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Fall prevention in the elderly

Koichi Kozaki

Abstract

Causes of falling are multi-factorial. Although it is not easy to identify specific causes of falling, it is necessary to detect the significant causes of falling in each individual. In particular, use of medications and indoor hazards are important factors. We need to give instructions to families who live together with older persons how to avoid dangers of falling. Exercise has been proven to provide beneficial effects to prevent falling, however it is necessary to consider exactly what and how much exercise one should prescribe to elderly individual who are at high risk of falling. In other words, it is important to give best approach to prevent falling after considering the status of the elderly.

Key words: *Dependent elderly, Fall-predicting score, Tai-Chi exercise, Individual assessment*
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Evaluation of risk of falls in patients at a memory impairment outpatient clinic

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Aim: We investigated the usefulness of the fall-predicting score, a simple screening test to identify patients at high risk of falls in outpatients with cognitive impairment.

Methods: This was a 1-year prospective study. Seventy-nine patients (28 men and 51 women, 78.1 ± 5.9 years old) in the Memory Impairment Outpatient Clinic of Kyorin University Hospital. History of falls in the past year, record of falls in the follow-up period (1 year), fall-predicting score, time of standing on one foot, timed Up & Go test, tandem gait, functional reach, grip strength, maximum circumference of the legs and blood laboratory tests were measured.

Results: Of the 79 subjects, 38 (48.1%) had experienced falls in the past year, and 29 (36.7%) experienced falls during the follow-up period. Comparing the two groups with and without a history of falls during the follow-up period, a significant difference was observed in fall-predicting score, timed Up & Go test, tandem gait and functional reach. Logistic regression analysis revealed that fall-predicting score was the only significant determinant for predicting future falls. Furthermore, fall-predicting score correlated with timed Up & Go, duration of standing on one foot, functional reach, grip strength and tandem gait. When the χ^2-test was performed to investigate the correlation between individual items of the fall-predicting questions and falls during the follow-up period, "Do you use a stick when you walk?" and "Are there any obstacles in your house?" showed a significant difference ($P < 0.05$).

Conclusion: Fall-predicting score is useful as a screening test to predict future falls in patients with cognitive decline.

Keywords: fall, fall-predicting score, memory impairment.

Introduction

The annual rate of falls in elderly people is reported to be 10–30% in Japan, and the rate is higher in women than in men and increases with age.[1,2] Because falls are a pivotal cause of bone fractures, a significant background of bed-ridden status in the elderly, establishing preventive measures against falls is important to decrease the number of bed-ridden elderly people. Falls occur through a combination of internal and external factors, such as impaired balance and decreased muscle strength,[3,4] poor vision, neurological disorders, orthostatic hypotension, cognitive impairment,[5] use of medication such as psychotropics[6] and hazardous indoor

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environment.[7] To identify elderly people with a high risk of falls caused by these complex factors, Toba *et al.* created the fall-predicting score,[8] a self-answered questionnaire with 21 items, as a simple screening test (Appendix). A cross-sectional investigation in community-dwellers found that the fall-predicting score was significantly related to past history of falls.[8] In addition, in a 6-month prospective study of community-dwellers, Okochi *et al.* found that the fall-predicting score was useful for predicting future falls.[9] It was also shown, using the fall-predicting score, that regular exercise is beneficial to prevent falls in elderly women.[10] Although the usefulness of the fall-predicting score has been tested in the general population, no study has been performed in patients with cognitive impairment. Although cognitive impairment is reported to be a significant cause of falls, it is not easy to examine the location, time and number of falls in these patients. In the present study, we examined the usefulness of the fall-predicting score in outpatients at the Memory Impairment Clinic of Kyorin University Hospital. To obtain data of falls as accurately as possible, we prepared a fall-recording notebook and instructed all the patients and their family to record the circumstances of falls whenever they happened. In addition to the fall-predicting score, cognitive function, use of prescribed medication, laboratory tests including bone metabolic markers, bone mineral density and fall-related physical functions were also examined to investigate the significance of each test in falls and determine the correlation between fall-predicting score and each test.

Methods

This study was performed in 98 consecutive outpatients (men, 32; women, 66), who were cognitively declined but able to verbally communicate with other people, at the Center for Comprehensive Care of Memory Disorders at Kyorin University Hospital. The mean age of the patients was 78.5 ± 6.1 years old (range, 61–91 years old). In each patient, history of falls in the past year, daily use of medication, fall-predicting score[8] (self-answered questionnaire, Appendix), fall-related physical examination (duration of standing on one foot with open eyes, timed Up & Go test, tandem gait, functional reach, grip strength and maximum circumference of the legs), cognitive function (Mini-Mental State Examination, MMSE), blood biochemical parameters (total protein, albumin, calcium, phosphate, blood urea nitrogen [BUN], creatinine, Fe, glycosilated hemoglobin, total cholesterol, low-density lipoprotein [LDL]-cholesterol and triglyceride), bone metabolic markers (type I collagen cross-linked N-telopeptide [NTx] and bone-type alkaline phosphatase) and bone mineral density (dual energy X-ray absorptiometry [DXA]) were determined. In addition, a fall-recording notebook was handed to each patient and their family, and they were instructed to fill out the circumstances of when, where and how the patient fell during the follow-up period. Every time the patient attended the clinic, the fall-recording notebook was examined. One year after the first visit, fall-predicting score was determined and fall-related physical examination was performed again. The diagnosis of individual cognitive impairments was made using the following diagnostic standards: Alzheimer's disease (AD); National Institute of Neurological and Communicative Disorders and Stroke – Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA),[11] vascular dementia (VaD); NINDS – Association Internationale pour la Recherche et l'Enseignenent en Neurosciences (NINDS-AIREN),[12] dementia with Lewy bodies (DLB); the guidelines for diagnosis of dementia with Lewy bodies consortium (2005),[13] mild cognitive impairment (MCI); Mayo Clinic criteria,[14] frontotemporal lobar degeneration (FTLD); a consensus on clinical diagnostic criteria,[15] depression; and the Geriatric Depression Scale.[16]

Statistical analysis

SPSS software (ver. 12.0) was used for analysis. Based on the data recorded in the fall-recording notebook, the cause, location and time of falls were examined. Two groups of subjects, those who experienced falls during the follow-up period and those who did not, were compared by Student's t-test for continuous variables such as age, blood test results, bone metabolic markers and bone mineral density, or by Mann–Whitney test for all the other discrete variables. The correlation between the use of medication and falls was examined by χ^2-test. Logistic regression analysis was performed to determine significant independent variables for the occurrence of falls during the follow-up period. Pearson's correlation coefficient was determined to examine the relationship between the fall-predicting score and each fall-related physical examination.

Ethical consideration

This study was approved by the Medical Ethical Committee of the Kyorin University. We explained this study clearly, and obtained written consent from all participants and their guardians (mainly family members). All the data were stored and analyzed carefully to preserve the subjects' anonymity and protect their privacy.

Results

Ninety-eight consecutive outpatients were recruited in this study. They were cognitively declined, but able to verbally communicate with families, caregivers, and doctors (MMSE: 9–30 points, mean ± SD: 22.8 ± 5.1,

Table 1 Characteristics of study subjects

Age, mean ± SD	78.1 ± 5.9
Sex (male : female)	28:51
MMSE, mean ± SD	22.8 ± 5.1 (9–30)
Fall-predicting score, mean ± SD	8.8 ± 4.1
Type of cognitive impairment, n (%)	
MCI	30 (38.0%)
AD	18 (22.8%)
VaD	8 (10.1%)
Mixed type	6 (7.6%)
Depression	6 (7.6%)
DLB	5 (6.3%)
FTLD	4 (5.1%)

Full marks of the fall-predicting score is 21 points. AD, Alzheimer disease; DLB, dementia with Lewy bodies; FTLD, frontotemporal lobar degeneration; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; SD, standard deviation; VaD, vascular dementia.

