

Features of Potentially Reversible Dementia in Elderly Outpatients

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A standardized evaluation was carried out in two separate groups of patients with dementia to determine the features that characterize those with potentially reversible or treatable dementia. In both groups, Alzheimer's-type dementia was the most common diagnosis (65% and 70%); the most common cause of potentially reversible cognitive impairment was medication toxicity. In both groups, patients with potentially reversible dementia had a shorter duration of symptoms, less severe dementia and used more prescription drugs. Because of this association, these features may be considered risk factors but are not distinguishing or diagnostic features of patients with potentially reversible dementia. Other, previously undetected, treatable illnesses not often considered in the differential diagnosis of potentially reversible or treatable dementia were also prevalent in these patients.

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A careful, systematic evaluation has been recommended for all patients with possible dementia¹⁻⁸ because some of these patients do not have dementia but another illness mimicking dementia⁵ and because treatable diseases may cause potentially reversible dementia.^{6,9} Therefore, a precise diagnosis of the type of dementia and its causes is of critical importance for effective patient care.

We recently found¹⁰ that diagnostic outcomes of evaluating elderly outpatients with possible dementia differ somewhat from those reported in series containing primarily younger patients.^{1,2,5,9,11-15} We also observed that patients with potentially reversible dementia showed improvement; many patients, however, did not revert completely to normal as they frequently had coexistent irreversible dementia. Nonetheless, the reversible condition had clearly caused excess disability. Comparison of clinical features of patients with potentially reversible and irreversible dementia showed group differences that could alert physicians to patients with unnecessary disability¹⁰ if these differences were found in other groups of patients. In this paper we report the results of studies in another 200 patients to further define differences between patients with potentially reversible and those with

irreversible dementia and, in particular, to determine if these differences are common to two groups of patients.

Patients and Methods

Case-selection criteria, the diagnostic evaluation and diagnostic criteria have been described previously.¹⁰ In the first study, 107 patients were enrolled prospectively from 1978 to 1980¹⁰ and in the second 200 from 1980 to 1982.¹⁶

All patients in the 1980-1982 sample met the following four entry criteria: (1) older than 60 years; (2) having possible global cognitive impairment on the basis of the patient or family complaining of symptoms such as forgetfulness, confusion, inability to care for self and slow thinking; (3) having symptoms for at least three months' duration, and (4) willing to undergo diagnostic evaluation and to participate in follow-up for at least one year after evaluation. Informed consent was obtained from patients, family members or guardians. Of 209 consecutive patients referred for evaluation between 1980 and 1982, 200 satisfied the enrollment criteria. Of the nine exclusions, five were too young and four did not agree to a follow-up.

Patients in the 1978-1980 sample met the first three entry

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ABBREVIATIONS USED IN TEXT

ATD = Alzheimer's-type dementia
 DSM III = *Diagnostic and Statistical Manual of Mental Disorders*, third edition
 SD = standard deviation
 WAIS = Wechsler Adult Intelligence Scale

criteria. The diagnostic evaluation was done as part of their regular patient care. Consent to participate in follow-up was not obtained at the time of evaluation; follow-up information was sought for all patients one year after initial evaluation.

Evaluation

All patients were evaluated by an internist (E.B.L.) and a psychiatrist (B.V.R.). Internal medicine evaluations consisted of a complete history and a physical examination with formal neurologic examination including mental status testing. If possible, a family member or friend accompanied the patient to provide and verify details of the history. The Mini-mental State test¹⁷ and the Dementia Rating Scale¹⁸ were used for both groups. The psychiatric evaluation explored the problem areas as perceived by the patient and family and included detailed examination for dementia and depression using criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, third edition (DSM III).¹⁹

As part of the medical evaluation, all patients with possible dementia received a standard laboratory evaluation, including those tests recommended for evaluating dementia.^{3,6} This evaluation has been described in detail elsewhere.^{10,16}

