Postgrad Med J (1992) **68**, 673 - 676

Clinical Reports

'Pseudo-Alzheimer's' and primary brain tumour

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Summary: Primary brain tumour may present in the elderly purely as a dementing illness before the onset or detection of sensorimotor neurological symptoms or signs. Although neurological examination may indicate no definite signs, close attention to accepted DSM-IIIR and NINCDS-ADRDA diagnostic criteria for primary degenerative dementia and 'probable' Alzheimer's disease respectively will suggest a process other than a degenerative one. This was the case in two patients with primary brain tumour presenting clinically with dementing illness similar to but distinct from Alzheimer's disease.

Introduction

Although Alzheimer's disease (AD) is the single most common cause of dementing illness in the elderly population, there are a number of causes of dementia other than AD which must be considered in this age group. The only wholly reliable test for AD is brain tissue pathological analysis; however in recent years clinical diagnostic criteria for AD have been published, that is, Diagnostic and Statistical Manual (3rd Rev.) (DSM-IIIR) criteria[1] for 'primary degenerative dementia' (Table I) and National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria[2] for 'probable AD' (Table II). On follow-up post-mortem pathological studies, the NINCDS-ADRDA criteria have been found to be 81-87% accurate.[3,4] Cognitive impairment is a well documented but uncommon isolated presentation of primary brain tumour. Because of the increasing prevalence of AD in the ageing population in general and in the over-75 age group in particular, in which there is an estimated dementia prevalence of 15-25%,[4] AD can be too readily diagnosed without due regard for the clinical diagnostic criteria. Primary brain tumour may behave clinically like AD, but the distinction is clearly demonstrated in the application of these criteria as in the following two cases.

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Accepted: 19 February 1992

Case 1

In December 1990, a 78 year old widow was referred by her general practitioner for assessment of a 3 month history of 'forgetfulness, confusion and disorientation in time and place: ?Alzheimer's disease.' It was evident from her daughter's collateral history that there had been a 3 month history of subacute onset of confusion and memory failure dating from the death of a close friend, and that this confusion had been associated with a grief reaction. Since that time, confusion had increased progressively. The patient herself complained of 'poor memory, especially names', 'feeling depressed' and of 'a muzzy feeling in the head'. There were no other specific symptoms. Her general health had been 'good' up to 3 months previously. The patient was not considered markely depressed, and she did not satisfy DSM-IIIR criteria for major depressive disorder. Eight years previously, she had suffered a skull fracture associated with loss of consciousness lasting 'several hours'. Computed tomography at that time indicated no gross intracranial structural lesion and she had no apparent cognitive problems arising from this event. She was taking no medications. There was no known family history of senile dementia or other psychiatric disorder.

On examination, she was alert and attentive. Her Mini-Mental State Examination[5] score was 16/30, suggesting a moderately severe cognitive disorder. She scored 1/18 on the Hachinski Ischaemic Index,[6] making multi-infarct disease a less likely cause for her dementia. On the Cornell Depression Scale[7] she scored 6/33 (normal). The DAT (Dementia Alzheimer Type) Inventory[8] score was 19/20, showing consistency with a diagnosis of AD. Her Clinical

Table I DSM-IIIR criteria for the diagnosis of 'Primary Degenerative Dementia' of the Alzheimer type (source: ref. 1)

DSM-IIIR criteria for primary degenerative dementia	*Patient 1*	*Patient 2*
A. Dementia		
1. Impairment of short-term and long-term memory	Yes	Yes
2. At least *one* of the following:	Yes	Yes
(a) impaired abstracting abilities		
(b) impaired judgement		
(c) other disturbances of intellectual function such as		
(i) aphasia		
(ii) apraxia		
(iii) agnosia		
(iv) constructional difficulty		
3. Cognitive disturbances sufficient to interfere with work or usual social activities or relationships with others	No	Yes
4. The patient is not delirious	Yes	Yes
5. Disorder not attributable to any other cause such as major depression	Yes	Yes
B. Insidious onset with progressive deteriorating course	No	No
C. Exclusion of other specific causes of dementia by history, physical examination, and laboratory tests	Yes	No

Table II NINCDS-ADRDA criteria for 'Probable DAT' (Dementia of the Alzheimer Type) (source: ref. 2)