Table 2 Occurrence of falls in year before and year after initiating the study

	Falls in past year, *n*	No falls in past year, *n*	Total, *n*
Falls in follow-up period, *n*	18	11	29
No falls in follow-up period, *n*	20	30	50
Total, *n*	38	41	79

Table 1). Seventy-nine subjects were able to be followed for one year. Eighteen subjects discontinued the study because of hospitalization or moving to other facilities, and one patient died. The type of cognitive impairment in the 79 subjects is shown in Table 1; two leading causes were mild cognitive impairment (MCI) and Alzheimer disease (AD).

A total of 76 falls occurred during the one-year period before the study and during the follow-up period. Falls occurred in 38 (48.1%) of the 79 subjects in the year before the study, and in 29 subjects (36.7%) during the follow-up period. Thirty-two falls (42.1%) occurred outdoors, 31 (40.8%) indoors, and 13 (17.1%) were unable to be identified. Frequent locations of falls were the street (25.0%) and backyard (6.6%) for outdoors, and the living room (10.5%), hallway (7.9%), bathroom (6.6%) and entrance (5.3%) for indoors. Regarding the time when falls occurred, 22 falls (28.9%) occurred in the morning and 36 (47.4%) in the afternoon. Falls in the morning occurred most frequently between 10.00 and 11.00 hours, accounting for 58.3% of falls in the morning. Falls in the afternoon occurred most frequently between 18.00 and 19.00 hours, accounting for 24% of those in the afternoon. Fall rate according to the type of cognitive impairment was 80% DLB, 75% FTLD, 50% VaD, 50% depression, 28% AD, 27% MCI and 17% mixed type, showing that the fall rate in DLB patients was significantly higher than that in MCI patients ($P = 0.038$).

In the two groups with and without a history of falls in the year before the study, 18 of 38 subjects (47.4%) with prior falls experienced falls in the follow-up period, and 11 of 41 subjects (26.8%) without prior falls experienced falls in the follow-up period (Table 2). Although the fall rate during the follow-up period in the group with a history of falls was higher than that in the group without a history of falls, statistically significant difference was not found between the two groups.

Next, a comparison was made between the two groups with and without falls during the follow-up period with regard to age, blood test results, cognitive function (MMSE), fall-predicting score, bone mineral density, fall-related physical functions and medication. No significant difference was found between the two groups in age, all blood test results, bone mineral density, MMSE and use of all medications. With regard to medication, non-significant but higher occurrence of multiple falls ($P = 0.054$ by χ^2-test) was found in the users of hypotensive drugs. On the other hand, a significant difference in the fall-predicting score, timed Up & Go, duration of standing on one foot and functional reach was confirmed (Table 3).

Next, logistic regression analysis was performed with four items that showed a significant difference between patients with and without a history of prior falls, as well as age and sex as independent variables, and with the experience of falls during the follow-up period as a dependent variable. As a result, only the fall-predicting score was a significant factor ($P = 0.047$, odds ratio (OR) = 1.2, Table 4). When the correlation between each question of the fall-predicting score and the experience of falls during the follow-up period was analyzed by χ^2-test, a significant difference ($P < 0.05$) was found in two questions, "Do you use a stick when you walk?" and "Are there any obstacles in your house?", while a tendency for a difference ($0.05 < P < 0.1$) was observed in four questions, "History of tripping", "Can you cross a road within the green signal interval?", "Is there any difference in level within your home?" and "Do you have to walk up and down a steep slope around your house?".

When the correlation between the fall-predicting score and individual fall-related physical functions was analyzed, a significant correlation was confirmed in grip strength ($r = -0.408$), duration of standing on one foot ($r = -0.338$), timed Up & Go ($r = -0.352$), functional reach ($r = -0.341$) and tandem gait ($r = -0.453$).

Table 3 Comparison of fall-related question items between two groups with and without falls during follow-up period

	Total (n = 79)	With falls (n = 29)	No falls (n = 50)	P-value
Age	78.1 ± 5.9	78.3 ± 5.0	78.0 ± 6.4	0.749
Sex (M : F)	28:51	13:16	15:35	0.226
MMSE, points	22.8 ± 5.1	22.9 ± 4.9	22.6 ± 5.3	0.605
Fall-predicting score, points	8.7 ± 4.1	10.5 ± 4.2	7.8 ± 3.8	0.021
Max circumference of legs, cm	32.1 ± 3.1	32.6 ± 3.1	31.8 ± 3.1	0.306
Grip strength (major hand), kg	14.1 ± 6.5	14.3 ± 7.7	14.0 ± 5.8	0.859
Duration of standing on left foot, s	10.1 ± 8.7	7.8 ± 7.7	11.3 ± 9.0	0.076
Duration of standing on right foot, s	11.0 ± 18.3	7.2 ± 7.3	13.1 ± 21.9	0.046
Timed Up & Go, s	15.4 ± 6.3	17.3 ± 7.0	14.4 ± 5.8	0.028
Tandem gait, steps	5.3 ± 4.3	4.9 ± 4.1	5.6 ± 4.5	0.495
Functional reach, cm	24.2 ± 6.2	22.7 ± 6.5	25.1 ± 5.9	0.026

Data are shown by mean ± standard deviation.

Table 4 Logistic regression analysis of falls during follow-up period

	OR	P-value	95% CI
Age		0.238	0.84–1.05
Sex		0.056	0.10–1.03
Fall-predicting score, points	1.2	0.047	1.00–1.37
Duration of standing on one foot (right), s		0.558	0.90–1.06
Timed Up & Go test, s		0.682	0.92–1.13
Functional reach, cm		0.330	0.85–1.06

Odds ratio (OR) significant at the $P < 0.05$ level or greater are indicated. CI, confidence of interval.

Discussion

Ninety-eight consecutive outpatients were recruited in this study. They were cognitively impaired, but able enough to tell whether they fell or not within a few hours. The correctness of the information of falling was improved by utilizing a fall-recording notebook, and instructing the patient and the family to record the circumstances of falling whenever it happened. The fall rate in the past year (48.1%) and that during the follow-up period (36.7%) were higher than the reported fall rates of community-dwelling elderly people (10–30%). This is probably because activities of daily living (ADL) of our study subjects, who were outpatients at a memory impairment clinic, was lower than that of community dwellers, and patients with cognitive impairment are more prone to falls. In this study, the rate of indoor and outdoor falls was comparable. This is probably because the patients at our memory impairment clinic stayed inside longer than community dwellers, who showed a higher rate of falls outdoors than indoors,[17] and shorter than people in nursing homes, who showed a higher rate of falls indoors than outdoors.[18] Regarding the time of day when falls occurred, 28.9% happened in the morning and 47.4% in the afternoon. With regard to the relations of the location and time when falls occurred, it appears that falls occurred outside in the morning and inside in the evening. When we examined fall rate by the type of cognitive deficit, it was revealed that the fall rate in DLB patients was higher than that in MCI patients ($P = 0.038$), and the duration of standing on one foot in DLB patients was significantly shorter than that in MCI patients. This agrees with the inclusion criterion of "repeated falls" in the diagnosis of DLB. The fall rate during the follow-up period in subjects with a history of falls in the past year (47.4%) was higher than that in subjects without a history of falls (26.8%), though the difference did not reach statistical significance. Considering several reports showing a past history of falls as a future falls risk, further investigation with a larger number of subjects is needed before drawing a conclusion.

