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Frequency and Clinical Characteristics of Early-Onset Dementia in Consecutive Patients in a Memory Clinic

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Key Words
Early-onset dementia · Alzheimer's disease · Frontotemporal lobar degeneration · Dementia with Lewy bodies · Memory clinic

Abstract
Aims: To investigate the frequency, rate of causes of dementia, and clinical characteristics of early-onset dementia in consecutive patients of a memory clinic. ***Methods:*** A total of 668 consecutive demented patients were involved in this study. We examined the distribution of patients' diagnosis, differences in sex, education, dementia severity and cognitive function at the first visit, and the duration from onset to consultation. We also examined the changes in the proportion of subjects during the research period. ***Results:*** There were 185 early-onset patients, 28% of all demented patients. No significant differences were observed between the early-onset and late-onset dementia groups in Clinical Dementia Rating and Mini-Mental State Examination score at the first consultation, but the duration from onset to consultation was significantly longer in the early-onset group. In the early-onset group, the rates of patients with Alzheimer's disease and dementia with Lewy bodies were relatively low and the rate of patients with frontotemporal lobar degeneration was relatively high. There were no significant differences in the proportion between either demented subjects and nondemented subjects or early-onset dementia patients and late-onset dementia patients during the research period. ***Conclusion:*** We conclude that early-onset dementia is not rare and its clinical characteristics and causes are different from late-onset dementia.

Introduction

Early-onset dementia (EOD), with onset in those younger than 65 years, has a large psychological and economical impact on patients and caregivers because of their leading role in the society and family at the disease onset. However, EOD has been underrecognized until today and social support services for EOD patients are not enough compared with those for late-onset dementia (LOD) patients.

Although there are some studies about early-onset Alzheimer's disease (AD) [1–3], there are few systematic studies about cognitive function in and clinical features of EOD of the non-Alzheimer type [4, 5]. Further, epidemiologic data on relatively rare causes of dementia, in-

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Table 1. Clinical characteristics of EOD patients and LOD patients

	EOD patients (n = 185; 27.7%)	LOD patients (n = 483; 72.3%)	p
Age at consultation, years	58.3 ± 11.0	77.9 ± 5.6	
Sex ratio (M:F)	94:91	188:295	0.007
Education[1], years	11.4 ± 2.8	9.5 ± 2.5	0.000
MMSE score at first consultation[2]	18.4 ± 7.8	18.4 ± 6.4	0.978
CDR at first consultation (0.5:1:2:3)[3]	50:50:53:12	108:167:148:34	0.326
Duration from onset to consultation, months	59.6 ± 70.8	35.7 ± 25.9	0.000

Those who could not undergo MMSE or CDR at their first consultation or whose caregivers' information on patients' education was inaccurate were excluded.

[1] n = 628.

[2] n = 637.

[3] n = 622.

cluding dementia with Lewy bodies (DLB) and frontotemporal lobar degeneration (FTLD), are insufficient because pure cross-sectional or population studies are impractical for rare diseases [6]. Therefore, we aimed to clarify the frequency of EOD, rate of causes of dementia, and clinical characteristics of EOD in consecutive patients of our memory clinic.

Method

A total of 861 consecutive patients visiting the Higher Brain Function Clinic of the Department of Neuropsychiatry, Ehime University Hospital between January 1997 and September 2005 were examined. Of the 861 patients assessed, more than 80% resided in the Ehime prefecture, within a 100-km radius of the hospital, at their first consultation. The Ehime prefecture is a rural area of Japan with 1.5 million people, 21% of whom are over 65 years old. Our clinic is one of the few specialized clinics for demented people where we can evaluate patients with brain MRI and HMPAO-SPECT. More than 40% of all patients were referred from other doctors. Fifty percent of referrals were received from psychiatrists who are experts in demented patients to some degree, and the others were received from general physicians and geriatricians.

All patients were seen by senior neuropsychiatrists and underwent physical and neurological examinations. Thirty-three patients who came to our clinic only once or who could not undergo neuroimaging examination were excluded, as they could not complete enough evaluations for us to make a clear diagnosis. Patients were assessed with a comprehensive neuropsychological test battery, which included the Mini-Mental State Examination (MMSE) [7], Clinical Dementia Rating (CDR) [8], together with standard psychiatric evaluations to exclude major functional psychiatric disorders such as schizophrenia and mood disorders. All patients underwent brain MRI, except those with cardiac pacemakers who underwent brain CT instead. Almost all patients underwent HMPAO-SPECT except those who could not because of their behavioral symptoms. Patients were also assessed with screening blood tests including vitamin B_{12}, folic acid and thyroid function.

Dementia was diagnosed according to the *Diagnostic and Statistical Manual of Mental Disorders*, 3rd edition revised [9]. Patients with AD satisfied probable AD criteria developed by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association [10], and patients with vascular dementia (VaD) satisfied the criteria of the National Institute of Neurological Disorders and Stroke and the Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) [11]. DLB was defined according to the consensus guidelines for the clinical diagnosis of DLB [12]; FTLD was diagnosed according to the international consensus criteria [13]. Standard diagnostic criteria were also applied to dementia of other etiologies.

Information about onset of dementia was routinely and systematically queried from caregivers, and it was emphasized that 'onset' is the time when caregivers first noticed changes from the patients' premorbid state which should be substantive and not a long-standing character trait. One hundred and sixty patients were excluded as they did not fulfill the diagnostic criteria for dementia; 668 patients were included in this study. Among these nondemented patients, there were 31 patients with schizophrenia or delusional disorder, 19 patients with depression or anxiety disorder and 17 normal healthy subjects. The distribution of patients' diagnosis, differences in sex, educational level, severity of dementia according to CDR at the first visit, cognitive function according to MMSE at the first visit, and the duration from onset to consultation were compared between the EOD group (onset before the age of 65 years) and LOD group (onset after the age of 65 years). We examined the distribution of onset age and sex according to the causes of dementia in EOD patients. We also examined the changes in the proportion of subjects during the research period.

Data analyses were carried out using the SPSS-PC software package. Statistical differences between the EOD group and LOD group were assessed by the t test for age, education, duration from onset to consultation and MMSE score, and by the χ^2 test with post hoc Fisher's exact test for sex, CDR, distribution of diagnosis, and proportion of subjects. All examinations were conducted after obtaining informed consent from all subjects or their caregivers.