Diagnosis

Diagnoses were based on the results of the original evaluation, diagnostic tests and a subsequent summary visit. In the 1980-1982 study group, diagnoses were reviewed and confirmed by a consensus group that reviewed the results of the history, physical and neurologic examinations; psychiatric evaluation; laboratory tests including computed tomographic scans; neuropsychologic tests—including the Wechsler Adult Intelligence Scale (WAIS), the Wechsler Memory Scale and Fuld Object-Recall tests—and a summary visit. The group included the internist who evaluated the patient, a psychiatrist, a psychologist, a neuropathologist-neurologist (S.M.S.) and the public health nurses (C.G.C., N.M.C.) who coordinated the evaluation and followed the patients.

Diagnostic criteria have been described in detail^{10,16} and included the research diagnostic criteria²⁰ for organic brain syndrome (impaired orientation and memory plus one of the following: impaired calculation, attention, abstraction or comprehension and no evidence of delirium or impairment of consciousness). In general, the consensus group based the diagnosis of Alzheimer's-type dementia (ATD) on the criteria proposed by Eisdorfer and Cohen.²¹ The guidelines were as follows:

- Loss of global cognitive function to a level that compromised a patient's ability to adapt to the environment;
- Progressive deterioration;
- Duration of at least six months;
- Absence of other illnesses causing dementia.

On mental status examination, the patient showed impairment in at least two of the following abilities: learning, attention, memory or orientation *plus* one of the following cognitive

skills: calculation, abstraction and judgment and comprehension. All patients with a diagnosis of ATD had evidence of memory loss. Other causes of dementing illness were either excluded or listed as contributing causes of dementia if the patient was judged to otherwise have typical Alzheimer's-type dementia. Patients having ATD who also had signs of Parkinson's disease (rigidity, coarse tremor, bradykinesia, shuffling gait and the like) were diagnosed as having ATD with Parkinson's disease. If signs of Parkinson's disease preceded dementia or were predominant, patients were classified as having Parkinson's disease causing dementia. A diagnosis of multi-infarct dementia was based on a Hachinski ischemic score greater than 7 points²² and excluded when the score was less than 4.²² The diagnosis of a major affective disorder was based on DSM III criteria.¹⁹

Patients were classified as having potentially reversible dementia by the internist (E.B.L.) at the summary visit in the 1978-1980 group and by the internist with the consensus group confirmation in the 1980-1982 group. This classification was based on the investigator's assessment that the disease diagnosed caused cognitive impairment and that the cognitive impairment was likely to improve with appropriate treatment.

Follow-up

All patients in the 1980-1982 study group were followed for at least 12 months after evaluation. Outcomes were based on the overall clinical assessment and the results of neuropsychological testing including the Mini-mental State test, the Dementia Rating Scale, the WAIS, the Wechsler Memory Scale and the Fuld Object-Recall test. Follow-up information in the 1978-1980 study group was sought between 1980 and 1982 and was based on physician evaluations, an audit of medical records and interviews with family members or acquaintances of the patients. Improvement or "reversibility" in cognitive function was based on the findings of neuropsychological tests and reports from family members and caregivers. Objective improvement was defined as at least a 2-point change in the Mini-mental State score, at least 1.5 points on the Dementia Rating Scale or at least 10 points on the WAIS or Wechsler Memory Scale. The duration of improvement had to be at least one month to be considered more than just a change due to normal variation unrelated to treatment.

