

CLINICAL FEATURES OF ALZHEIMER'S DISEASE IN A REGIONAL MEMORY CLINIC IN HONG KONG

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Abstract

Symptomatology of Alzheimer's Disease (AD) had been widely reported in Caucasian populations. Local data was lacking in Hong Kong. The aim of the present study was to review the clinical features of Alzheimer's disease in a regional Memory Clinic in Queen Mary Hospital. This was a retrospective case series analysis. Case records of patients attending the Queen Mary Hospital's Memory Clinic from 1/1/1997 to 30/6/2000 were reviewed. All patients who had probable AD (i.e. AD) by NINCDS-ADRDA criteria were recruited. Demographic data, presenting symptom, cognitive and non-cognitive symptoms, cognitive assessment scores, functional status and place of residence were documented and analyzed. Results: 96 AD patients were recruited. 72.9% were female. The mean age at first visit was 77.3 years (s.d.= 6.55 years). The interval between symptom onset and first visit was 3.1 years (s.d.=2.0 years). 90.6% presented to the clinic because of poor short-term memory. 83.3% had non-cognitive symptoms at clinical presentation. These included behavioural changes (59.4%), perceptual/psychotic changes (51.0%), sleep (27.1%) and mood (24.0%) changes. In conclusions, the clinical features of AD among Chinese elderly patients in a regional Memory Clinic in Hong Kong shared many common features to those reported by Caucasian studies. There was a delay in symptom onset and in the proper assessment at the Memory Clinic

Keywords: Alzheimer's Disease, Clinical features

Introduction

In Hong Kong, dementia occurs in 6.1% of elderly people aged 70 and over. Alzheimer's Disease (AD) accounts for 64.6% of all dementia¹. AD has well described clinical features, which may be categorized into cognitive and non-cognitive symptoms with functional impairment consequently. The presence of memory impairment as one of the first cognitive manifestation of AD has been reported in Caucasian studies². Non-cognitive symptoms like affective instability, psychotic symptoms and behavioural disorders are common in AD. These symptoms occur in approximately 90% of patients in overseas studies³. Behavioral disturbances often compel families to seek long-term care for AD patients⁴. They may also cause significant distress for the patient as well as burden for the family caregiver.

Treatment of both cognitive and behavioral abnormalities can improve the quality of life of the patient and caregiver. Therefore, the recognition of cognitive and non-cognitive presentations of AD is important because these symptoms have implications for diagnosis, prognosis and treatment. However, local published data on the prevalence and impact of clinical features of AD in Hong Kong is lacking.

The objectives of this study were to review the clinical features of AD in a Memory Clinic case series.

Method

Study Population / subjects

Between 1/1/1997 and 30/6/2000, 288 patients attended the Memory Clinic of Queen Mary Hospital. These patients were referred from different sources. Among the 288 subjects, 109 (45.4%) had probable AD according to criteria from DSM-IV⁵ and the National Institute of Neurological and Communication Disorders and Stroke - Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA)⁶. 13 of them were found to have coexisting vitamin B12 deficiency. These 13 cases were excluded from this study in view of the possible negative effect of vitamin B12 deficiency on cognition. Therefore, 96 probable AD patients were selected for subsequent analysis.

Review of Medical Records in this Study

This was a retrospective case series analysis. During the case review process, particular attention was paid to the clinical presentations, symptoms and physical findings to ensure that the diagnosis of probable AD was made in accordance with the NINCDS-ADRDA criteria⁶.

Study variables:

Ninety-six subjects who had probable AD were eligible for detailed analysis. Information on the following parameters was extracted from the records. These included demographic data (gender, age at presentation, age of onset of dementia illness, education and marital status), presenting symptoms and duration of illness before first clinic visit, cognitive symptomatology, non-cognitive symptomatology, vascular risk factors, assessment scores namely Mini-Mental State Examination (MMSE)⁷, Geriatrics Depression Scale (GDS-30)⁸, Hachinski Ischaemic Score (HIS)⁹, Barthel Index on Activities of Daily Living Scale (BADL)¹⁰, Lawton's Instrumental Activities of Daily Living Scale (IADL)¹¹ and Clinical Dementia Rating (CDR)¹². The type of accommodation at first visit was documented. Any change in the type of accommodation (for example, from home to institution) was recorded. If possible, the time of institutionalization was also noted so as to estimate the duration of illness from onset of symptom to institutionalization.

The criteria for some of the symptoms are defined as below:

Poor comprehension = failure to perform any one procedure in the 3-step command in the MMSE test.

Word-finding difficulty = difficulty in finding

the name of an object as reported by patients or their carers.