NINCDS-ADRDA criteria for 'probable Alzheimer's'	*Patient 1*	*Patient 2*
1. Dementia established by standardized mental status questionnaire and confirmed by neuropsychological testing	Yes	Yes
2. Deficits in two or more areas of cognition	Yes	Yes
3. Progressive worsening of memory and other cognitive functions	Yes	Yes
4. No disturbance of consciousness (delirium)	Yes	Yes
5. Onset of illness between 40 and 90 years of age	Yes	Yes
6. No systemic or brain disorder to account for the progressive mental status changes	Yes	No
7. Diagnosis of DAT supported by the following:		
(a) progressive deterioration of specific skills such as language (aphasia), motor skills (apraxia), or perceptual regnition (agnosia)	Yes	No
(b) impaired activities of daily living and altered patterns of behaviour	No	Yes
(c) positive family history of similar disorders (particularly if DAT confirmed by neuropathological examination)	No	No
(d) Laboratory results such as:		
(i) normal CSF	N/A	N/A
(ii) normal or non-specific EEG slowing	N/A	N/A
(iii) cerebral atrophy on neuroimaging procedures with progression on serial testing	No	No

Dementia Rating (CDR)[9] was 1.0, indicating established but mild dementia. The patient was right-handed, and the main positive findings on examination were marked dysnomia and undressing/dressing dyspraxia. Examination of the cranial nerves, visual fields, fundi, gait and fine movement were all normal. Light touch, pinprick and vibration sensations were intact and symmetrical in the upper and lower limbs. A 4–5 cm pulsatile mass was detected in the epigastrium, consistent with abdominal aortic aneurysm.

Routine 'secondary dementia' screen sedimentation rate, haematological and biochemical profiles, serum thyroxine, serum B12 and red cell folate levels, plasma VDRL and TPHA, electrocardiogram and chest radiograph were all unremarkable. A check on the DSM-IIIR criteria for 'Primary Degenerative Dementia' and the NINCDS-ADRDA criteria for 'probable AD' showed a pattern which was divergent from a diagnosis of AD, in that there had been a relatively rapid onset and progression of the dementing process (see

Tables). Computed tomographic (CT) images of the brain showed a multilocular cystic mass in the left temporoparietal area slightly hypodense before contrast and which enhanced strongly after contrast. Brain biopsy showed glioblastoma multiforme. There was no evidence of AD on this biopsy. The patient was treated palliatively and died 3 months later.

Case 2

An 80 year old woman was referred for assessment of 'senile dementia', and with a view to arrangement of long-term care. The patient was very confused and unable to give a cogent history. A collateral history from a daughter-in-law indicated that the patient had become confused with steady deterioration which, 2 months prior to presentation, worsened rapidly with poorly comprehensive speech, wandering in the locality, increasing agitation and insomnia, and the onset of urinary incontinence. She has been prescribed mianserin and temazepam 2 months previously for increased agitation and 'early morning wakening' which was considered to signify agitated depression. However her confusion and agitation failed to improve on this treatment.

The main findings on physical examination were nominal and receptive dysphasia. Her Mini-Mental State Examination score was 4/30; however, the receptive dysphasia and dysnomia were considered to account for this low score to a large degree. Her Hachinski Ischaemic Scale score was 3/18, making multi-infarct disease unlikely and she was not considered clinically depressed. Her overall cognitive testing indicated moderately severe dementia. Cranial nerve examination was normal and there were no peripheral motor or sensory deficit detectable; plantar responses were downgoing. Other physical examination was unremarkable. Her dementia screen tests detected a serum B12 of 130 ng/l indicating possible deficiency.

Because of the relatively rapid progress of confusion over a 6 month period, greatly accelerated in the 2 months prior to presentation, and profound receptive dysphasia, rather than a true global cognitive dysfunction, the symptom complex was thought to be atypical of AD. Also, the clinical course had not been a steadily progressive one as is the usual pattern with AD. CT (Figure 1) showed an extensive, infiltrating left hemispheric lesion with surrounding oedema and a midline shift effect, suggestive of a high-grade malignant primary brain tumour. She was referred for a neurosurgical opinion with a view to brain biopsy. However, she deteriorated a short time after her CT scan, and remained too unwell to tolerate the biopsy procedure. She died 6 weeks after presentation. Consent for post-mortem was not obtained.

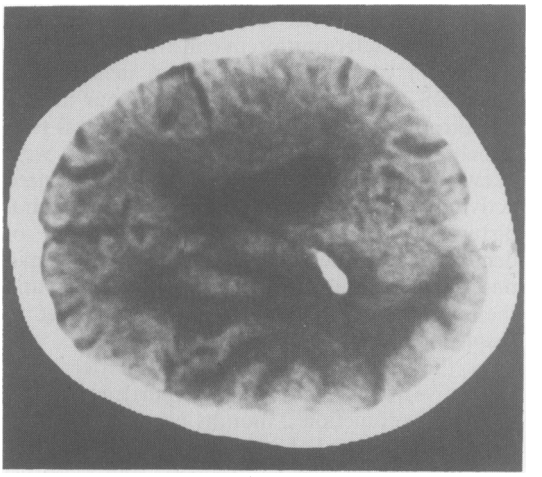

Figure 1 Control transaxial CT image of brain in case 2, showing an infiltrating lesion extending from the frontal to the occipital areas, with subtotal obliteration of the left lateral ventricle, marked white matter oedema and midline 'shift'.