Data Analysis

Data were analyzed using Student's *t* test, analysis of variance and the χ^2 test for statistical significance.²³

Results

Mean age (\pm standard deviation [SD]) in the 1978-1980 group was 75.8 ± 8.1 years and 75.7 ± 7.5 years in the 1980-1982 group. The demographic features have been reported in more detail elsewhere^{10,16} and were comparable in both groups. In the second group, 31% of patients were living alone at the time of evaluation, 44% were living with a spouse and 14% were living with another relative. Most patients (72%) lived in their own homes or apartments; 10% lived in unsupervised housing for the elderly, and only 8% were in nursing or convalescent homes at the time of evaluation. The mean duration of memory loss (as determined by asking a

family member or close acquaintance) was 42.0 months (SD = 31.1). The mean Mini-mental State score was 19.1 (SD = 7.9, range 0 to 30, with the higher score reflecting less impairment), indicating that the severity of dementia varied, with the average patient being moderately demented.

The distribution of dementia diagnoses is shown in Table 1. Alzheimer's-type dementia was the predominant diagnosis and was associated with Parkinson's disease in 7 patients (7%) in 1978-1980 and 12 patients (6%) in 1980-1982. Other "irreversible" dementias included progressive supranuclear palsy, posthypoxic encephalopathy, Parkinson's disease associated with dementia and posttraumatic encephalopathy, among others. It was not uncommon for patients to have more than one condition that was judged to contribute to dementia; thus, there are more diagnoses than patients in both groups. Furthermore, a mutually exclusive classification was often difficult. For example, one patient with confusion due to chronic alcohol intoxication could also have been classified as potentially "reversible" for Table 1, especially because the confusion cleared with total abstinence. In addition, 29 patients (27%) in the 1978-1980 group and 48 (24%) in the 1980-1982 group were diagnosed as having coexistent depression and dementia.

The causes of potentially reversible or treatable dementia are shown in Table 2. In both groups, the most common causes were medication side effects followed by hypothyroidism. An overlap between the causes listed in Table 2 also presents a problem of classification because some metabolic abnormalities were medication side effects, such as insulin-induced hypoglycemia.

Patients classified as having potentially reversible dementia were compared with patients with so-called irreversible dementia. Features that were significantly different in patients with potentially reversible dementia in the 1978-1980 study group (shorter duration, less severe dementia and the use of more prescription drugs) were also significantly different in the larger 1980-1982 study group (Table 3). Drugs used significantly more frequently in the reversible subgroup were sedative-hypnotics ($P < .01$) and antihypertensives. Two differences appeared in the 1980-1982 group comparisons between potentially reversible and irreversible subgroups that were not present in the 1978-1980 comparison; patients with potentially reversible dementia were more likely to have a history of falling (50% versus 25%, $P = .008$) and were more likely to show previously undetected abnormalities of the feet on physical examination, such as debilitating ingrown toenails (40% versus 14%, $P < .001$).

The investigation of patients in both groups resulted in the diagnosis of a surprisingly large number of other medical diseases. The 1978-1980 group had 48 patients who had 88

other previously unrecognized but treatable diseases diagnosed, all of which were judged to be important clinically because they contributed to dysfunction or caused symptoms.¹⁰ A total of 248 other medical diagnoses were made in the 124 patients in the second group.¹⁶ Table 4 shows some of the more common, previously unrecognized but treatable illnesses diagnosed in both groups of patients. The miscellaneous category includes illnesses like metastatic breast cancer, seborrheic dermatitis, acne rosacea, decubitus ulcers, other forms of medication toxicity, hypertension and transient ischemic attacks, among others.

In the 1978-1980 group, 13 patients with potentially reversible dementia were evaluated at least six months after the initial evaluation, and 11 had improvement in cognitive function. In eight of these patients, however, persistent worsening consistent with an Alzheimer's-type dementia eventually developed. In the 1980-1982 group, 18 of 30 patients with potentially reversible dementia showed persistent improvement at one-year follow-up. Of these 18 with persistent improvement, 7 did not meet the criteria for objective improvement documented on psychometric tests but were judged