Impaired calculation = failure to perform any two (out of three) question related to calculation as set in the semi-structured interview form.

1. How many 10-cents coins are there in one dollar? - answer is TEN
2. How many 50-cents coins are there in HK\$6.5? - answer is THIRTEEN
3. To subtract 3 sequentially and start from 20. - answer 17,14,11,8,5,2

Apraxia = inability to carry out motor activities despite intact motor function as reported by patients or their carers

Construction apraxia is the failure in the task of copying two intersecting pentagons in the MMSE assessment test.

Judgement and problem solving problem:

1. *difficulty in handling household emergency* = it is worse than before for the patient to handle a household emergency like plumbing water leak or fire at home as reported by the carer
2. *Trouble with money management* = loss of ability to cope with small sums of money (e.g. make change, leave a small tip) or loss of ability to handle complicated financial/ business transactions (e.g. balance check book, pay bills) as reported by carer

Impaired abstract thinking ability = failure of the patient to answer two or more (out of four) of the questions about similarities and differences asked by interviewer in the semi-structured assessment.

1. How are Onion and Lettuce alike? Answer is VEGETABLE
2. How are Desk and Bookcase alike? Answer is FURNITURE or BOTH HOLD BOOKS
3. Can you tell me what is the difference between Lie and Mistake? Answer is ONE DELIBERATE, ONE INTENTIONAL
4. Can you tell me what is the difference between River and Sea? Answer is ONE NON-SALTY, ONE SALTY.

Statistical analyses

Descriptive analyses for all variables were first performed. Student's t-tests were used for continuous variables. Chi-square statistics or Fisher's Exact test were used for categorical data. A p-value of less than 0.01 was regarded as

Table 1: Gender differences in demographic characteristic, baseline scores and number of domains of cognitive and non-cognitive symptoms at first visit (n=96)

	Men (n=26)	Women (n=70)	p value
Age at first visit (years)	76.3±7.3	77.7±6.3	0.36
Age at onset of disease (years)	74.0±7.2	74.2±6.9	0.93
Duration of illness before first visit (years)	2.25±0.99	3.5±2.2	<0.001*
Marital status			0.008*
Married	61.5%	31.4%	
Widowed/ single/ divorced	38.5%	68.4%	
Years of education†	6.3±5.1	3.1±4.4	0.004*
Number of cognitive domain	5.8±1.5	5.9±1.6	0.77
Number of non-cognitive domain	1.7±1.1	1.6±1.1	0.76

* denotes statistically significant (p<0.01)

† denotes n=94

statistically significant to correct for multiple comparison. The Statistical Package for the Social Sciences (SPSS) 7.5 for Windows was employed for statistical analyses.

Results

Demographic characteristics

Among the 96 AD patients, 18 (18.7%) lived at home. 70 (72.9%) were female. The mean age at first visit was 77.3 (SD 6.6) years. Nearly half (45.7%) of the subjects were illiterate. The mean number of years of education attained was 3.93 (4.8) years. There was no gender difference as regard to age (male 76.3±7.3 years vs female 77.7±6.3 years; p=0.36). There were more women who were either widow, divorced or single than the men (68.4% vs 38.5% in men, p=0.008). Female patients were more likely to be illiterate as compared to the male group (54.3% vs 20.8%; p=0.005). The mean

education level among the women was 3.1 ±4.4 years as compared to 6.3±5.1 years in men (p=0.004). Women had longer duration of symptom before consultation (3.5 years in female versus 2.3 years among male). (Table 1).

The mean MMSE on presentation was 15.5±5.4 with a GDS of 7.9±5.6. Likelihood of vascular dementia was low with a mean HIS of 1.45. Most of them was independent in BADL but disable with instrumental ADL (mean BADL at 18.1±3.5, IADL at 4.9±2.4).

65.6% of the patients had mild dementia with CDR 0.5 or 1. 25.0% had moderate dementia (CDR 2) and only 9.4% had severe dementia with CDR 3.

Cognitive Symptoms (Table 2)

Overall 88 (91.7%) patients presented to the clinic because of cognitive symptoms alone. 7 (7.3%) presented with non-cognitive symptoms alone. One patient (1.0%) presented with mixed cognitive and non-cognitive symptoms.

At presentation, all AD patients had poor short-term memory. Only 5.2% reported poor long-term memory at first visit.

Three-quarters (74.0%) had disorientation in time, place or person. Disorientation in place and time were very common. They occurred in 60.4% and 51.0% of the patients respectively. Disorientation in person was present in approximately one-quarter (25.0%) of patients.