Discussion

Although AD is the most common cause of dementia in the elderly population, important 'secondary' causes of dementia such as primary malignant brain tumour may easily be overlooked if a high index of suspicion is not maintained. Application of the DSM-IIIR criteria for 'Primary Degenerative Dementia' and the more specific NINCDS-ADRDA criteria for 'Probable' AD is important in the accurate diagnosis of primary degenerative dementia. A divergence from the 'typical' pattern of AD as judged by these criteria led to the correct diagnosis in these cases. In the first case, the progression of cognitive impairment had been more rapid than one would expect in AD. The patient had moderately severe cognitive failure at presentation, only 3 months after onset of symptoms. The history of cognitive impairment in AD patients is usually more insidious, present for more than 6 months in most cases. DSM-IIIR criteria were not satisfied in that the patient's daily activities remained normal as did her relationships with her family, and there was no behaviour disturbance. Her cognitive deficits were primarily of language, praxis and calculation – all dominant parietal lobe functions. Non-dominant parietal function as assessed by constructional praxis (intersecting pentagons test on the MMSE) was

intact. In patients with established AD one would expect some deterioration in constructional praxis in tandem with dominant parietal deficits. The NINCDS-ADRDA criteria, which favour the use of neurophysiological and neuroradiological tests to help confirm a diagnosis of 'probable AD', were likewise not supported by the absence of impaired activities of daily living, absence of behavioural disturbance and absence of family history of dementing disorders. Thus the relatively rapid onset, the focal nature of the cognitive deficit and the failure to satisfy AD diagnostic criteria led to suspicion of a focal space-occupying lesion.

In the second case, the initial pattern was suggestive of AD. However, the rapid deterioration in cognitive function 2 months prior to presentation was not typical of AD. This deterioration was characterized by marked dysnomia and receptive dysphasia indicating a left parietal lobe deficit. She also rapidly developed urinary incontinence and a marked behaviour disorder suggesting impaired frontal lobe function. She was not clinical delirious and the borderline B12 deficiency, low-dose psychotropics and 'depression' were not considered sufficient to explain the clinical picture. Thus, item 6 in the NINCDS-ADRDA criteria for AD (Table II) was not satisfied in this case with focal neurological features and possible B12 deficiency.

We believe that primary malignant brain tumour is an understated cause of 'secondary' dementia in the elderly. Brain tumour dementia may closely mimic the clinical pattern of AD as in these two cases. However attention to the details of the DSM-IIIR and NINCDS-ADRDA diagnostic criteria for AD will lead to less errors in dementia diagnosis. As these cases illustrate, patients presenting with a progressive dementing illness of less than 3 months' duration, or initial slow cognitive decline followed by a more rapid deterioration, or with a relatively isolated area of cognitive dysfunction, must be assumed to have focal pathology until proved otherwise.

References

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 3rd ed. rev. American Psychiatric Press, Washington, D.C., 1987.
2. McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D. & Stadlan, E.M. Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984, **34:** 939–944.
3. Tierney, M.C., Fisher, R.H., Lewis, A.J. *et al.* The NINCDS-ADRDA Work Group criteria for the clinical diagnosis of Alzheimer's disease: a clinicopathological study of 57 cases. *Neurology* 1988, **38:** 359–364.
4. Joachim, C.L., Morris, J.H. & Selkoe, D.J. Clinically diagnosed Alzheimer's disease: autopsy results in 150 cases. *Ann Neurol* 1988, **24:** 50–56.
5. Henderson, A.S. The epidemiology of Alzheimer's disease. *Br Med Bull* 1986, **42:** 3–10.
6. Folstein, M.F., Folstein, S.E. & McHugh, P.R. 'Mini-mental state': a practical method for grading the mental state of patients for the clinician. *J Psychiatr Res* 1975, **12:** 189–198.
7. Hachinski, V.C. Illiff, L.D., Zhilka, E. *et al.* Cerebral blood flow in dementia. *Arch Neurol* 1975, **32:** 632–637.
8. Alexopoulos, G.S., Abrams, R.C., Young, R.C. & Shamoian, C.A. Cornell scale for depression in dementia. *Biol Psychiatry* 1988, **23:** 271–284.
9. Hughes, C.P., Berg, L., Danziger, W.I., Coben, L.A. & Martin, R.L. A new clinical scale for the staging of dementia. *Br J Psychiatry* 1982, **140:** 566–572.