TABLE 1.—Distribution of Dementia Diagnoses in 2 Study Groups

Diagnosis of Dementia	1978-1980 (N=107)		1980-1982 (N=200)	
	Number Diagnoses	Patients, Percent	Number Diagnoses	Patients, Percent
Alzheimer's-type dementia	74	69	149	75
Multi-infarct dementia	4	4	3	2
Alcohol-related dementia	4	4	8	4
Other "irreversible" dementia	3	3	18	9
Potentially "reversible" dementia	15	14	30	15
Not demented	15	14	15	8
Totals	115		223	

TABLE 2.—Causes of Potentially Reversible Dementia in 2 Study Groups

Cause of Dementia	1978-1980 (N=107)	1980-1982 (N=200)
	Patients, Number	Patients, Number
Medication side effect	5	19
Hypothyroidism or myxedema	4	6
Subdural hematoma	2	0
Other metabolic causes*	1	5
Other†	3	0
	15	30

*Causes included hyperparathyroidism (2), hypoglycemia (2) and hyponatremia (2). In both patients with hypoglycemia, this developed as a drug (insulin) side effect, and the use of diuretics undoubtedly contributed to hyponatremia in both patients with this metabolic cause.

†Transient ischemic attacks, rheumatoid vasculitis and manic-depressive illness associated with dementia syndromes.

TABLE 3.—Features of Reversible Dementia in 2 Groups of Patients

Features of Dementia	1978-1980			1980-1982		
	Reversible (N=15)	Irreversible (N=77)	P Value	Reversible (N=30)	Irreversible (N=155)	P Value
Duration, mo	28.5 ± 15.7*	51.7 ± 55.7	.01	33.7 ± 24.0	44.1 ± 32.4	.027
Severity of dementia†	20.0 ± 4.8	14.5 ± 7.8	.04	21.3 ± 8.0	16.3 ± 9.3	.001
Prescription drugs, number	2.5 ± 2.1	1.4 ± 1.4	.02	3.4 ± 2.1	1.7 ± 1.9	<.001

*Values expressed as mean ± standard deviation.
 †Mini-mental State score.

“clinically” improved by family members and research nurses. Likewise, 7 of the 30 patients with potentially reversible dementia in the 1980-1982 group experienced transient reversal of cognitive dysfunction that did not persist at the time of one-year follow-up.

Discussion

Dementia is an extremely common disorder in the elderly.²⁴ Until recently, most series of demented patients have focused on younger patients.^{1,2,5,9,11-15} This series confirms our original research¹⁰ and the finding of Fox and co-workers,²⁵ among others, that ATD is the most common cause of dementia in this population. A more surprising finding is the paucity of mass or destructive central nervous system disease causing dementia in elderly patients. This difference may be related to the long duration of dementia in outpatients and to the relative infrequency of such illnesses as normal-pressure hydrocephalus, brain tumor and subdural hematoma; these are all rare diseases, especially in ambulatory patients, and have probably been overrepresented in hospital-based series of patients with dementia.^{1,2,5,9,11-15,25} By contrast, conditions like Alzheimer’s disease, hypothyroidism and medication toxicity are more common, do not necessarily result in hospital admission and, thus, predominate in our series of patients. Because dementia is more prevalent in elderly outpatients, studies of this group of patients should be of particular value to clinicians. These epidemiologic factors need to be considered in evaluating patients and in formulating diagnostic strategies.

The validity of dementia diagnoses is important in a study focusing on diagnostic evaluation. We prospectively established diagnostic criteria using the available literature. In addition, review of each case by a multidisciplinary consensus group provided another important validation step, given the clinical nature of most diagnoses. Finally, each patient in the 1980-1982 group was followed systematically to ascertain if the clinical course validated our initial diagnosis. We are not aware of other studies of the diagnostic evaluation of dementia that have taken such a systematic and arduous approach to validate diagnostic results. Even though newer criteria for ATD have been published²⁶ and Hachinski’s criteria for multi-infarct dementia have been questioned,²⁷ our follow-up experience, including autopsy in more than 40 patients, has largely confirmed our clinical and consensus diagnoses¹⁶ and has not produced any diagnostic surprises.