The percentage of subjects having disorientation increased with increasing severity of dementia as measured by CDR (Figure 1). It increased from 31% to 70%, 96% and 100% for CDR of 0.5, 1.0, 2.0 and 3.0 respectively. In advanced dementia (CDR 3.0), 56% had complete disorientation of time, place and person. Among those with disorientation in place

Table 2: The prevalence of different domains of cognitive and non-cognitive symptomatology (n=96)

Cognitive domains	n (%)
Poor memory	100%
Disorientation	74.0%
Apraxia	80.2%
Calculation problems	68.8%
Language problems	57.3%
Impaired abstracting ability	90.6%
Impaired executive function	85.4%
Agnosia	22.9%
Impaired attention	5.2%
Non-cognitive domains	
Behavioral changes	59.4%
Perceptual changes/ psychotic symptoms	51.0%
Sleep changes	27.1%
Affective disorders	24.0%
Appetite changes	1.0%

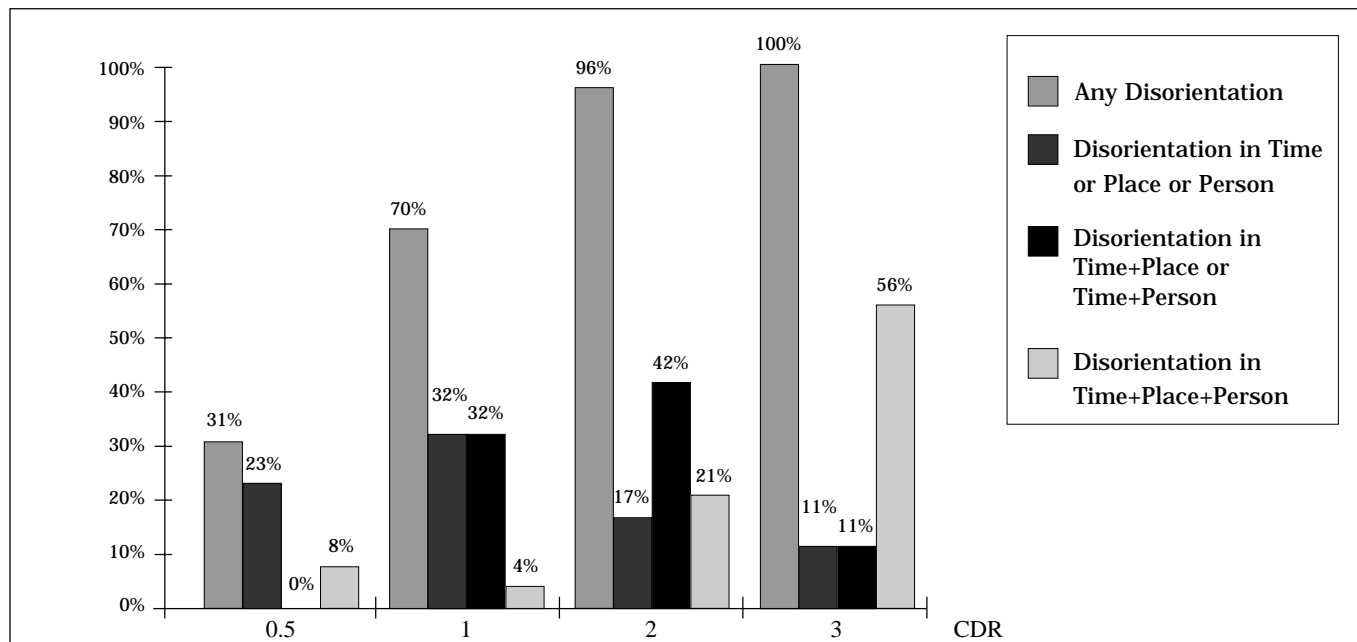


Figure 1: Prevalence of disorientation in general and disorientation of different types among subjects with different stages of dementia as measured by CDR. (Any disorientation means disorientation in time, place or person or any combination of them.)

(n=58), 38 (65.5%) had history of “getting lost in street”.

Apraxia was found in 80.2%. 68.8% had impaired calculation. 57.3% expressed various degree of language difficulties at first visit. These included poor comprehension (45.8%) and word-finding difficulties (26.0%).

Abstracting thinking ability was impaired in 90.6%. Impaired executive function, judgement or problem solving ability occurred in 85.4% of subjects. 63.5% found difficulties in handling household emergency, 54.2% had trouble with money management and 44.8% had impaired ability in household chores.