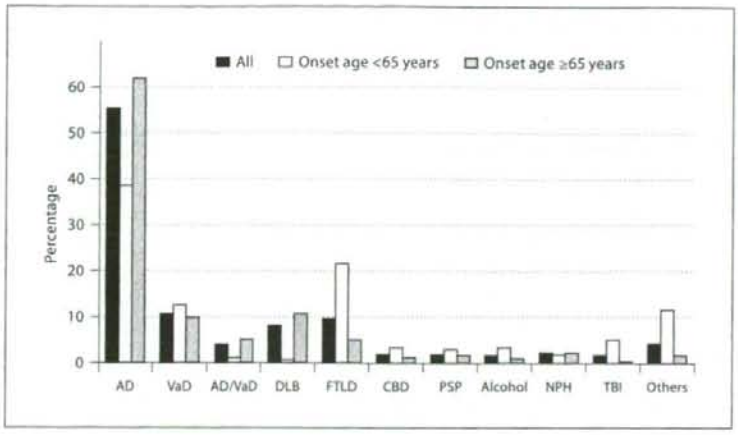

Fig. 1. Rate of causes of dementia in all patients, EOD patients and LOD patients. CBD = Corticobasal degeneration; PSP = progressive supranuclear palsy; alcohol = alcohol-related dementia; NPH = normal pressure hydrocephalus; others = dementia of other etiologies.

Result

Table 1 shows the clinical characteristics of the total 668 patients with dementia, comparing the EOD group and LOD group.

There were 185 EOD patients, 27.7% of all demented patients. In these EOD patients, mean age at consultation was 58.3 years and the sex ratio was almost equal (M:F = 94:91), meaning there were significantly fewer females than in the LOD group. Educational level was significantly higher than in LOD patients. There were no significant differences between the two groups in CDR and MMSE score at the first visit, but duration from disease onset to consultation was significantly longer in the EOD group compared to the LOD group.

Figure 1 shows the rate of causes of dementia in all patients, EOD and LOD groups.

Among all demented patients, AD was the most frequent cause of dementia (55.4%), followed by VaD (10.5%), FTLD (9.4%) and DLB (8.1%). Among EOD patients, AD was also the most frequent cause of dementia (38.5%). FTLD was the second most common cause of dementia (21.4%), followed by VaD (12.6%) and traumatic brain injury (TBI) (4.9%), and there were only a few DLB patients (0.5%). There were statistically significant differences between the EOD and LOD groups in the frequency of AD ($p = 0.000$), DLB ($p = 0.000$), FTLD ($p = 0.000$), alcohol-related dementia ($p = 0.031$), and TBI ($p = 0.000$). Neurosyphilis, carbon monoxide intoxication and post-encephalitis were relatively common in EOD patients with other etiologies.

Table 2. Changes in the proportion of subjects during the research period

	Demented		Nondemented	Total
	EOD	LOD		
1997–1999	39	146	56	241
2000–2002	69	164	63	296
2003–2005 (Sept.)	77	173	74	324
Total	185	483	193	861

Among all EOD patients and early-onset AD patients, the number of patients increased as the onset age got older, and there were no large differences in sex distribution in any generation. Among early-onset VaD patients, the number of patients increased with increasing onset age, and there were more males. Among early-onset FTLD patients, the number of patients increased after the age of 45 years, but no constant tendency was found in the sex ratio.

The changes in the proportion of subjects during the three sequential research periods are summarized in table 2.

Although the number of subjects increased with the passage of time in all groups, there were no significant differences in the proportion between either demented subjects and nondemented subjects or EOD patients and LOD patients. Among the demented patients, the severity of dementia according to CDR at the first consultation did not differ during the research period.

Discussion

This is a systematic study to reveal the clinical characteristics of EOD in consecutive patients over a period of 8 years at a memory clinic in Japan. It is worthy of notice that nearly 30% of the demented patients had an age of onset of less than 65 years.

Comparing with other studies in Japan, Miyanaga et al. [14] estimated that there are a total of 25,000 EOD patients (32 patients per 100,000 population) in Japan, only a few percent of more than 2 million demented patients. Yokota et al. [15] reported that only 34 patients (7.3%) had an age of onset of less than 65 years out of a total of 464 demented patients from their outpatients of psychiatric hospitals in Japan. Both studies showed a much fewer number of EOD patients than our study. Comparing with other countries, Harvey et al. [5] estimated that there are 54 EOD patients per 100,000 population in their epidemiological study in the UK, almost the same number as the one previously reported in Japan. An outpatient study in Denmark showed that a total of 314 patients per 1,000 demented patients were aged less than 60 years [4], an outpatient study in the USA reported that 29.3% of 948 demented patients were EOD patients [16], and a UK study showed that the proportion of EOD patients was 28.6% [17]. All these results are consistent with our result. An outpatient study in Brazil showed that 46.6% of all demented patients were EOD patients [18], a relatively high number compared to other studies. There may be more EOD patients in Japan than previously reported.

In our study, the sex ratio in the EOD group was almost equal, whereas there were more females in the LOD group. In fact, many epidemiological studies revealed that there were more female patients among the demented elderly [19–21], while there were more males among EOD patients [5, 14]. This may be because there are more male-related causes of dementia, such as VaD or alcohol-related dementia, in EOD groups. There is a possibility that the sex ratio of AD is affected by onset age, as some studies mentioned that there are more males in early-onset AD patients than in late-onset AD patients [3].

The education level was significantly higher in EOD groups. This may be due to changes in the educational system in Japan after World War II.

As there were no significant differences between the EOD and LOD groups in CDR and MMSE score at the first consultation, we performed this analysis with all causes of dementia together; however, cognitive function and severity of dementia could not be discussed for each cause of dementia. Therefore, further assessments are needed on cognitive function and psychiatric symptoms for all causes of dementia.

It is noteworthy that in EOD patients the duration from disease onset to consultation is longer than in LOD patients. Therefore, it seems that the progress of dementia in EOD patients is slow, even though the severity of dementia is equal between the two groups. However, in patients with AD, which is the major cause of dementia, early-onset groups are known to show a more rapid progression than late-onset groups [22, 23]. Therefore, we suppose that in EOD patients it takes longer to correctly diagnose the disease because early-onset patients are sometimes misdiagnosed as having psychiatric disorders such as schizophrenia or mood disorders. Furthermore, EOD groups consist of not only patients with neurodegenerative disorders or cerebrovascular diseases but also of patients with many heterogeneous causes of dementia, such as TBI or neurosyphilis. These pathologies sometimes require more time to be diagnosed by specialists in dementia. This misdiagnosis might have led to the under-recognition of EOD, and hence, to the underestimation of its prevalence. This issue is important from a socioeconomic point of view, and we need to inform people further about EOD.

There are also a few noteworthy findings in the classification of causes of dementia in our study. Among our patients, 12.6% of all EOD patients had VaD and there was no significant difference between that number and the number of LOD patients (9.7%). Although several epidemiological studies have reported that VaD was more common in patients aged less than 65 years compared with elderly patients [3, 18, 24], our result was not consistent with these findings. The distribution of the diagnoses of VaD is influenced by the specificity and sensitivity of the criteria used in each study, and the NINDS-AIREN criteria are known to be the strictest criteria, requesting onset of dementia within 3 months following a recognized stroke [25, 26]. This low prevalence of VaD in our study may be because we used the NINDS-AIREN criteria to diagnose VaD, and young patients may not have recognized their strokes. Furthermore, as our series of patients are outpatients of the neuropsychiatry department, there is a possibility that there might be few subjects with clear neurological symptoms due to cardiovascular disease.