It is reported that diabetes,[19] frailty,[20] sarcopenia[21] and osteoporosis[22] are causes of muscle weakness, impaired balance and a decrease in walking speed, leading to the occurrence of falls. In this study, we did not find a correlation between falls and any blood laboratory test results including hepatitis B surface antigen 1c (HbA1c), bone metabolic markers, bone mineral density and maximum circumference of the legs. Regarding the correlation between medication and falls, it was shown that psychotropics[23,24] and polypharmacy[25] are risk factors for falls. Therefore, a decrease or termination of the use of medication including psychotropics is recommended to prevent falls.[26,27] Although no significant correlation was found between falls and the use of any drugs in this study, users of hypotensive drugs tended to show a higher occurrence of multiple falls by χ^2-test ($P = 0.054$).

It is reported that balance disorder and muscle weakness are risks for falls, and that fall-related physical functions such as timed Up & Go test,[28,29] tandem gait,[30] duration of standing on one foot,[31] functional reach[32] and grip strength[33] were shown to be related to falls. When the two groups with and without the occurrence of falls during the follow-up period were compared, a significant difference was found in timed Up & Go test, duration of standing on one foot and functional reach in this study. The fall-predicting score was different between the two groups, while their cognitive level was comparable. To understand the significant factor(s) predicting future falls in these subjects with comparable levels of cognitive impairment, we performed logistic regression analysis, including factors which showed significant difference between fallers and non-fallers as independent variables. As a result, we found that only the fall-predicting score was a significant factor. This implies that fallers with cognitive dysfunction could be predicted by performing a fall-predicting questionnaire.

Fall-predicting score is a simple screening test created by Toba *et al.* It is a self-answered questionnaire to detect persons with a high risk of falls. In cross-sectional analysis of the correlation between falls and past history of falls in community dwellers, a significant correlation was confirmed for the items "History of tripping", "Can you cross a road within the green signal interval?", "Do you use a stick when you walk?", "Do you have knee pain?", "Do you feel dizzy at times?", "Can you squeeze a towel tightly?" and "Are there any obstacles in your house?".[8] In addition, in the 6-month prospective study performed by Okochi *et al.* in community dwellers, the items; "History of falls within the past year?", "Do you feel your walking speed has declined recently?", "Do you use a stick when you walk?", "Is your back bent?" and "Do you take five or more prescribed medicines?" were significant predictive factors for future falls.[9] In our prospective study of elderly female subjects who exercise regularly, it was found that five items – age ($P < 0.001$, OR = 1.1), "History of falls within the past year?" ($P < 0.001$, OR = 3.8), "History of tripping" ($P = 0.003$, OR = 2.3), "Can you squeeze a towel tightly?" ($P = 0.030$, OR = 3.0) and "Do you have to walk up and down a steep slope around your house?" ($P = 0.048$, OR = 1.6) were significant fall-related items.[10] As shown above, the significance of each question item in relation to falls differed depending on the subjects and the design of the study. Nevertheless, there is no doubt that the fall-predicting score is a simple and useful screening test to predict future falls. When the fall-predicting score and each fall-related physical examination was compared, a significant correlation was confirmed for the duration of standing on one foot, timed Up & Go, functional reach, as well as tandem gait and grip strength. Therefore, it is suggested that the fall-predicting score could be performed at any place instead of time-consuming fall-related physical examination.

In conclusion, fall-predicting score can predict future falls in patients with cognitive decline. Because a good correlation of the fall-predicting score with individual fall-related physical examinations was found, fall-predicting score could be used as a screening test to detect individuals at high risk of falls.

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Appendix

Items of fall-predicting score (questionnaire)

Q1. History of tripping. Yes, 1; No, 0.
Q2. Can you climb stairs without help? Yes, 0; No, 1.
Q3. Do you feel your walking speed has declined recently? Yes, 1; No, 0.
Q4. Can you cross a road within the green signal interval? Yes, 0; No, 1.
Q5. Can you walk 1 km without stopping? Yes, 0; No, 1.
Q6. Can you stand on one foot for about five seconds? Yes, 0; No, 1.
Q7. Do you use a stick when you walk? Yes, 1; No, 0.
Q8. Can you squeeze a towel tightly? Yes, 0; No, 1.
Q9. Do you feel dizzy at times? Yes, 1; No, 0.
Q10. Is your back bent? Yes, 1; No, 0.
Q11. Do you have knee pain? Yes, 1; No, 0.
Q12. Do you have a problem with your vision? Yes, 1; No, 0.
Q13. Do you have a hearing problem? Yes, 1; No, 0.
Q14. Do you think you are forgetful? Yes, 1; No, 0.
Q15. Do you feel anxious about falling when you walk? Yes, 1; No, 0.
Q16. Do you take five or more prescribed medicines? Yes, 1; No, 0.
Q17. Do you feel unsafe because your home is dark? Yes, 1; No, 0.
Q18. Are there any obstacles in your house? Yes, 1; No, 0.
Q19. Is there any difference in level within your home? Yes, 1; No, 0.
Q20. Do you have to use stairs in daily living? Yes, 1; No, 0.
Q21. Do you have to walk on a steep slope around your house? Yes, 1; No, 0.

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Association of plasma sex hormone levels with functional decline in elderly men and women

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Aim: We aimed to determine whether plasma sex hormone levels are associated with activities of daily living (ADL), cognition, depression and vitality in elderly individuals with functional decline.

Methods: Two hundred and eight consecutive persons 70 years or older (108 men and 100 women; mean ± standard deviation, 81 ± 7 years) with a chronic stable condition, receiving long-term care at a long-term care facilities located in Nagano Prefecture, Japan, were enrolled. Plasma total testosterone, free testosterone (only in men), dehydroepiandrosterone (DHEA), DHEA sulfate (DHEA-S) and estradiol levels were determined in the morning after an overnight fast. Comprehensive geriatric assessment was performed including basic ADL by Barthel Index, instrumental ADL, cognitive function by Hasegawa Dementia Scale – Revised, mood by Geriatric Depression Scale and ADL-related vitality by Vitality Index.

Results: Simple regression analysis showed that, in men, plasma total and free testosterone levels were associated with basic ADL ($R = 0.292$ and $R = 0.282$), instrumental ADL ($R = 0.261$ and $R = 0.408$), cognitive function ($R = 0.393$ and $R = 0.553$) and vitality ($R = 0.246$ and $R = 0.396$), while DHEA(-S) was associated with cognitive function, and estradiol with cognitive function as well as vitality. In women, the only significant correlation was between DHEA(-S) and basic ADL. Adjustment for age and nutritional markers did not influence the associations of plasma sex hormone levels with functional scores except for that of free testosterone with Barthel Index.

Conclusion: These results suggest that sex hormones have sex-specific associations with physical and neuropsychiatric functions in elderly individuals, and that endogenous testosterone is related to global function in elderly men.

Keywords: activities of daily living (ADL), comprehensive geriatric assessment, dehydroepiandrosterone sulfate, estradiol, testosterone.

Introduction

In addition to the abrupt reduction in estrogen production in women during the menopause, both men and women experience an age-associated decrease in the levels of androgens.[1-3] Physical and neuropsychiatric

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function also declines with age; however, the association of sex hormones with functional decline is not fully understood. One nursing home study found that a higher total testosterone (T) level was associated with better activities of daily living (ADL) performance such as transferring and eating among frail elderly men, while estrone and dehydroepiandrosterone (DHEA) levels were inversely related to ADL in women.[4] Although several observational studies examining the relationship between endogenous androgen and cognitive function in elderly men have also been published,[5–8] most surveys have investigated only a few aspects of functions rather than the whole spectrum and have been carried out based on community samples of white people in Western countries. In addition, many studies are restricted to one sex and few have focused on frail or disabled elderly individuals.