Non-cognitive symptomatology (Table 2)

Non-cognitive symptoms were present in 83.3% among the AD patients. Among the 5 domains of non-cognitive symptomatology, behavioral change was the most commonly encountered form, which occurred in 59.4%. The second most common domain was perceptual / psychotic changes (51.0%). Sleep and mood changes were present in 27.1% and 24.0% respectively. Only 1% reported having appetite change.

15.6% had depressive features and only a minority of them were taking anti-depressant. Irritability occurred in 10.4%. Apathy and anxiety was present in 3.1% and 1.0% respectively. All patients did not fulfill the Major Depression criteria (by DSM-IV criteria) after careful review by our

psychogeriatrician.

Delusional or paranoid ideations was found in 47.9%. 63.0% were in the form of “delusion of stealing”. Hallucinations occurred in 10 (17.4%) of patients with delusions. Interestingly visual hallucination was more common than (90%) auditory hallucination.

Approximately one quarter (24.0%) had some change in temper. Disturbing, aggressive and unusual behaviours occurred in 11.5%, 8.3% and 7.3% respectively.

Discussion

72.9% AD patients seen in our Memory Clinic were female. This finding is consistent with most epidemiological studies that the prevalence of AD is higher in women than men. The mean duration of illness before first visit was 3.1 years. This was more than double the recently reported figure of 1.2 years from a Caucasian dementia population¹³. The delay between the onset of cognitive symptoms and referral for diagnosis among our Chinese group could be related to the traditional and cultural belief that poor memory and impaired cognitive function is a “normal ageing” feature in older persons. It is important to arouse the public’s awareness about the existence of AD and the availability of treatment (e.g. Acetylcholine esterase inhibitors and vitamin E) in order to slow down the progression of disease. In agreement with previous findings¹³⁻¹⁵, the present study has demonstrated that women was more

likely to be referred late relative to men. Some authors have suggested that men are more likely to become aggressive and abusive¹⁶ and hence they would require an earlier referral. However, in our patients, the prevalence of non-cognitive symptoms and in particular aggressive behavior, among the two sexes did not differ significantly.

Disorientation occurred in 74.0% of subjects. Our study showed that disorientation increased with increasing severity of dementia as measured by CDR. Mild dementia with CDR 0.5 or 1.0 usually develops disorientation in time and/ or place initially. With progression of the disease, AD subjects will get disorientation in person as well. In advanced stage, over 50% of AD patients are characterized by complete disorientation in time, place and person. This sequence of loss of orientation from the sphere of time, to place, and lastly to person is consistent with the disease progression through different stages of AD¹⁷

Among our patients with disorientation in place, 65% had a past history of "getting lost in the street". This is an alarming figure because it may imply that a significant proportion of AD patients may get injury or even risk of death from complications like dehydration or other accidents when they are separated from their caregiver. Tragic news regarding the discovery of dead body of demented patients has been reported previously in Hong Kong¹⁸. Particular attention has to be given to this group to avoid endangerment after loss.

Executive aspects of cognition, such as planning, sequential organization, judgement and problem solving abilities are considered core functions. They are affected in early stage of AD¹⁹. 85% of our subjects had impaired executive function. This refers to the ability to appropriately handle the day-to-day challenges that occur at home, work or social situations. Most of the caregivers (>60%) reported that the demented subjects had difficulties in handling household emergency. This is important in management if we want to prevent accidents in this at-risk group.

Although non-cognitive symptoms were not the most common presenting complaints, they were present in the majority of the AD patients (83.3%) at initial visit. This finding was comparable to another published study which reported that more than 90% of AD patients had a non-cognitive symptom³. The number of domains of non-cognitive symptom per AD subject was less than that of cognitive symptoms in both sexes (1.6 vs 5.8; Table 1). Patients who have psychiatric or behavioural

symptoms predominantly were more likely referred to a Psychiatric Clinic or a psychogeriatrics unit for assessment. Of the non-cognitive symptoms, behavioral change was found to be the most common symptom. It was present in 60%. Behavioural symptoms that were stressful to the caregiver would include aggressive, disruptive/disturbing, and unsafe behaviours. These occurred in less than 12%. This figure varies between different studies. Verbal and physical aggression occurred in 17% to 51% of AD in overseas studies^{20, 21} while this was present in 3.1 and 6.3% in this study. Mega MS et al²² had found that the most common behavioral abnormality in AD was apathy (72%), followed by agitation (60%). These two behavioral changes were present in 3.1% and 10.4% of our AD patients respectively. Studies also varied widely in the reported prevalence of non-cognitive symptoms in AD. Different reports had different figures of prevalence for the different domains of non-cognitive symptoms. The reasons are multiple. Firstly, the distinction between cognitive and non-cognitive symptoms is often not very clear. Secondly, there is variability in the definitions of specific behaviors. Some studies report behaviors as occurring only when they are identified as problems, while others include them in prevalence estimates whenever they occur. Thirdly, different types of sampling may give rise to different prevalence figures. For example, behavioral problems are more commonly found in institutions than in the community.