Among our patients, DLB was the second most common cause of dementia (10.9%) in the LOD group while there were only a few DLB patients (0.5%) in the EOD group. Although there were little epidemiological data on clinically diagnosed DLB compared with research on au-

topsy patients, some investigations on EOD reported a low prevalence of DLB patients [4, 5, 27]. These findings suggest that the onset age of DLB seems to be considerably old.

Among our patients, FTLD was the second most common cause of dementia following AD among the EOD group (21.4%; AD/FTLD = 1.8:1) while it was relatively rare among the late-onset patients (4.9%; AD/FTLD = 12.5:1). Although this rate of FTLD in the EOD group is higher than in other studies in Japan [14, 15], it is not a surprising rate compared with those in other countries. Many studies in Western countries report that FTLD is the second most common cause of dementia following AD among early-onset patients [6, 28–30]. An epidemiological study in the UK showed that the rate of FTLD was 15.7% out of a total of 108 demented people aged <65 years, whereas the rate of AD was 25% (FTD/AD = 1:1.6) [29]. Although there are some familial and genetic cases among FTLD patients in Western countries and the pathoetiologic background of FTLD in Japan may be different from that in Western countries [28, 31], our results suggest that FTLD in Japan has been underestimated until now.

Turning to the changes of the proportion of subjects during the three sequential research periods, there were no significant differences between either demented subjects and nondemented subjects or between EOD patients and LOD patients. This result suggests that the proportion of EOD and LOD patients was not affected by the recent trend of increased awareness of dementia, although the number of all patients increased. Moreover, the severity of dementia at the first consultation did not differ during the research period. This may suggest that early diagnosis and early referral are still not enough even today. Further information about dementia for families and for general physicians is required.

There are a few methodological issues that should be taken into consideration to fully appreciate our results. Firstly, this study is based on memory clinic patients in the department of neuropsychiatry of a university hospital, thus it is not a purely community-based epidemiological study. Referral bias may affect the proportion of each diagnosis in this study. Relatively common causes of dementia such as AD or VaD may be treated by general physicians, and physicians may refer patients with aphasia or motor neuron symptoms to other neurological referral centers. Younger patients may be threatened with loss of employment due to dementia, which may lead the family and the general physician to refer the patient to a specialist. Older patients may have less opportunity of referral because of their age. This possible selection bias may affect the proportions of EOD and LOD patients. However, as we mentioned above, pure cross-sectional or population studies are impractical for rare diseases, and many epidemiological studies of dementia are intended for people over 65 years of age. Therefore, an assessment of a large number of consecutive patients at a memory clinic might be important. Furthermore, as our clinic is one of the few specialized clinics for demented people in our regional area where we can evaluate patients with MRI and HMPAO-SPECT, we believe our result is not inaccurate. Secondly, determining the age of onset and the duration of degenerative dementia is difficult. This study is based on the retrospective recall of caregivers, and it can be claimed that the informants' memories may have been inaccurate. Thirdly, in this study we clinically diagnosed AD, VaD, DLB, FTLD and other causes of dementia according to consensus diagnostic criteria. We did not perform pathological confirmations, so we cannot discuss the pathological background of our diagnoses. However, we routinely used the Neuropsychiatric Inventory [32] and Stereotypy Rating Inventory [33] for all patients in order to assess the psychiatric and behavioral symptoms of the patients. Moreover, we used a comprehensive frontal function assessment battery including motor series, conflicting instruction, digit span, word fluency test, trail making test, and the Stroop color-word test, for those in whom FTLD was suspected. As described previously, all patients underwent brain MRI and almost all patients underwent HMPAO-SPECT. All the patients with FTLD showed either frontal/temporal lobe atrophy on MRI, or frontal/temporal hypoperfusion on HMPAO-SPECT. Even when frontal system dysfunction was detected by neuropsychological tests in some patients with AD and VaD, they did not show frontal lobe atrophy on MRI or frontal hypoperfusion on HMPAO-SPECT. Therefore, we believe that our clinical diagnosis of the causes of dementia is the most accurate possible.

In conclusion, EOD patients are not rare, at least in memory clinics. There are many atypical causes of dementia among EOD patients such as FTLD or TBI, so clinicians have to take into consideration the specific clinical symptoms and histories of these diseases when examining such patients. Since in EOD patients the duration from their disease onset to consultation is longer, further information for the public and social support services for EOD patients are required.

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Do family caregivers perceive more difficulty when they look after patients with early onset dementia compared to those with late onset dementia?

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SUMMARY

Objective To compare family caregiving situations for patients with early onset dementia (EOD) and late onset dementia (LOD), and to identify the specific problems experienced by relatives caring for EOD patients.

Methods The participants were chosen from 92 consecutive caregiver–patient dyads, comprising co-residing family caregivers and outpatients who fulfilled the diagnostic criteria for dementia. The patients were assessed according to cognitive function, neuropsychiatric disturbances and the severity of dementia. The caregivers completed a self-administered questionnaire that included items on their sociodemographic status and caregiving situation. Caregiver burden was assessed by the Japanese version of the Zarit Burden Interview.

Results In total, 68 dyads were eligible for the analysis, 14 of which included patients with EOD and 54 of which included patients with LOD. There were no significant differences between the two groups in terms of patient clinical features, duration of caregiving, number of hours during which caregivers were relieved per day or number of hours of caregiving per day. No significant associations were detected between the type of dementia and caregiver characteristics (such as health status) or caregiver burden, even after adjusting for confounding variables. However, the caregivers of EOD patients had greater perceived difficulties due to patient behavioural disturbances than did the caregivers of LOD patients.

Conclusions Our findings demonstrated that additional resources, such as care services, should be provided for sufferers of EOD, in order to allow family caregivers to cope with difficulties associated with patient behavioural problems. Copyright © 2007 John Wiley & Sons, Ltd.

KEY WORDS — family caregivers; early onset dementia; presenile dementia; late onset dementia; senile dementia; care services

INTRODUCTION

It is well established that caring for a relative with dementia is a difficult task, which can lead to stress, physical and mental health problems, and even high morbidity and mortality among family caregivers (Baumgarten *et al.*, 1992; Schulz *et al.*, 1995; Kiecolt-Glaser *et al.*, 1996; Schulz and Beach, 1999; Kiecolt-Glaser *et al.*, 2003; Vitaliano *et al.*, 2004). Most previous studies of this issue have focused on older patients with dementia (that is, individuals aged ≥65 years). However, Freyne *et al.* (1999) demonstrated that caregivers of early onset dementia (EOD) patients (that is, individuals aged < 65 years) were more likely to have a longer duration of caregiving, less social support and a heavier

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caregiver burden than those caring for late onset dementia (LOD) patients. Previous studies have also indicated that situations involving younger caregivers and/or younger patients are associated with an increased caregiver burden (Freyne *et al.*, 1999; Schneider *et al.*, 1999).