Thus, additional data are needed to elucidate the relationship between plasma hormone levels and functional status in elderly individuals with functional decline to better understand the application of hormone replacement therapy to bring about the most beneficial effects. In our preliminary study in a small sample of frail elderly men, a higher plasma T level was associated with higher functional scores.[9] To extend this pilot study, we included a larger sample of elderly men and women with functional decline, and evaluated whether sex hormone levels, including DHEA sulfate (DHEA-S) and estradiol, are associated with functioning on the basis of comprehensive geriatric assessment.

Methods

Study design and participants

In this cross-sectional observational study, 208 consecutive persons aged 70 years or older (108 men aged 70–95 years and 100 women aged 70–93 years; mean ± standard deviation, 82 ± 7 and 81 ± 6 years, respectively) who attended health service facilities for the elderly (facilities that provide nursing care and rehabilitation services to elderly people with disability, "Mahoroba-no-Sato") located in Nagano Prefecture, Japan, were enrolled. The participants were in a chronic stable condition and receiving Long-term Care Insurance either for facility admission or day-care service. The principal exclusion criteria were malnutrition (serum albumin, <3.5 mg/dL), extremely low ADL status (Barthel Index,[10] <50), malignancy, acute inflammation (fever, white blood cell count of >10 000/mL, or other signs of infection within 4 weeks before enrollment), severe anemia (blood hemoglobin, <10.0 g/dL) and overt endocrine diseases because these diseases may affect both plasma sex hormone levels and functions. The following information was collected from medical history charts or by interviewer-administered questionnaire; past medical history, present diagnosis of any disease, medication and nutritional intake. Comorbid conditions included in the current analysis were hypertension, chronic heart disease (angina, myocardial infarction, congestive heart failure, arrhythmia), stroke, osteoarthropathy (arthritis, rheumatism, osteoporosis, history of fractures) and diabetes mellitus. We also obtained data on anti-androgenic treatment or intake of glucocorticoids, opiates or hormone supplements which could affect plasma hormone levels, but no subject was taking any of these. The institutional review board of Kikyogahara Hospital approved the study protocol, and all participants or their families gave written informed consent.

Hormone measurements

Blood samples were obtained from the participants in the morning after an overnight fast, and plasma hormone levels, in addition to blood cell counts and blood chemical parameters, were determined by a commercial laboratory (Health Sciences Research Institute, Yokohama, Japan). Free-T, DHEA-S and DHEA were assayed using sensitive radioimmunoassays. Total-T and estradiol were assayed using chemiluminescence immunoassays with minimum detection limits of 7 ng/dL (0.2 nmol/L) and 4 pg/mL (14.7 pmol/L), respectively. The intra-assay coefficients of variation for these measurements were less than 5%.

Functional and anthropometric measurements

Trained nurses and physical therapists visited the participants at the health service facilities and performed comprehensive geriatric assessments. Basic ADL was assessed by Barthel Index,[10] instrumental ADL (IADL) by Lawton and Brody's IADL,[11] cognitive function by Hasegawa Dementia Scale – Revised (HDS-R, 30-point scale),[12] mood by Geriatric Depression Scale (GDS, 15 items)[13] and ADL-related vitality by Vitality Index (10-point scale).[14] In the current study, three items (food preparation, household tasks and laundering) were removed from the original version of Lawton and Brody's IADL scale to assess men; thus, IADL scale ranged 0–5 points in men and 0–8 in women. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

Statistical analysis

Data were analyzed using SPSS statistical software (version 11.0). Data were compared between men and women using the Student's t-test for continuous variables and χ^2-tests for categorical variables. Pearson's simple correlation coefficients were determined by plasma sex hormone levels, age and functional measures. Standardized regression coefficients from multivariate linear regression analysis of functional measurements in relation to age, nutritional markers and plasma hormone levels were determined. An unpaired Student's *t*-test was used for the differences in hormone levels and functional status according to associated diseases. $P < 0.05$ was considered statistically significant.

Results

The characteristics of the study subjects are presented in Table 1. Sex differences were found in the levels of hemoglobin and total cholesterol, and also in the percentage of subjects with heart disease and stroke. On average, subjects showed mild-to-moderate functional decline, and scores of Barthel Index, HDS-R and Vitality Index were higher in women than in men. Plasma level of total-T in male cohorts was lower than that reported in healthy elderly men,[15] but comparable to those in frail elderly men.[4] All plasma hormone levels were significantly higher in men than in women.

In simple regression analysis, age was negatively correlated with most of the functional scores except for instrumental ADL and GDS in men and GDS in women (data not shown). Because an age-associated decline of plasma sex hormone levels[1–3] and an influence of nutritional status on hormone levels[16,17] have been reported, we analyzed the correlations between hormone levels, age and BMI (Table 2). However, only free-T in men was significantly associated with age, and only total-T in women was correlated with BMI. Because DHEA, testosterone and estradiol have precursor-metabolite relationships in the steroid-hormone biosynthesis cascade, we evaluated the correlations between each of the plasma hormone levels (Table 2). Some, but not all, plasma sex hormone levels showed significant correlations in both sexes.

Table 1 Distribution of variables in study subjects

	Men	Women
No. of subjects	108	100
Age, years	82 ± 7 (70–95)	81 ± 6 (70–93)
Nutritional parameters		
Body mass index, kg/m²	21.8 ± 3.3 (15.1–29.0)	22.9 ± 3.8 (16.0–33.6)
Hemoglobin, g/dL	13.7 ± 1.7 (10.4–18.7)	12.8 ± 1.3 (10.0–15.6)**
Albumin, g/dL	4.2 ± 0.3 (3.5–4.9)	4.2 ± 0.3 (3.5–4.9)
Total cholesterol, mg/dL	181 ± 32 (119–273)	205 ± 33 (126–288)**
Chronic diseases		
Hypertension, *n* (%)	31 (28.7)	36 (36.0)
Heart disease, *n* (%)	9 (8.3)	19 (19.0)*
Stroke, No. (%)	35 (32.4)	19 (19.0)*
Osteoarthropathy, *n* (%)	23 (21.3)	31 (31.0)
Diabetes mellitus, *n* (%)	10 (9.3)	14 (14.0)
Functional parameters		
Barthel Index	84 ± 17 (50–100)	93 ± 9 (60–100)**
Instrumental ADL†	2.6 ± 2.0 (0–5)	5.9 ± 2.3 (0–8)
HDS-R	19 ± 7 (2–30)	23 ± 6 (5–30)**
Vitality Index	9.2 ± 1.1 (5–10)	9.7 ± 0.6 (6–10)**
GDS	5.6 ± 3.2 (0–13)	5.4 ± 3.0 (0–13)
Hormones		
Total testosterone, nmol/L	14.8 ± 5.8 (2.5–30.5)	1.3 ± 0.6 (0.2–2.9)**
Free testosterone, pmol/L	22.2 ± 8.7 (3.1–43.4)	
DHEA-S, µmol/L	1.75 ± 1.18 (0.26–5.47)	1.34 ± 0.54 (0.38–2.70)**
DHEA, nmol/L	7.63 ± 3.82 (2.43–25.7)	4.86 ± 2.08 (1.04–11.1)**
Estradiol, pmol/L	109.4 ± 48.1 (14.7–228.0)	59.5 ± 38.9 (14.7–206.7)**

Probability values of chronic diseases were compared between men and women by χ^2-test; *$P < 0.05$. Age, nutritional parameters, functional parameters (except for instrumental ADL) and hormone measurements were compared between men and women by Student's *t*-test; **$P < 0.001$. Values except those for chronic diseases are shown as mean ± standard deviation (range). †Lawton and Brody's instrumental ADL scale ranges 0–5 points in men and 0–8 in women, respectively. ADL, activities of daily living; DHEA, dehydroepiandrosterone; DHEA-S, dehydroepiandrosterone sulfate; GDS, Geriatric Depression Scale; HDS-R, Hasegawa Dementia Scale – Revised.