Perceptual or psychotic symptoms are common in AD. It has been reported in overseas studies that delusions occurs in 11 to 73% of all AD, visual or auditory hallucinations in 3 to 67% and misidentification of persons or places in 5 to 30%²³. In the present study, these features were present in 48%, 10% and 3% respectively. In our study, AD patients with delusions were older than those without. An association was found between delusion and hallucination in our AD patients. This was consistent with findings of another study³, though another authors had reported no association of these two symptoms²².

Regarding mood changes, the most commonly reported symptom were depressive features, which occurred in 15% of the subjects. Significant depression was commonly reported in AD, occurring in 25% to 30% of the patients and depressive symptomatology is much more common. In our study, we had excluded patients who had major depression by DSM-IV criteria⁵. There was a low prevalence of anxiety in our study. Only 1% of the

subjects reported anxiety symptoms. This was in great contrast to overseas figure of 48% to 70%^{22, 24}. This low figure could be due to under-reporting from patients or caregiver, or that the interviewer has not asked for this symptom specifically or the difference in the definitions of anxiety used in the studies.

Limitations

This was a retrospective study. Hence, some symptoms that might be present at presentation or follow-up might not have been documented. This would contribute to under-estimation of prevalence of some symptoms. However, this was not very likely in our Memory Clinic, which employed a semi-structured format in the history taking and physical examination. The majority of the clinical features had been carefully documented with this format. Secondly, the subjects were from a Memory Clinic of a regional hospital and were not from a population sample. Thirdly, cognitively impaired patients from psychiatric or psychogeriatric services were not included. Therefore our subjects might not represent the all AD patients in the community. This possibly limited the generalization of our results to all AD patients. On the other hand, the diagnosis of AD might be inaccurate without careful assessment in general out-patient clinic. Our AD patients had been assessed with great details and the clinical diagnosis of probable AD were made in accordance to the NINCDS-ADRDA criteria which meant a diagnostic accuracy of at least 90%. The findings of our study therefore reflected quite accurately the symptomatology of AD in Hong Kong.

Conclusion

Clinical features and course of Alzheimer's Disease (AD) have been reported in Caucasian population. This is the first local study on the clinical features of Hong Kong Chinese AD patients in a Memory Clinic in Hong Kong. The presenting symptoms and clinical characteristics of AD patients are in agreement with those reported in the Caucasian group. On the average, AD patients present with poor short-term memory approximately 3.1 years after symptom onset and at the age of 77.3 years. The duration of illness at first visit is long compared to that in Caucasian AD patients. Poor awareness of early features of AD may be a reason. Future studies may investigate the impact of various AD treatments on the symptomatology and progression of disease among AD patients in Hong Kong.

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LEARNING POINTS

- 1. There was an interval of 3.1 years between symptom onset and first consultation. This may reduce the efficacy of potential treatment.**
- 2. Besides cognitive impairment, 83.3% of AD patients had non-cognitive symptoms.**
- 3. The commonest non-cognitive symptoms, in order of frequency, were behavioral changes, perceptual changes / psychotic symptoms, sleep changes and affective disorders.**

LISTEN TO YOUR PATIENT

A 78 years old residential inmate was regularly followed up at specialist clinics for her diabetes mellitus and asymptomatic ischemic heart disease.

She was put on nitrate, beta blocker, and oral hypoglycemic agents. She had repeated syncope in the past 18 months. Frequency of syncope increased over the past six months and she was repeatedly admitted into hospital. 24 hours Holter and echocardiogram were done twice, yet findings could not explain her problem. Nitrate was stepped up with presumed diagnosis of ischemic heart disease precipitating the syncope. Old aged home staff consulted CGAT for advice. Patient was asked to describe her symptom. She spontaneously flowed out that the syncope usually occurred in the morning while having her breakfast. There was usually some belching / bloating sensation

at the epigastrium, and syncope occurred seconds afterwards. Working diagnosis of deglutition syncope was made. Her nitrate was taken off. She was advised to eat slower and avoid hard food. Since then she had no recurrent syncope.

History taking among elderly is sometimes difficult. Yet it can be most revealing. Elderly commonly has multiple pathology. Investigations will be positive in many occasions, yet un-related to the presenting or underlying problems. History taking is most important in underpinning the diagnosis / problem in elderly.

Remember to allow time for patients to tell their stories and be a good listener.

Christopher Lum