Therefore, it is clearly important to assess the problems faced by caregivers of EOD patients, and to ensure that they receive appropriate external assistance and social support. The formal care services in Japan provided under the Long-Term Care (LTC) insurance scheme is one of the important sources of social support. Kumamoto *et al.* (2006) reported that the use of such care services reduced feelings of burden among the caregivers of frail elderly patients. However, the LTC insurance scheme might be less easy for sufferers of EOD to access, as it is mainly targeted at individuals aged ≥65 years. The shortage of service provision has been indicated in other countries such as Ireland and the UK (Freyne *et al.*, 1999; Chaston *et al.*, 2004; Coombes *et al.*, 2004). This might be partly due to the fact that the issue has yet to be recognized as a public-health concern, owing to the relatively small prevalence of EOD sufferers compared with LOD sufferers (Karasawa, 1992).

There is a need to raise awareness of EOD as a public-health concern, and to identify the unmet requirements of EOD sufferers and their family caregivers with respect to caregiving situations, specific difficulties and caregiver burden-associated factors. The objectives of the present study were thus to compare family caregiving situations for individuals with EOD and LOD, and to clarify the specific problems experienced by the caregivers of the former.

METHODS

Participants

The subjects were chosen from a total of 92 caregiver–patient dyads, comprising co-residing family caregivers and consecutive outpatients seen at Ehime University Hospital, Japan, between June 2004 and December 2005. Informed consent was obtained from all of the subjects. Differential diagnoses were made by employing the NINCDS–ADRDA (McKhann *et al.*, 1984) for probable Alzheimer's disease, consensus criteria (Neary *et al.*, 1998) for Frontotemporal lobar degeneration, DSM-IV (American Psychiatric Association, 1994) for Vascular dementia, and consensus guidelines (McKeith *et al.*, 1996) for Dementia with Lewy bodies. Patients were assessed in terms of their cognitive function, neuropsychiatric disturbances and the severity of dementia, using the Mini-Mental State Examination (MMSE; Folstein *et al.*, 1975), the Neuropsychiatric Inventory (NPI; Cummings *et al.*, 1994; Hirono *et al.*, 1997) and the Clinical Dementia Rating (CDR) scale (Hughes *et al.*, 1982), respectively. The age at first hospital visit of the patients was identified from their charts.

Measures

The caregivers responded to a set of self-administered questions that included items addressing their socio-demographic status. The caregivers were also asked to state the number of hours per day they provided care for the patients and the number of months that they had cared for them. In addition, they were asked to estimate the number of hours per day that they were temporarily relieved of their duties or were able to leave the patients.

The health status of the caregivers was evaluated using two subscales of the 28-item General Health Questionnaire (GHQ; Goldberg and Hillier, 1979; Narita, 1994): the somatic symptoms subscale, and the anxiety and insomnia subscale. The sums of the scores in each subscale according to a four-point Likert scale were used as indices of the somatic symptoms and anxiety and insomnia of the caregivers, respectively, and ranged from 0 (healthiest) to 21 (least healthy). The Cronbach's coefficient alpha values for the somatic symptoms and anxiety and insomnia were 0.858 and 0.898, respectively.

The perceived difficulties caused by patient behavioural disturbances were assessed using 15 items from the Troublesome Behaviour Scale (Asada *et al.*, 1994, 2000). The caregivers were asked to state how much difficulty they experienced due to patient behavioural disturbances according to a four-point Likert scale. All of the items were summed, in order to reveal the perceived difficulties caused by patient behavioural disturbances, with scores ranging from 0 (little difficulty) to 45 (a lot of difficulty). The Cronbach's alpha value was 0.879.

Caregiver burden was assessed using the Japanese version of the Zarit Burden Interview (J-ZBI), which has well-documented validity and reliability (Arai *et al.*, 1997).

Statistical analyses

We divided the caregiver–patient dyads into two groups based on the age of the patient at their first visit to the hospital: those aged <65 years were assigned to

the EOD group, and those aged ≥65 years were assigned to the LOD group. The characteristics of the two groups were compared using Fisher's exact tests or Mann–Whitney tests. The associations among the patient variables and the caregiver variables were analyzed using the Spearman's rank order correlation coefficients for both groups. The associations between the probability of EOD and the caregiver variables were evaluated by calculating the odds ratios (OR) with 95% confidence intervals (CI). Logistic regression models were used to estimate the crude ORs and the ORs adjusted for the potential confounding factor. The independent variables were assumed to be continuous in view of their goodness-of-fit to the data. In addition, Mantel extension tests were used to assess linear trends across the tertile categories of the caregiver measures, with the exceptions of anxiety and insomnia, and perceived difficulties due to patient behavioural disturbances. These variables were classified into three groups, in order to include a similar number of subjects in each category.

The criterion for statistical significance was $p < 0.05$ for all analyses. All calculations were performed using SAS version 9.1.3 for Windows (SAS Institute Inc., Cary, NC).

RESULTS

Characteristics of patients and caregivers

In total, 24 of the 92 caregiver–patient dyads were excluded from the analysis due to missing data (14 dyads) or because the individuals were not living together (10 dyads). Of the 68 dyads that were eligible for further analyses, 14 were assigned to the EOD group and the remaining 54 were assigned to the LOD group.

Table 1 shows the characteristics of the patients and their caregivers in the two groups. There were no significant differences in cognitive function (MMSE), behavioural disturbances (NPI) or the severity of dementia (CDR) between the EOD and LOD patients. The caregivers in the EOD group were significantly younger and more likely to have a job than those in the LOD group.

Family caregiving situations in the EOD and LOD groups

There were no significant differences between the two groups in the caregiving situations (Table 2). The perceived difficulties caused by patient behavioural disturbances appeared to be greater in the EOD group, although this trend was not statistically significant.

Correlations of caregiver and patient variables

Among the EOD group, the caregivers' anxiety and insomnia and J-ZBI score were positively correlated with the patient NPI score (Table 3). On the other hand, among the LOD group, there were significant associations between most of the caregiver variables and the patient NPI and CDR scores (Table 4).

Health, difficulties and burden of caregivers in the EOD and LOD groups

The crude ORs of the EOD and LOD groups showed no significant differences in any of the caregiver variables (model 1; Table 5). Adjusting for patient age slightly increased the ORs (model 2). Additional adjustments were made for the NPI and CDR scores (model 3), because they were strongly correlated with the caregiver variables (see above). The results demonstrated that caregivers of EOD patients were more likely to perceive difficulties due to patient behavioural disturbances than caregivers of LOD patients (p value for trend = 0.041). Although the OR for the anxiety and insomnia of caregivers was found to be significant, no linear trend was observed across the categories of the variable (p value for trend = 0.182).

