HDS-R and Mini-Mental State Examination (MMSE) were 9 and 17, respectively (cutoff point for dementia = 23/24[16]). EEG revealed diffuse slow-wave activity on bilateral hemispheres. Chronic ischemic changes were shown by 3T MRI, mainly in the bilateral periventricular areas, with unremarkable atrophy in the medial temporal lobes. These neuroimage findings suggested that cognitive dysfunction was not caused by specific neurodegenerative disease. Steroid medications were reduced by 3 mg/day because there was suspicion of steroid delirium. Polymyalgia rheumatica was not worsening. In October, the HDS-R score recovered to 14, but was accompanied by symptoms of anxiety. She was discharged from the hospital in November. In January of the next year, with 2.5 mg/day of PSL, she was again admitted to our Department of Neuropsychiatry owing to violence against her husband and jealous delusions. From February, PSL was tapered off, and her psychiatric symptoms were dismissed in response to steroid reduction. EEG revealed focal 7–9-Hz slow wave in some areas, although basic activity was alpha rhythm. Steroid-induced delirium may be overlapped in the early course of hospitalization. No site-specific brain atrophy was shown on 3T MRI (Figure 2a). Cerebral blood flow on SPECT showed no decrease in blood flow in the posterior cingulate gyrus, precuneus, or parietal lobe (Figure 2b), so there was no suggestion of Alzheimer's disease. DAT scan and MIBG myocardia scintigraphy showed no particular findings of dementia with Lewy

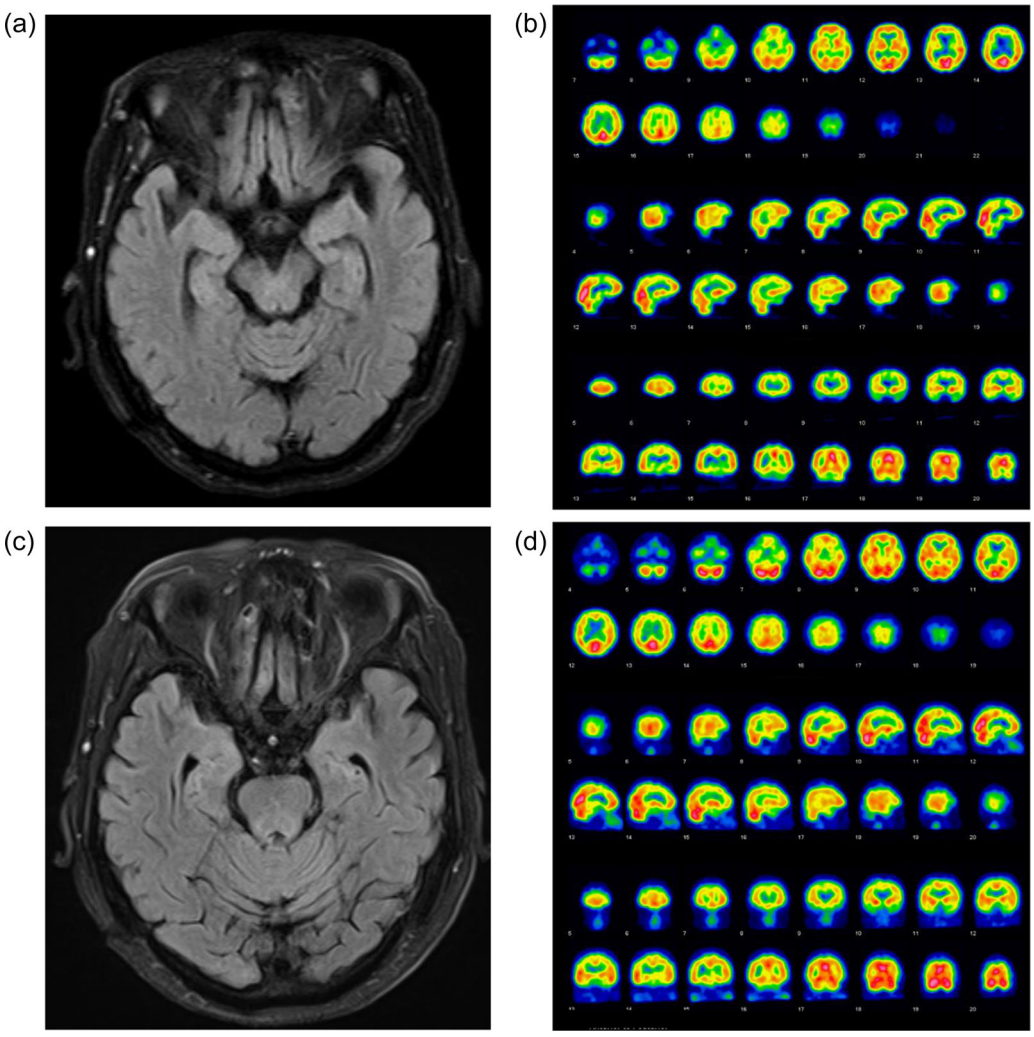

FIGURE 2 Case 2: (a,c) 3T magnetic resonance imaging (MRI) and (b,d) single-photon emission computed tomography (SPECT). In the MRI, the patient's left is shown on the right of the images. In the SPECT, axial view is shown from the feet to head, sagittal view is displayed from right to left, and coronal view is lined up from anterior to posterior.