Table 2 Correlation between plasma sex hormone levels, age and body mass index

	Age	BMI	Total-T	Free-T	DHEA-S	DHEA	Estradiol
Men							
Age	–	0.035	–0.121	–0310**	–0.254	–0.111	–0.047
BMI		–	0.006	0.026	–0.177	–0.151	–0.055
Total-T			–	0.672***	0.043	0.075	0.476***
Free-T				–	0.468***	0.392**	0.414***
DHEA-S					–	0.382**	0.342*
DHEA						–	0.084
Estradiol							–
Women							
Age	–	–0.187	0.079		–0.062	0.017	–0.028
BMI		–	0.320*		0.121	–0.070	0.040
Total-T			–		0.202*	0.355**	0.162
DHEA-S					–	0.561***	0.131
DHEA						–	0.097
Estradiol							–

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$. All data are presented as Pearson correlation coefficients. BMI, body mass index; DHEA, dehydroepiandrosterone; DHEA-S, dehydroepiandrosterone sulfate; Free-T, free testosterone; Total-T, total testosterone.

We also assessed whether plasma hormone levels were different between individuals with or without chronic diseases including hypertension, heart disease, cerebrovascular disease, osteoarthropathy and diabetes mellitus, using a Student's *t*-test, but there were no significant differences in hormone levels according to these conditions (data not shown). On the other hand, a significant difference was observed in Barthel Index scores between subjects with and without cerebrovascular disease in men (77 ± 16 vs 86 ± 16, $P < 0.01$).

The associations between plasma hormone levels and functional scores were evaluated. As shown in Table 3, in men, plasma total-T and free-T levels were positively correlated with functional scores except for GDS. DHEA(-S) and estradiol were positively correlated with cognitive function, and DHEA and estradiol were associated with Vitality Index as well. In contrast, in women, a significant correlation was observed only between DHEA(-S) and Barthel Index.

Multiple regression analysis revealed that the associations between sex hormones and functions were independent of age and BMI except that the associations between free-T and Barthel Index in addition to DHEA and vitality were not significant after adjustment. The statistical results were similar when serum albumin or total cholesterol was entered into the regression model instead of BMI (data not shown).

Because all measured sex hormones were associated with HDS-R in men, we entered free-T, DHEA-S and estradiol into the regression model as covariates in addition to age and BMI (Table 4). Free-T remained a significant determinant of HDS-R, while DHEA-S and estradiol did not hold a significant association with HDS-R. When a stepwise model (forward selection) was used to test for the determinants for HDS-R with the same five covariates, the *P*-value for the regression was minimized when only free-T was chosen as a variable ($R^2 = 0.227$, overall *P*-value for the regression <0.05).

Discussion

The present study demonstrated that men with higher plasma T levels had better ADL, cognitive function and vitality. Also, a higher estradiol level was related to better cognitive function as well as vitality, and a higher DHEA(-S) level was related to better cognitive function. In women, DHEA(-S) level was related to higher basic ADL, but T and estradiol levels showed no correlation with functional scores. The positive associations between sex hormones and functional scores were independent of age and nutritional status, suggesting that plasma sex hormone levels, especially that of testosterone in men, are independently related to functional status in elderly individuals.

Concerning cognitive function, our findings are consistent with the results of the previous observational studies examining the relationship between endogenous androgen and cognitive function in elderly men.[5,7,8] Several interventional studies have shown an improvement in spatial cognition and working memory after treatment with T, suggesting that T might have a beneficial effect on cognitive function.[18–21] Also, DHEA(-S), the most abundant circulating steroid in both sexes and the biosynthetic precursor of T, has been shown to have neurotrophic and neuronal remodeling activity.[22,23]

Table 3 Linear regression model of hormone levels on functional scores unadjusted and adjusted for age, and age and body mass index

	Total-T	Free-T	DHEA-S	DHEA	Estradiol
Men					
Unadjusted					
Barthel Index	0.292**	0.282**	0.094	−0.058	0.110
Instrumental ADL	0.261*	0.408**	0.239	0.140	0.129
HDS-R	0.393***	0.553***	0.390*	0.393**	0.266*
Vitality Index	0.246*	0.396***	0.210	0.297*	0.291*
GDS	−0.103	−0.097	−0.181	−0.027	−0.060
Adjusted for age					
Barthel Index	0.250**	0.183	0.044	−0.077	0.107
Instrumental ADL	0.255*	0.402***	0.216	0.137	0.124
HDS-R	0.366***	0.488***	0.317*	0.361**	0.243*
Vitality Index	0.218*	0.348***	0.160	0.176	0.288*
GDS	−0.068	−0.065	−0.146	−0.024	−0.005
Adjusted for age and BMI					
Barthel Index	0.281**	0.112	0.101	0.109	0.114
Instrumental ADL	0.229*	0.414**	0.314*	0.400*	0.053
HDS-R	0.340**	0.443**	0.329*	0.480**	0.236*
Vitality Index	0.285*	0.321*	0.140	0.227	0.292*
GDS	−0.067	−0.015	−0.013	0.002	0.079
Women					
Unadjusted					
Barthel Index	0.085		0.280*	0.293*	−0.068
Instrumental ADL	−0.050		0.071	0.171	0.071
HDS-R	−0.051		0.080	−0.034	0.121
Vitality Index	−0.076		0.167	0.091	0.043
GDS	0.004		−0.087	−0.014	0.052
Adjusted for age					
Barthel Index	0.120		0.225*	0.288*	−0.068
Instrumental ADL	−0.003		0.041	0.166	0.052
HDS-R	−0.028		0.038	−0.037	0.120
Vitality Index	−0.060		0.140	0.089	0.043
GDS	−0.008		−0.066	−0.012	0.052
Adjusted for age and BMI					
Barthel Index	0.142		0.269*	0.221*	0.035
Instrumental ADL	−0.067		0.092	0.178	0.046
HDS-R	−0.110		0.045	−0.051	0.106
Vitality Index	−0.103		0.137	0.043	0.104
GDS	0.063		−0.020	0.038	0.056

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$. Data are presented as standardized regression coefficients. ADL, activities of daily living; BMI, body mass index; DHEA, dehydroepiandrosterone; DHEA-S, dehydroepiandrosterone sulfate; Free-T, free testosterone; GDS, Geriatric Depression Scale – 15 items; HDS-R, Hasegawa Dementia Scale-Revised; Total-T, total testosterone.

In addition, our recent study showed that a low plasma T level is related to endothelial dysfunction in middle-aged men,[24] suggesting a mechanistic link between T and cerebrovascular function.

With respect to mood, although some large scale epidemiological studies[25,26] failed to show a clear correlation between T and depression in middle-aged men, another study has shown that low T levels are associated with depression in healthy elderly men.[27] The reason is unknown but it might be due simply to the cohort difference between community-dwelling healthy men and frail elderly men, or to the low reliability of GDS in demented people.[14] In the current study, in men, estradiol was also associated with cognitive function and vitality. However, multiple regression analysis with both free-T and estradiol as covariates suggested that estradiol is merely a marker as a metabolite of androgens and does not exert a direct action on neuropsychiatric

Table 4 Multiple regression analysis on cognitive function with free-T, DHEA-S and estradiol as covariates in addition to age and BMI in men

	HDS-R β	*P*
Age	−0.346	0.087
BMI	0.091	0.649
Free-T	0.466	0.030
DHEA-S	0.011	0.964
Estradiol	−0.213	0.321

β, standardized regression coefficient; BMI, body mass index; DHEA-S, dehydroepiandrosterone sulfate; Free-T, free testosterone; HDS-R, Hasegawa Dementia Scale – Revised.

function in men consistent with the results of cross-sectional studies.[5,7,8]