DISCUSSION

Patients with EOD and LOD in the present study did not show differences in their clinical features, including cognitive function, behavioural disturbances and disease severity. Nevertheless, a multiple logistic regression analysis demonstrated that the caregivers of the EOD patients had greater difficulties in coping with patient behavioural disturbances than the caregivers of LOD patients. This implied that a difference in a factor other than patient clinical features caused additional difficulties for caregivers coping with behavioural disturbances of EOD sufferers.

Although relatively few studies have compared the psychosocial effects of differences in the onset of dementia on patients, previous finding should be noted. Prohaska *et al.* (1987) noted that people generally tend to attribute their symptoms to aging, especially older individuals or those with less-severe symptoms. Hence, the psychosocial effects of a disease might vary between patients depending upon the point in their lives at which the symptoms occur.

The early onset of disease could potentially have a greater impact on their behaviour and clinical features,

Table 1. Characteristics of patients and caregivers in the EOD and LOD groups

	Early onset ($n = 14$)	Late onset ($n = 54$)	p value[a]
Patient			
Age	60.5 [59.0, 63.0]	78.0 [72.0, 80.0]	<0.001
Years since first visit to the hospital	1.5 [0.0, 4.0]	1.0 [0.0, 2.0]	0.255
Female	7 (50.0)	24 (44.4)	0.769
Diagnosis			
Alzheimer's disease	10 (71.4)	32 (59.3)	0.081
Vascular dementia	1 (7.1)	7 (13.0)	
Frontotemporal lobar degeneration	3 (21.4)	2 (3.7)	
Dementia with Lewy bodies	0 (0.0)	9 (16.7)	
Other types of dementia	0 (0.0)	4 (7.4)	
Cognitive function (MMSE)[b]	20.0 [13.0, 23.0]	22.0 [18.0, 25.0]	0.220
Behavioural disturbances (NPI)	11.5 [9.0, 19.0]	8.5 [4.0, 24.0]	0.832
Severity of dementia (CDR)			
0	0 (0.0)	1 (1.9)	0.344
0.5	4 (28.6)	19 (35.2)	
1	3 (21.4)	17 (31.5)	
2	5 (35.7)	10 (18.5)	
3	2 (14.3)	7 (13.0)	
Caregiver			
Age	61.5 [57.0, 66.0]	70.0 [63.0, 74.0]	0.011
Female	8 (57.1)	44 (81.5)	0.078
Relationship to the patient			
Spouse as caregiver	13 (92.9)	39 (72.2)	0.152
Adult child as caregiver	0 (0.0)	7 (13.0)	
Daughter-in-law as caregiver	0 (0.0)	7 (13.0)	
Other	1 (7.1)	1 (1.9)	
Employment status[c]/employed	8 (57.1)	14 (26.4)	0.052
Subjective economic status			
High	2 (14.3)	8 (14.8)	0.771
Middle	7 (50.0)	32 (59.3)	
Low	5 (35.7)	14 (25.9)	

Data are shown as the median [25 percentile, 75 percentile] or n (%).
[a]Calculated using the Fisher's exact test for nominal variables and the Mann–Whitney test for ordinal/interval variables between the EOD and LOD groups.
[b]One missing data point in each group.
[c]One missing data point in the LOD group.

which might increase the difficulties and burdens experienced by their caregivers. Young age among caregivers of dementia patients has also been identified as a predictor of increased burden (Freyne *et al.*, 1999; Schneider *et al.*, 1999). This implies that younger caregivers are less likely to be sufficiently prepared for the role, perhaps due to reduced understanding and acceptance of the disease.

In the current study, we did not identify a greater caregiver burden, but rather greater perceived difficulties by the caregivers of the EOD group. However, behavioural disturbances of patients with dementia clearly increase the risk of caregiver burden (Coen *et al.*, 1997; Donaldson *et al.*, 1998; Arai and Washio, 1999; Coen *et al.*, 1999; Rymer *et al.*, 2002). Thus, the fact that the caregivers in our study perceived difficulties in coping with patient behavioural disturbances could be regarded as a precursor of caregiver burden. The difficulties perceived by the caregivers of the EOD patients might therefore eventually lead to caregiver burden if appropriate assistance is not provided.

The assistance provided to family caregivers can include formal care services that are intended to

Table 2. Caregiving situation in the EOD and LOD groups

Caregiving situation	Early onset ($n = 14$)	Late onset ($n = 54$)	p value[a]
Duration of caregiving (months)	24.0 [13.0, 36.0]	24.0 [6.0, 55.0]	0.574
Hours of caregiving per day	4.5 [3.3, 8.0]	2.0 [0.0, 4.5]	0.054
Hours caregivers are relieved per day	2.0 [1.5, 8.0]	4.0 [2.0, 24.0]	0.368
Caregiver measure (score)			
Somatic symptoms[b]	8.5 [7.0, 13.0]	9.0 [4.0, 12.0]	0.474
Anxiety and insomnia[b]	10.0 [9.0, 13.0]	8.0 [5.0, 12.0]	0.106
Perceived difficulties due to patient behavioural disturbances[c]	9.0 [4.0, 15.0]	4.0 [0.0, 13.0]	0.053
Caregiver burden (J-ZBI)[d]	21.0 [15.0, 36.0]	18.0 [11.0, 34.0]	0.686

Data are shown as the median [25 percentile, 75 percentile].
[a]Calculated using the Mann–Whitney test for ordinal/interval variables between the EOD and LOD groups.
[b]Scores ranging from 0 to 21.
[c]Scores ranging from 0 to 45.
[d]Scores ranging from 0 to 88.

Table 3. Correlations between patient and caregiver variables in the EOD group ($n = 14$)

	1	2	3	4	5	6	7	8	9
1. Patient age	1.000								
2. Caregiver age	0.709*	1.000							
Patient measure									
3. Cognitive function (MMSE)	−0.146	−0.135	1.000						
4. Behavioural disturbances (NPI)	0.115	0.138	−0.284	1.000					
5. Severity of dementia (CDR)	0.058	0.079	−0.626**	0.307	1.000				
Caregiver measure									
6. Somatic symptoms	−0.114	−0.180	0.095	0.368	0.065	1.000			
7. Anxiety and insomnia	0.027	−0.100	−0.077	0.544**	0.087	0.652**	1.000		
8. Perceived difficulties due to patient behavioural disturbances	0.353	0.414	−0.178	0.440	0.485	0.159	0.527	1.000	
9. Caregiver burden (J-ZBI)	0.058	0.176	−0.287	0.774*	0.450	0.449	0.641**	0.413	1.000

Spearman's rank order coefficient;
*$p < 0.01$; **$p < 0.05$.