Bodies. One year after discontinuation of PSL, persistent cognitive impairment without psychiatric symptoms was observed with the HDS-R score of 11. Two years after discontinuation of PSL, the HDS-R score was 24, indicating some improvement in cognitive function, although there was still some difficulty in delayed playback, object calling, and retroactive recitation, indicating some improvement in cognitive function. She could no longer live fully independently by herself and required assistance with cooking, shopping, and dressing. SPECT and 3T MRI at the same time revealed no degenerative disease-specific patterns (Figure 2c,d).

DISCUSSION

We present two cases of acute cognitive impairment induced by steroids with details of their clinical course and longitudinal follow-up. In both cases, cognitive decline appeared in an acute course after the start of steroid treatment, and continued for several months without degenerative disease-specific findings in structural 3T MRI and nuclear medicine tests. Each patient's cognitive and daily function partially recovered over a period of about 2 years in response to decrease or discontinuation of steroid medication, but this was insufficient to restore premorbid life function levels. These cases suggest that cognitive function can be acutely impaired by steroids, but it is to some extent reversible over the course of the next few years, although some loss of function remains. To our knowledge, these are the first reported geriatric cases of a long-term course of steroid dementia over a long-term course with detail of differential diagnoses using several neurodegenerative disorder-related biological makers. This report provides insight into the clinical course and biological basis of steroid dementia.

Animal studies have shown that high doses of corticosterone may be neurotoxic to the hippocampus and may affect glucocorticoid receptors in the hippocampus and prefrontal cortex.[17–21] Glucocorticoids, whose receptors are present in high density in the hippocampal CA1 of humans, including elderly people, are known to act on neurons in the central nervous system in a dose- and exposure-time-dependent manner, and they may be involved in neuroplasticity.[22] In humans, it has been suggested that long- or short- term steroid exposure reduces hippocampal volume,[23,24] and from a neuroimaging point of view, partial reduction in blood flow has been reported as an effect of high steroid doses on the brain.[4] One case report of 10-year-old boy with glucocorticoid medication showed longitudinal cognitive deficit and reduced hippocampal volume and decreased activity in the left posterior frontal and left parietal lobes.[5] These findings suggest that there may be direct or indirect neurotoxicity caused by the use of steroids.

Systemic immune disease itself may have caused impairment of cognitive function in these two cases. However, cognitive decline appeared or continued after improvement of interstitial lung disease in Case 1 and of polymyalgia rheumatica in Case 2. While both patients underwent physical rehabilitation during hospitalization to prevent disuse syndrome, low activity during hospitalization may have impacted upon cognitive decline. Moreover, aging-related cognitive decline may have partially existed or developed during the 2-year follow-up period in these elderly patients. In general, steroid-induced cognitive dysfunction has not yet been demonstrated and it is difficult to clearly rule out several factors, so definitive diagnosis of steroid dementia should be made cautiously.

There are several limitations to this report. In both cases, accurate cognitive function tests were not performed before the onset of the disease, so difference in function before and after steroid treatment is difficult to quantify. In addition, it is desirable to quantify and evaluate cognitive dysfunction and psychiatric symptoms simultaneously.

CONCLUSION

In steroid therapy, attention should be paid to the appearance and progression of cognitive dysfunction and to the presence and degree of residual cognitive function after tapering of steroid medication. Cognitive function should be appropriately assessed before, during, and after the start of steroid treatment. Detailed differential diagnosis of neurodegenerative disorders and longitudinal follow-up is required when cognitive dysfunction is observed after initiation of steroid therapy.

AUTHOR CONTRIBUTIONS

Natsuko Ikeda and Shun Takahashi conceptualized the case report. Shinichi Yamada, Masahiro Yamamoto, Katsunori Tanaka, Takao Fujii, Tomikimi Tsuji, and Sohei Kimoto provided the clinical insights. Natsuko Ikeda wrote the first manuscript draft and Shun Takahashi assisted writing the paper. All authors contributed to and have approved the final manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICS APPROVAL STATEMENT

Not applicable.

PATIENT CONSENT STATEMENT

Written informed consent for publication of the case report was obtained from the patient in Case 1 and from the patient's daughter in Case 2.

CLINICAL TRIAL REGISTRATION

Not applicable.

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