Because T has anabolic effects on muscle and may improve cognition, our findings on the association of T with ADL are not surprising. While several observational studies have demonstrated the correlation of endogenous testosterone with muscle mass and strength[28–31] and physical performance[4,32] in older men, interventional surveys have provided mixed findings[33–38] and the studies using healthy men have found only increased muscle mass and strength but not improved physical function.[35–38] In addition, results of studies investigated the correlation between endogenous testosterone and fall risks are inconsistent.[30,32] Future interventional studies enrolling frail and/or disabled elderly men might clarify the causal relationship between testosterone and frailty. Although the correlation between sex hormones and physical function or ADL in women is contradictory across studies,[39–43] our findings are consistent with one report showing that the plasma level of DHEA(-S) is related to basic ADL in middle-aged to elderly women.[39]

The explanations for the sex difference in the correlation between hormones and function could be due to sex differences in hormone secretion and metabolism.[41,44,45] In fact, plasma estradiol level in women was approximately half of that in men, and distributed in a narrow range (52% cases fell into a range of 14.7–53.1 pmol/L), providing a possible explanation for no association of estrogen levels with functioning in women. Measurement of active forms of estrogens such as free or bioavailable estradiol, although the assays are not available in Japan, might show some significant correlations with functional levels; however, most of the previous studies investigating the relationship between endogenous estrogen levels and physical performance or cognitive function in postmenopausal women, including one study that measured bioavailable estradiol levels, found negative results.[46–50] Accordingly, in the ranges of circulating endogenous hormone levels, estradiol may not be related to functional levels in older women. On the other hand, information on the sex-specific distribution of steroid hormone receptors is limited. Recently, Bezdickova *et al.* reported that nuclear androgen receptor staining was observed in the mammillary body, precentral gyrus and hippocampus in the human male brain but not in the female brain.[51] The sex difference in the correlation between hormones and functions should be further determined based on the ligand–receptor relationship.

The limitations of our study should be acknowledged. First, we cannot exclude an influence of the associated diseases or the comorbid condition on our results, although no significant differences were observed in hormone levels or functional status in subjects with or without chronic diseases, except that the Barthel Index was significantly lower in male subjects with cerebrovascular disease. Second, only free-T was measured as the active form of T by radioimmunoassays instead of bioavailable or calculated free-T, because sex hormone-binding globulin and direct assays of bioavailable T were not available. Finally, it should be recognized that our results were obtained from a cross-sectional study and do not provide direct evidence of a causal relationship; therefore, it is possible that high sex hormone levels were the result of enhanced physical or mental health.

In summary, our cross-sectional survey revealed that sex hormones have sex-specific relationships with physical and neuropsychiatric function in elderly individuals. In men, endogenous androgen is independently associated with ADL, cognitive function and vitality. Although it has been reported that testosterone or DHEA supplementation in healthy elderly men did not affect physical or cognitive function,[37,38] our findings suggest that elderly men with functional decline could be a better target for androgen replacement to improve physical and cognitive function.

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〈症例報告〉

II型呼吸不全を契機に診断された運動ニューロン疾患を伴う前頭側頭型認知症(frontotemporal dementia with motor neuron disease) の1例

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要　約　症例は79歳の女性で，もの忘れを主訴として2006年に杏林大学付属病院もの忘れセンターを受診し，脳血管性認知症の診断にて加療されていたが，2007年にもの忘れ症状が進行し，認知機能検査値の低下も認められた．また，発語も復唱で字性錯語や吃音の出現も認めた．治療として塩酸ドネペジル5 mg/日の内服を開始したが，経過中にII型呼吸不全を合併し，神経所見から運動ニューロン疾患を疑い，針筋電図を施行した結果，下位運動ニューロンの脱神経所見を認めたことから，運動ニューロン疾患を伴う前頭側頭型認知症の診断に至った．以上，本例は短期記憶障害で発症した後，非流暢性失語をきたし，II型呼吸不全を発症して初めて運動ニューロン疾患を伴う前頭側頭型認知症と診断された症例である．
Key words：非流暢性失語，運動ニューロン疾患を伴う前頭側頭型認知症，II型呼吸不全

（日老医誌　2009；46：557–561）

緒　言

前頭側頭型認知症（FTD）は運動ニューロン疾患（MND）を伴う病型があることが報告[1]されており，近年では前頭側頭型認知症と筋萎縮性側索硬化症（ALS）との間に病理学的な共通点が指摘されていることから，両者は同一の病態を背景とする疾患群と考えられている[2]．ALSは進行すると呼吸障害が出現し，根本的な治療法がない状況下で人工呼吸器を使用することの是非が倫理的に問題視されている．今回，我々は非流暢性進行性失語（PNFA）を疑われ，経過観察中にII型呼吸不全をきたし，最終的に運動ニューロン疾患を伴う前頭側頭型認知症（FTD-MND）と診断された症例を経験したので報告する．

症　例

＜症例＞79歳女性，右利き，主婦．

＜主訴＞何度も同じことを訊く．

＜家族歴＞特記事項なし．

＜既往歴＞59歳：椎間板ヘルニア，痔核（ope），狭心症（PTCA施行），喫煙歴なし．

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＜外来受診時の現病歴＞2005年頃より元気がなくなり，家計簿をつけなくなったり，料理をしなくなり，できあいのものを買ってくることが多くなった．また，同じことを繰り返し訊くことが多くなったため，夫と息子に連れ添われ2006年6月に当院もの忘れセンターを受診した．身体所見として両側の膝蓋腱反射の軽度亢進を認めるのみで構音障害や脱力は認めず，また明らかな失語症状も認めなかった．神経心理検査でMMSE 23点と軽度から中等度の認知障害と，GDS 7点と抑うつ傾向を認めた．

2006年7月に画像検査を施行し，頭部MRIでは前頭葉および側頭葉皮質優位の萎縮，大脳基底核に多発するラクナ梗塞とPVH（periventricular hyperintensity）とDWMH（deep white matter hyperinsensity）を認めた（図1）．また^{99m}Tc-ECDシンチでは，eZISにて両側前頭前野と左側頭葉皮質に－2SD以上の血流低下を認めた（図2）．

以上の結果より脳血管性認知症（VaD）と診断し，シロスタゾール50 mg/日の内服を開始したが，頭痛を訴えたため8月よりニセルゴリン15 mg/日の投与に変更された．

＜外来の経過＞2006年8月にMMSE 27点まで改善が見られたが，2006年12月受診時に発語困難があり，他覚的にも「るりもはりもてらせばひかる」の復唱がやや困難であった．また同時期にMMSE 20点まで低下が