Table 4. Correlations between patient and caregiver variables in the LOD group ($n = 54$)

	1	2	3	4	5	6	7	8	9
1. Patient age	1.000								
2. Caregiver age	−0.021	1.000							
Patient measure									
3. Cognitive function (MMSE)	−0.104	0.041	1.000						
4. Behavioural disturbances (NPI)	0.076	−0.181	−0.219	1.000					
5. Severity of dementia (CDR)	0.130	−0.105	−0.678*	0.535*	1.000				
Caregiver measure									
6. Somatic symptoms	0.332**	−0.153	0.056	0.315**	0.264	1.000			
7. Anxiety and isomnia	0.248	−0.123	−0.140	0.488*	0.396*	0.760*	1.000		
8. Perceived difficulties due to patient behavioural disturbances	0.224	−0.167	−0.253	0.572*	0.523*	0.355**	0.366*	1.000	
9. Caregiver burden (J-ZBI)	0.138	−0.147	−0.189	0.630*	0.576*	0.583*	0.735*	0.504*	1.000

Spearman's rank order coefficient;
*$p < 0.01$; **$p < 0.05$.

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Table 5. ORs of the EOD and LOD groups associated with caregiver variables pertaining to health, perceived difficulties and caregiver burden

Caregiver measure	Model 1	Model 2		Model 3	
	Crude OR (95% CI)	Age-adjusted OR* (95% CI)	*p*-value for trend†	Age-/NPI-/CDR- adjusted OR** (95% CI)	*p*-value for trend†
Somatic symptoms	1.05 (0.92, 1.21)	1.17 (0.91, 1.62)	0.558	1.33 (0.95, 2.19)	0.731
Anxiety and insomnia	1.09 (0.96, 1.25)	1.24 (0.94, 1.80)	0.112	2.18 (1.06, 9.98)	0.182
Perceived difficulties due to patient behavioural disturbances	1.05 (0.99, 1.14)	1.22 (1.03, 1.68)	0.062	1.29 (1.05, 2.06)	0.041
Caregiver burden (J-ZBI)	1.00 (0.97, 1.04)	1.05 (0.97, 1.15)	0.669	1.08 (0.98, 1.25)	0.731

*Adjusted for patient age by a logistic regression model.
**Adjusted for patient age, and CDR and NPI scores by a logistic regression model.
†*p*-value for trend calculated by the Mantel extension method using categorized variables.

address caregiving needs and to promote social networking. Recent community-based studies have supported the notion that relatively few services are available for EOD patients and their family caregivers (Freyne *et al.*, 1999; Chaston *et al.*, 2004; Coombes *et al.*, 2004). Moreover, it has been suggested that poor provision of care services could prolong the duration of caregiving, consequently leading to the isolation of caregivers of EOD patients. It is therefore essential that additional resources should be allocated to sufferers of EOD, in order to allow family caregivers to better cope with the difficulties caused by patient behavioural problems and to develop more appropriate formal and informal sources of social support.

A couple of limitations to the present study should be noted. First, the small sample size made it difficult to generalize the findings. Second, patient age at first visit to the hospital was used to distinguish EOD patients from LOD patients. This cut-off point remains possible that misclassification could induce bias into the results. Third, as the present study focused on one time point of a long disease trajectory, further investigation will be needed to assess whether the clinical features of the EOD and LOD patients progress differently over a longer time span.

Despite these considerations, our study has several strengths. First, it is one of only a few studies to compare the psychosocial effects of the onset of dementia on patients and their family caregivers. Second, we found a significant difference in the perceived difficulties caused by patient behavioural disturbances in the caregivers of the two groups. Overall, our findings provide valuable insights that could be used to improve the current services for EOD patients and their family caregivers. We strongly believe that improved knowledge will enhance public awareness, and promote more accessible care services, which will benefit both EOD patients and their caregivers.

KEY POINTS

- Previous reports have indicated the shortage of service provision for patients with EOD and their family caregivers. However, relatively few studies have compared the psychosocial effects of differences in the onset of dementia on patients.
- The caregivers of EOD patients in the present study had greater perceived difficulties due to patient behavioural disturbances than did the caregivers of LOD patients, although patients with EOD and LOD did not show differences in their clinical features.
- Additional resources, such as care services, should be provided for sufferers of EOD, in order to allow family caregivers to cope with difficulties associated with patient behavioural problems.

CONFLICT OF INTEREST

None.

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特　集　ピック病・再考

ピック病の症状・経過について

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抄　録

ピック病は脱抑制，常同行動や自発性の低下などの特徴的な社会行動の障害や人格変化を呈する疾患群であり，潜行性に発症して比較的進行が早いことが知られている．しかしながら現在まで多数例での長期の自然経過の報告はほとんどなく，病期分類に関しても前頭葉優位型と側頭葉優位型を区別して行ったものはない．ピック病の臨床病理相関を明らかにし，おのおのの亜型での症状と経過を明らかにすることが求められる．

Key words：Pick's disease, frontotemporal dementia, behaviour, progress, staging

老年精神医学雑誌 18：591-597，2007

はじめに

およそ100年前にArnold Pickが前頭-側頭葉の限局性萎縮と特徴的な精神症状や言語症状を呈する症例を報告し[31]，その後の嗜銀性神経細胞封入体（ピック小体）の発見を経て，1926年にこの一連の臨床症状を呈する葉性萎縮例はピック病と命名された[22]．その後欧米ではピック小体の取り扱いをめぐってピック病の病理診断に関する議論が続いていた．

1980年代後半に，従来ピック病と呼ばれていた疾患群に対し，Manchesterのグループと Lundのグループがほぼ同時に類似の疾患概念を独立して発表し，1994年には両グループが共同でFTD（frontotemporal dementia）という臨床的・病理学的な概念を提唱して診断基準を示した[30]．しかし，このFTDにはそれまで側頭葉優位型ピック病と呼ばれてきた一群が含まれなかったため，1996年にManchesterのグループがFTLD（frontotemporal lobar degeneration）という上位概念を提唱し，これを臨床症状と萎縮部位から，前頭葉が主として障害されるFTD，側頭葉が主として障害されるSD（semantic dementia：意味性認知症），頭頂葉にまで病変が及ぶPNFA（progressive non-fluent aphasia：進行性非流暢性失語）に分類した[23]．

詳細なピック病の概念の変遷に関しては本稿の主題ではないが，本稿においてピック病という用語はピック小体の有無にかかわらず，広義の前頭葉優位型ピック病（FTDとほぼ同義）と側頭葉優位型ピック病（SDを中核とした一群）をあわせた用語として用いることを確認しておく．

ピック病の症状

ピック病の臨床症状に関しては，現在まで多くの精神科医によって詳細な記載がなされてきた．それらのうちで主要なものを表1に挙げる．前頭葉や側頭葉前方部が障害されるピック病においては，社会行動の障害や人格変化が主たる症状であ

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表1　ピック病の主要な症候学的記載

1926年	Stertz	前頭葉型と側頭葉型の臨床的特徴
1927	Schneider C	欲動的脱制止，滞続現象（stehende Symptom）
1934	Braunmühl & Leonhard	考え不精（Denkfaulheit）
1936	Guiraud	PEMA 症候群 (palilalie, écholalie, mutisme, amimie)
1938	古川	巣症状として失語，失書が著明
1947	Mallison	自動化した行為の一時的阻止，衝動亢進
1954	Klages	発動性減弱（Antriebsschwäche）
1981	吉田，松下	立ち去り行動
1985	Tissot	PES 症候群 (palilalia, echolalia, stereotypic behavior)
1999	田邊	わが道を行く行動