That is, all patients classified as having Alzheimer’s-type dementia, multi-infarct dementia or another so-called organic dementia had a clinical course consistent with the original diagnosis. Autopsy findings invariably showed the presence of organic brain disease; preliminary analysis of autopsies done on patients with a clinical diagnosis of ATD indicates more than 90% autopsy confirmation of the diagnosis, although coexistent neuropathologic disease (Pick’s disease, Parkinson’s disease, multiple infarcts) was present in some cases (E. B. Larson, MD, unpublished observations, June 1986).

The consistency of features associated with potentially reversible dementia deserves comment. Freemon and Rudd also observed a shorter duration of symptoms in patients with reversible dementia.²⁸ Thus, all three studies that have systematically tried to determine features of so-called reversible dementia have reported this finding. Another consistent finding was that reversible dementia was characterized by less severe symptoms. Less severe dementia was also correlated with a short duration and these two features are, therefore, interrelated. The other feature of this group, that patients with reversible dementia used a greater number of medications, reflects the predominance of medication toxicity as a cause of potentially reversible dementia in this series. Future research to confirm this finding and to improve detection and prevention of drug toxicity in the elderly is important given the high frequency of medication use^{29,30} and medication toxicity³¹ in older patients. Falling was also correlated with medication toxicity and reversibility in this study; medications causing confusion, especially the common drugs responsible for medication toxicity in our series (antihypertensives and sedative-hypnotics) will also cause gait instability and postural hypotension. The curious finding that patients with reversible dementia had more abnormalities of their feet probably represents a marker of neglect and inability to care for self³² because the abnormalities were typically ingrown or overgrown toenails.

These features of potentially “reversible” dementia obviously do not create non-overlapping subgroups nor do they “make” any unique diagnoses; rather, they are associations seen in a group of patients with diverse diagnoses. Furthermore, the potentially reversible causes of dementia are often found in patients with coexistent irreversible dementia, like ATD.¹⁰ The diagnoses are usually suspected or made based on the recognition of clinical syndromes. If our findings are generalizable and confirmed by others, they may help clinicians detect these patients more effectively by heightening awareness and suspicion in patients with these features. The information could also be useful for persons working with confused geriatric patients if they wish to focus more diagnostic surveillance on high-risk subgroups of patients. We hope others will study these and related issues in different populations.

Finally, even though this article focuses on detecting potentially reversible or treatable dementia, we do not wish to imply that clinicians should direct their efforts only on detecting and treating these reversible illnesses. Most patients with reversible dementia do have improvement but only four patients from the two series returned to normal. Overall, 25% to 30% of patients in the two studies showed objective improvement in cognitive function during follow-up,^{10,16} in-

TABLE 4.—Some Previously Unrecognized But Treatable Illnesses Diagnosed in 307 Patients Evaluated for Dementia, 1978-1982

Treatable Illness	Patients, Number
Depression	87
Parkinson’s disease	23
Low folate level	19
Osteoarthritis, rheumatoid arthritis, other arthritis	14
Urinary tract infection	12
Chronic obstructive pulmonary disease	9
Congestive heart failure	7
Iron deficiency anemia	5
Peptic ulcer disease	4
Other miscellaneous diagnoses	44

cluding some patients with "irreversible dementia." Thus, improvement may occur in patients with irreversible dementia. The existence of a large burden of previously undetected other medical illnesses along with considerable social and psychological problems experienced by these patients indicates it is not wise to focus strictly on detecting potentially reversible dementia.¹⁰ We believe that an attitude or statement implying that "there is nothing (more) we can do for you" after a dementia evaluation is perhaps the most discouraging and damaging message a patient and family can receive and usually is a barrier to effective patient care. Nonetheless, one goal of effective patient care should be to detect reversible conditions causing and exacerbating dementia, as these conditions are clearly part of the substantial burden of excess disability in elderly patients with dementia.

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