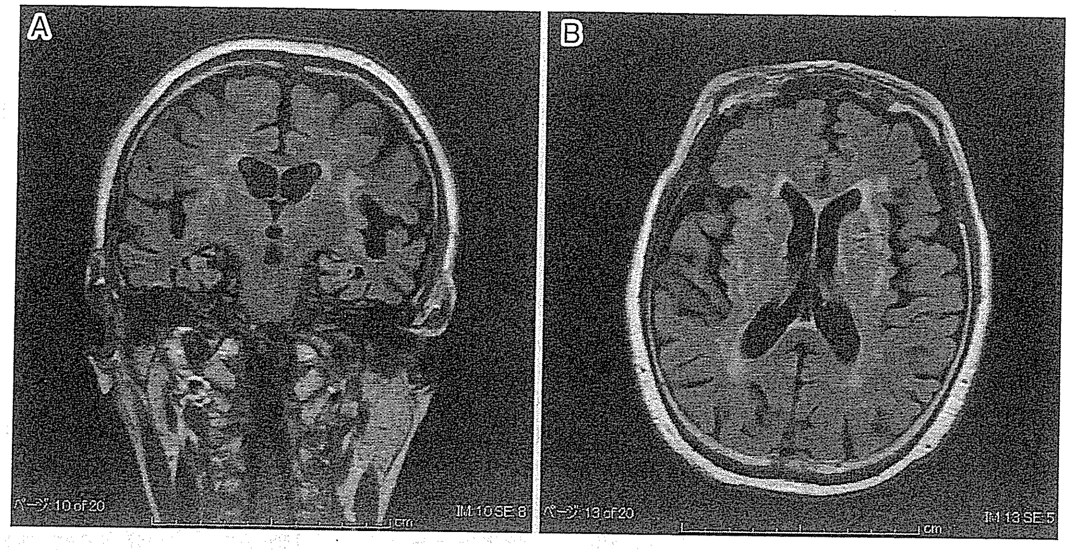

図1　頭部 MRI FLAIR　A：冠状断像　B：水平断像　前頭葉，側頭葉皮質に比較的軽度の萎縮を認める．

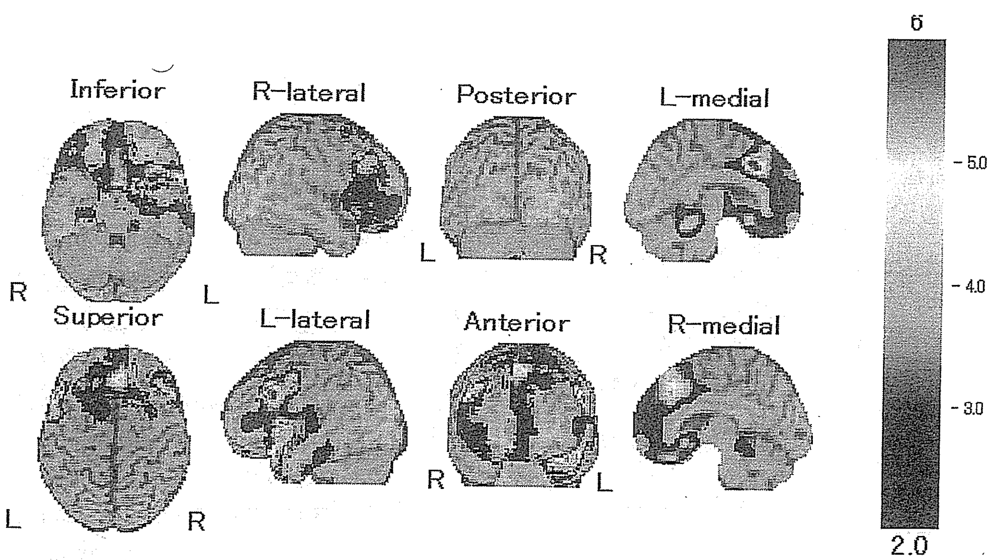

図2　^{99m}Tc-ECD シンチ e-ZIS 所見　両側前頭前野と左側頭葉皮質に血流低下を認める．

見られた．このため言語機能評価を行ったところ，標準失語症検査（SLTA）で口頭での複雑命令と文字での短文の理解がやや低下しており，また呼称の軽度低下が見られた．またレーブン色彩マトリックス検査では21点/36点と軽度の低下を認めた．2007年2月に再診した際は同じ事を繰り返し訊くことがさらに増加し，6月にはMMSE 16点まで低下した．また発語も復唱で字性錯語や吃音の出現も認め，初診時の頭部MRIにおける前頭葉と側頭葉の萎縮，および^{99m}Tc-ECDシンチでの両側前頭前野と左側頭葉皮質の血流低下から非流暢性進行性失語（PNFA）が疑われた．このため塩酸ドネペジル5 mg/日の内服を開始した．

2007年8月に嘔吐があり，他院で上下部内視鏡やCTなどを施行するも原因となる器質的病変は認めなかった．入院時は食欲に問題はなかったが，退院後一度嘔吐がありその後拒食が出現した．同月頭部MRI及び^{99m}Tc-ECD脳血流シンチを再検したが，初診時と大きな変化は認めなかった．そのため食欲低下は前頭葉障害に起因した“こだわり行動”と診断し，抑肝散7.5 g/日の内服を開始した．内服後も排便をしないのに頻回にトイレに

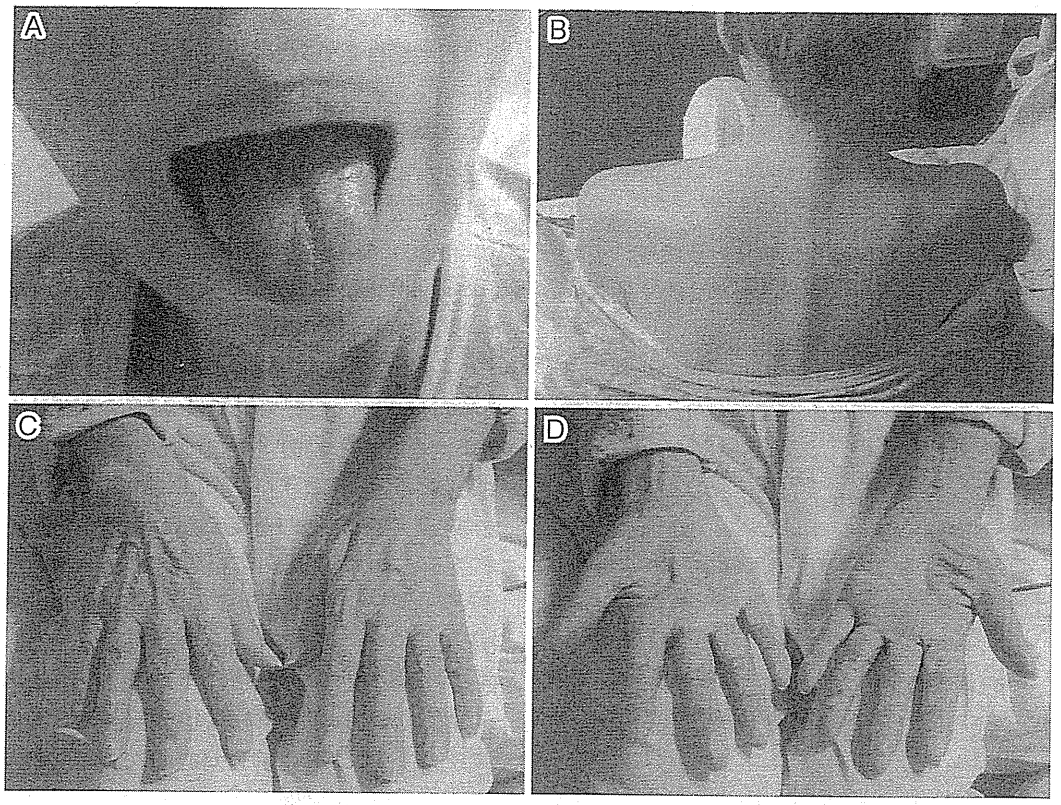

図3 A：舌萎縮 B：両側僧帽筋の萎縮 C：骨間筋の萎縮（手背側）D：母指球筋の萎縮（手掌側）

行く，毎日夕食で枝豆とビールしか取らない等の症状が見られたが，10月には通常の食事を全量摂取できるようになり，"こだわり行動"も消失した．

2008年1月より家で臥床している時間が増え，また発語量の減少と字性錯語の増加が見られ，意思を伝えるのが困難となった．MMSEは9点と低下が見られた．ただし言語理解は比較的保たれ，簡単な命令に従うことや書字は可能であった．

＜入院時の現病歴＞

2008年5月7日20時頃，夫が帰宅したところベッドの下に患者が転落しているところを発見した．呼びかけに返答がないため，救急車で当院救急外来を受診した．来院時意識レベルはやや改善したがまだ混濁状態であった．頭部MRIを施行したが急性期の脳血管障害は認めず．また血液ガス分析でII型呼吸不全を呈していたが，胸部レントゲン写真や胸部CTでは呼吸不全の原因となる器質的疾患を認めなかった．そのため精査加療目的で入院となった．