り，アルツハイマー病（Alzheimer's disease ; AD）のような記銘力障害や視空間機能障害は通常は目立たない．以下にピック病の主要な症状を概観する[1,8,12,14,30]．

1．精神症状・行動の障害

前頭葉優位型ピック病では病初期から出現する．側頭葉優位型ピック病では病期の進行にしたがって出現するとされてきたが，近年になり側頭葉優位型のピック病でも比較的早期から出現する可能性が示唆されている[1,30]．

1）病識の欠如

病初期より病識は欠如しており，とくに古典的な前頭葉優位型のピック病では病感すら失われていると感じられることが多い．そのためしばしば治療の導入に困難をきたす．

2）社会的対人行動の低下・脱抑制

本能のおもむくままに行動する「わが道を行く行動（going my way behavior）」が出現する[21]．具体的には礼儀，行儀作法が失われ，窃盗や盗食などの反社会的行動や軽犯罪もしばしば認められる（ただし本人には悪意はない）．これは前方連合野から辺縁系への抑制が外れた結果とも解釈できる．衝動的な暴力行為が認められることもあるが，これは常同行為が遮られたときに出現することが多い．このような脱抑制は前頭葉眼窩面の障害で出現するが，前頭葉全体に病変が進み自発性の低下が顕著になるとあまり目立たなくなる．

3）対人接触の調節障害・無関心

比較的病初期から認められ，自己の整容や身なりに対しても周囲への対応に関しても無関心になる．検査場面で自らは考えようとせずに検者にやらせようとしたり，よく考えずに即答したりする．これを「考え不精（Denkfaulheit）」と呼びその一部が無関心に関連していると考えられる．また診察場面で散見される立ち去り行動も無関心の関与が考えられている．

4）感情・情動変化

情意鈍麻，無表情が初期から出現しやすい．脱抑制と関連して多幸的に変化していることも多いが，焦燥感が強く不機嫌を呈していることもあり，一部には冷たく疎通性の得られない例もある．多幸的，児戯的な性格変化は前頭眼窩面の障害との関連が指摘されている．

5）自発性の低下

病状の進行に伴って意欲や自発性の低下が顕著になっていくことが多い．脳血管性認知症における自発性の低下との違いは，ピック病の場合は常同行動や落ち着きのなさと同居してみられること

がある点である．前述の「考え不精」は自発性の低下とも関連していると考えられている．一般的に自発性の低下は前頭葉内側面，とくに前部帯状回との関連や前頭葉穹窿面との関連が指摘されている[4,21]．

6）常同行動

日常生活において常同的な周遊（roaming），常同的な食行動，常同的な発話（反復言語，滞続言語など）を呈する[27]．これらはADとの鑑別にも重要となる症状である．生活が時刻表的になり，強迫性を帯びることもある．進行すると膝を手で擦り続けたり，手をパチパチと叩いたりするような反復行動がみられることもある．このような常同行動は基底核の病変によっても生じることから[18]，前方連合野から大脳基底核の抑制が外れた結果と理解できる[32]．

7）食行動異常

甘いものや味の濃いものへ嗜好が変わったり，大食になったり，決まった少数の食品や料理に固執する常同的な食行動が出現したりする場合が多い[15]．女性の場合調理が常同的となり，同じメニューばかり作るようになることもある．このような食行動異常はしばしばKlüver-Bucy症候群との関連で論じられる．

8）被影響性の亢進

日常生活場面では，介護者と同じ動作をするといった反響もしくは模倣行為，視覚に入った文字を読み上げる，他者への質問に先んじて応じるといった行為で現れる．これは前方連合野が障害されて後方連合野への抑制が外れ，後方連合野が本来有している状況依存性が解放された結果，すなわち外的刺激や内的要求に対する非刺激閾値が低下し，その処理が短絡的で反射的になったものと考えられる[31]．

9）転導性の亢進，維持困難

ある行為を持続して続けられない，注意障害あるいは運動維持困難との関連が考えられる．外界の刺激の有無にかかわらず，落ち着かないことが多い．前述の立ち去り行動も，この転導性の亢進との関連も考えられる．

2．言語症状

1）滞続言語（stehende Redensart），同語反復（palilalia），反響言語（echolalia）

滞続言語（stehende Redensart）は同じ話やフレーズを，質問の内容にかかわらず繰り返す発話を指す．病初期では意味のあるある程度まとまった文章であるが，しだいに短く内容も乏しくなっていくことが多い．同語反復（palilalia）は短い語句を繰り返し言う現象を指し，たとえば「今日は何日ですか」と尋ねると「14日，14日，14日…」などと反復する．反響言語（echolalia）は問われた言葉をオウム返しに言う現象を指し，たとえば「お名前は？」と尋ねると「お名前は」と答えたりする．これらの言語症状は前述の常同行動や被影響性の亢進との関連が指摘されている．また，同語反復はパーキンソン病や進行性核上性麻痺といった疾患でも生じることがあるが，これらの場合はピック病で生じる症状とは性質が異なる[11]．

2）語義失語

側頭葉優位型のピック病においては「語義失語」と呼ばれる特徴的な失語像を呈することが多い．この語義失語と呼ばれる失語像はArnold Pickの症例でもすでに報告されているが，近年になるまでその詳細な検討はなされてこなかった．

典型的な語義失語例では語の意味記憶が選択的に障害され，たとえば「鉛筆」を見せても名前が答えられない．語頭音を「エンピ」まで与えても語頭音効果がみられず，複数の物品から指し示すように指示しても，「鉛筆」を選ぶことができない．これらが通常の語想起障害，語健忘とは異なる点であるが，鉛筆を持って字を書くことは可能であり，物品としての意味は理解している．すなわち「えんぴつ」という語彙が欠落した状態である．この語義失語は左側頭葉の限局性の萎縮によって生じる．右側頭葉の障害あるいは両側性の障害では相貌の意味記憶障害や物品の意味記憶障害が生じ，親しい人間の顔も既知感がなくなるとい

ったことが出現する[13,32]．

3）進行性非流暢性失語

上記の失語症状以外にも，ピック病などの変性疾患によって失語が選択的に出現している時期の病態を表す用語として，進行性非流暢性失語がある．ただし病理学的には，ADや非特異的変化を呈する症例もこの概念に含まれている．この進行性非流暢性失語においては左シルビウス裂周囲や中心前回などに限局した病変があり，喚語困難や呼称障害で始まり，音韻性の錯語や意味理解の障害を伴う非流暢な失語が出現し，その他の認知症症状は目立たない．この一群についてはMesulamの緩徐進行性失語（slowly progressive aphasia without generalized dementia；SPA）や原発性進行性失語（primary progressive aphasia；PPA），FTLDの下位概念としてのPNFAなどなど互いにオーバーラップするが異なる臨床症候群が提唱されている[19,20,29]．

2 ピック病の経過

ピック病は潜行性に発症し，進行性の経過をたどる．経過は比較的早く，全経過を通じて10年以内に病状が進行することが多いといわれる．Cambridgeのグループはピック病剖検例61例の発症からの平均寿命は6.0 ± 1.1年であったと報告し[9]，San Franciscoのグループは臨床診断例103例で前頭葉優位型ピック病（FTD）の発症からの平均寿命は8.7 ± 1.2年であると報告した[26]．また前頭葉優位型ピック病（FTD）とADおのおの70例の進行経過を比較した研究では，前頭葉優位型ピック病はADに比べて有意に進行が早く，ADLの低下の速度も速いことが報告されている[25]．ただしここで注意しなければならないことは，前述のような精神症状のため，近年までピック病に対して早期からの抗精神病薬投与や精神科病院入院による加療が行われてきたという経緯がある点である．それらによる影響も少なからずあると考えられ，疾患の自然経過は依然として明らかではないといえよう．

長期にピック病の経過を観察した報告が近年まで少なかったため[23]，ピック病においてはADにおけるClinical Dementia Rating（CDR）[10]のような標準化された病期分類はない．古典的にはSchneider，BraunmühlとLeonhard，Sjögrenらなどにより3期に分類されてきた．比較的最近の病期分類としてはわが国では小林らの病期分類[16]（表2），欧米ではCummingsらによる分類などがある[3]（表3）．しかしながらこれらはピック病の臨床亜型を正確に鑑別したうえで分類したものではない．前頭葉優位型ピック病と側頭葉優位型ピック病では症状の出現頻度や出現順序が異なることも明らかになりつつあり[15]，少なくとも前頭葉優位型ピック病と側頭葉優位型ピック病はおのおの別に病期分類を行う必要がある．臨床亜型ごとに病期分類を明らかにすることが，正確な病態の把握および治療やケアの方法の確立につながると考えられる．

また最近では病理所見からの病期分類の試みもなされており，Sidneyのグループは剖検された前頭葉優位型ピック病の重症度を病理所見から4群に分類したうえで，それが認知症自体の重症度や経過年数と一致したと報告している[2,17]．

一般的には病初期に万引きなどの社会的逸脱行為が出現し，仕事や家事に対して無関心になる，同じことばかり繰り返すといった症状で周囲に気づかれることが多い．筆者らによる前頭葉優位型ピック病（FTD）と側頭葉優位型ピック病の中核をなすSDの初発症状の比較研究においては，前頭葉優位型ピック病は行動面での障害を中心とした多彩な初発症状があり，「自発性低下」と「常同行動」といった一見相反するような症状が並存して初発症状として多く認められた[28]．また，たとえば「とくにこれといった理由がないが，料理の味が落ちた」というような非特異的な日常生活上の変化も多かった．逆にある程度進行した前頭葉優位型ピック病で目立つ「易刺激性」や「食行動異常」は初発症状としてはそれほど多くはなかった．側頭葉優位型ピック病の中核をなすSDの

表2　ピック病の病期分類

第1期	欲動的脱制止を中心とする性格の変化が目立つが，知的能力などの障害は軽い
第2期	滞続言語，失語などの言語機能の障害，自発性の障害，特徴的な接触性障害および認知症が目立つ
第3期	精神荒廃が目立ち，無言，不潔症，症縮，原始反射などが出現し，ついには寝たきりの状態となる

（小林一成，新井平伊，池田研二，小阪憲司：Pick病のComputed Tomography．精神神経学雑誌，86：401-416，1984）

表3　ピック病の症状経過

第Ⅰ期 （発病から1～3年）	人格：関心の喪失 判断力：障害 実行能力：計画および抽象思考の低下 記憶：比較的保たれている 視空間見当識：正常 言語：正常あるいは失名辞，迂回操作 計算力：比較的保たれている Klüver-Bucy症候群：症状が部分的に顕在化 運動系：正常 脳波：正常
第Ⅱ期 （発病から3～6年）	言語：常同言語，言語理解不良，失語 記憶：比較的保たれている 視空間見当識：比較的保たれている 判断力：低下 実行能力：低下 運動系：比較的正常 脳波：基礎律動の徐波化 CT/MRI：前頭葉と側頭葉の両方または片方の局所性萎縮 PET/SPECT：両側前頭葉の低代謝あるいは低血流
第Ⅲ期 （発病から6～12年）	言語：緘黙あるいは意味不明の発話 記憶：低下 視空間見当識：低下 認識：高度に障害 運動系：錐体外路症状または錐体路症状と錐体外路症状の混在 脳波：全般性徐波あるいは前頭・側頭の徐波化 CT/MRI：前頭葉と側頭葉の両方または片方の局所性萎縮 PET/SPECT：両側前頭葉の低代謝あるいは低血流

（Cummings JL, Benson DF : Pick's disease. *In* Dementia ; A clinical approach, 2nd ed., ed. by Cummings JL, Benson DF, Butterworth-Heinemann, Boston, 1992）

初発症状は言語障害が多く，とくに喚語困難，錯語，語理解の障害が一般的であった．

中期になると前述した人格変化や行動異常が顕著になる．行動面では同じ行為を繰り返す常同行動が目立ち，習慣化した行動以外の生産的な行動は困難となる．また考え不精となり，周囲への態度は無配慮で非協力的なものとなるため，他者との疎通性が低下する．さらに滞続言語や反響言語なども目立つようになる．しかし，これらの人格面での変化に比べて記憶力や視空間認知能力はこの時期でも比較的保たれており，これがADとは大きく異なる点である．

末期になると，自発性が顕著に低下して膝をさすり続けるような反復行為が前景に立つ生活になる．さらに症状が進むと寝たきりになり，錐体路症状や錐体外路症状なども出現する．

なお，臨床例と剖検例をあわせた96例のピック病の予後を調査した研究では，緘黙や神経徴候，嚥下困難を伴う患者は生命予後が不良であったと報告されており[6,7]，前述のSan Franciscoのグループの報告では筋萎縮性側索硬化症を合併するタイプは予後不良であったとされている[20]．また前頭葉優位型ピック病31例を検討し，頭部MRI上で萎縮が顕著であったものは進行が早かったとした報告もある[5]．

おわりに

近年の疾患概念の変化によりピック病という用語は姿を消し，前述のFTLDあるいはFTDという概念がそれに変わるようになった．そのFTDも病理学的あるいは遺伝学的に多様な背景をもつ疾患集合であることが明らかになりつつある．しかし，新しい概念が複雑になればなるほど，臨床的にはピック病の概念が有用になることが多い印象もある．いずれにせよ，ピック病ないしFTLDの症状と経過を考えるうえで，今後はその組織病理学的な背景と臨床症状や経過との相関を明らかにし，臨床亜型ごとの特徴を抽出することが重要であると考える．

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