＜身体所見＞

意識E4V1M6，体温36.4℃，血圧143/113 mmHg，心拍数72 bpm整，SpO_2 99％（O_2マスク100％ 6 l/min）．

頭部：眼瞼結膜貧血なし，眼球結膜黄染なし．

胸部：呼吸音左側で減弱，肺雑音なし，心音に異常なし．

腹部：特記すべき事項なし．

四肢：関節腫脹及び変形なし，浮腫なし．

＜神経所見＞

脳神経：舌萎縮，両側胸鎖乳突筋および僧帽筋萎縮，構音障害あり（図3）．

運動：四肢に明らかな脱力なし，両側母指球筋萎縮あり．舌及び僧帽筋から両上肢にかけて筋線維束性収縮あり．

感覚：表在感覚に異常なし，深部感覚は失語により評価困難．

反射：上下肢の腱反射は両側ともやや亢進，咽頭反射および下顎反射は減弱も亢進も認めず，Babinskiおよび Hoffmann反射なし．

錐体外路症状：頸部にのみ固縮と振戦あり．

＜検査所見＞

血算：Hb 15.0 g/dl，Ht 46.4％，RBC 475万/μl，WBC 12,000/μl，Plt 25万/μl．

生化学：Na 137 mmol/l，K 3.3 mmol/l，Cl 92 mmol/l，Ca 9.4 mg/dl，BUN 16.8 mg/dl，Cre 0.4 mg/dl，TP 8.4 g/dl，Alb. 4.0 g/dl，T-Bil 0.7 mg/dl，ALP 178

IU/l，AST 35 IU/l，ALT 17 IU/l，LDH 279 IU/l，CK196 IU/l，Glu 157 mg/dl，CRP 0.2 mg/dl.

血液ガス：O_2マスク100％ 6 l/min pH 7.268，pCO_2 87.5 mmHg，pO_2 169 mmHg，HCO_3 38.6 mmol/l，BE 7.8 mmol/l，SAT 98.9％.

＜筋電図＞

安静時：上下肢に豊富な線維自発電位と陽性棘波を認め，上腕二頭筋に複合反復放電を認めた．また上肢に線維束自発電位を認めた．

随意運動時：上下肢で漸増が弱く，正常運動単位は下肢でしかみられなかった，特に上肢で多巣性かつ高振幅電位が多く観察された．

＜神経伝導速度＞異常なし．

＜入院後経過＞

II型呼吸不全に対しNIPPVによる呼吸管理を開始し，翌日には呼吸状態及び意識レベルは改善した．その後徐々にNIPPVからの離脱を行い，日中の使用は不要となった．意識レベルの改善後にSLTAを再検したところ，極端な発語の低下と言語理解の障害が出現していた．

呼吸不全の原因検索のため頭部MRI及び^{99m}Tc-ECDシンチを施行したが，急性期の脳血管障害は認めず，1年前に施行した同検査の結果と著変は認めなかった．また脳波にも異常を認めなかった．来院時の神経所見から運動ニューロン疾患を疑い，針筋電図を施行した結果，下位運動ニューロンの脱神経所見あり，筋萎縮性側索硬化症（ALS）と診断した．

以上より，本症例は進行性認知障害と自発語の減少を特徴とした失語，保続の出現を認め，運動ニューロン疾患を伴う前頭側頭型認知症（FTD-MND）と診断した．

考　察

前頭側頭型認知症（FTD）は前頭側頭葉変性症（FTLD）のひとつに分類され，そのうち運動ニューロン疾患を伴うものはFTD-MNDと呼ばれている．FTLDは認知症の中でアルツハイマー型認知症（AD），レビー小体型認知症（DLB）についで3番目に多く，認知症全体の12～20％を占めるとされている[1)2)]．FTLDのうちFTDは約半数を占め，FTDのうちMNDを合併するものは15％程度とされている[3)]．

三山らの26例の症例検討[4)5)]では，FTD-MNDは初老期に発症し比較的女性に多い．症状として短期記憶障害よりも脱抑制や意欲低下が目立ち，また自発語の減少をきたすが比較的言語理解は保たれる．また認知症の診断後約1年程度でMNDの合併が診断され，また進行期ではパーキンソニズムの出現もある．また発症から死亡までの期間は3年から5年であり，比較的下肢の筋力低下は軽く，死亡時まで歩行が可能な例も多いが，球麻痺による誤嚥性肺炎で致命的経過をとることが多いとされている[4)5)]．以上より本症例はFTD-MNDとして典型的な経過をたどっていると考えられる．

ALSでは呼吸不全が臨床的な問題であるが，ALS発症から慢性呼吸不全をきたすまでの期間は疾患の筋症状の進行速度が最も早い群でおおよそ1年程度と報告されている[6)]．FTD-MND例での呼吸不全の進行速度に関する検討はない．症例報告ではALSの経過中に急激な呼吸不全をきたした例[7)8)]や，肺炎を契機にALSと診断された例[9)]の報告があり，ALS単独例でも急激な呼吸不全をきたし呼吸不全の発見が遅れる例があると考えられる．また運動性失語にALSが合併した報告例では，発症後1年から1年半程度で呼吸筋麻痺による呼吸不全をきたしていた[10)11)]．三山らの症例報告では，FTD-MND例とALS単独例とで筋力低下部位の分布が異なることが報告されており，呼吸不全の発症時期も異なる可能性が考えられる．またFTD-MNDでは，失語によりに自覚症状の訴えが困難であったり，もしくは前頭葉障害による病識の無さから呼吸苦の訴えが目立たず，その結果II型呼吸不全の発見が遅れることも否定できない．

呼吸筋麻痺に対するNIPPVの使用についてはALSではその有効性が認められている[12)]がFTD-MNDではその有効性は検討されていない．ただしFTD-MNDにNIPPVを使用し，19カ月生存できた例[13)]も報告されており，FTDの合併が必ずしもNIPPVの使用を困難にするわけではないと考えられる．本症例も外来通院時にはFTD特有の“こだわり行動”が見られていたが，入院期間中にはそのような問題行動は消失しておりNIPPVの妨げることはなかった．FTD-MND例の呼吸不全に対するNIPPV使用の適応について，検討を重ねる必要があると考えられる．

認知症は高齢者のcommon diseaseであり，FTD-MNDもまれではない頻度で報告されている．本例は初診時に特異的な所見を欠いていたため脳血管性認知症と診断されていたが，失語症状の進行の後，II型呼吸不全が出現してはじめてFTD-MNDと診断を確定することができた．FTD-MNDの診断過程に非流暢性の失語をきたすことがある点で，本症例は老年科医にとって教訓的な一例と考えられた．

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Frontotemporal dementia with motor neuron disease diagnosed after the development of type II respiratory failure

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Abstract

A 79-year-old woman attended the Center for Comprehensive Care of Memory Disorders at the Kyorin University Hospital in 2006 due to forgetfulness. Her initial diagnosis was vascular dementia. In 2007, her cognition declined gradually. Then, impaired verbal fluency and stuttering, the symptoms of non-fluent aphasia, were presented. Thereafter, 5 mg/day donepezil hydrochloride was prescribed. She later suffered type II respiratory failure. Needle electromyography revealed denervation of lower motor neurons. This led to the diagnosis of frontotemporal dementia with motor neuron disease. Interestingly, before developing type II respiratory failure, cognitive decline and non-fluent aphasia occurred in this case.

Key words: *Non-fluent aphasia, Frontotemporal dementia with motor neuron disease, Type II respiratory failure*
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