Family Practice Grand Rounds

Senile Dementia

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DR. DEMETRIOS A. PAPADOPOULOS *(Clinical Assistant Professor, Department of Family Medicine)*: In 1978, 22 million people, or 10.9 percent of the United States population, were 65 years of age or older. It is estimated that by the year 2030, 51 million people, or 17 to 20 percent of the population, will make up this age group. Ten percent of persons over 65 years of age and 20 to 30 percent over 80 years of age have clinically important intellectual impairment. In 1980, $12 billion was spent to care for persons with chronic dementia, and a conservative estimate is that by the year 2030, $30 billion will be spent yearly.

The family physician must be skillful and knowledgeable in dealing with senile dementia. He or she must be capable of identifying the problem, competent in evaluating and determining the etiology of the problem, and, most important, able to devise a rational and cost-effective treatment program that deals with both the affected patient and members of the family. As our chairman, Dr. Hiram Curry, has aptly stated, "In caring for these persons, the energy requirement for care, the reduced quality of life, and the sorrow of loved ones are all beyond estimation."

Our Grand Rounds will focus on many aspects of senile dementia. We shall begin with a patient presentation and discussion of pathological findings. Next, we shall discuss the differential diagnosis and workup of dementia, and finally, we shall discuss the social assessment and family counseling aspects in the treatment of dementia.

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Patient Presentation

Mr. O. was a naval shipyard pipefitter who retired in his early fifties with a disability from a chronic back problem. Subsequently, he was divorced from his wife and lived what was described as "an existence isolated from his family." At 63 years of age he was admitted to the hospital for treatment of a vertebral compression fracture as a result of an automobile accident.

During the hospitalization, family members reported that over the previous five years there had been slowly evolving mental changes such as religious preoccupations and nocturnal hallucinations. Mr. O. had been responsible for four recent minor automobile accidents related to reckless driving. On several occasions he had become lost when driving in areas with which he had been familiar most of his life. There was no recent history of excessive alcohol intake. The family history was significant in that two sisters had psychiatric problems and "possible dementia" and an uncle "became senile at an early age."

Mental status examination revealed Mr. O. to be alert and jovial with a shallow affect. His speech rambled, but he was mainly organized and coherent. He could not recall the day or month and insisted it was the year 1991. He could not remember the length of the present hospitalization, nor could he recall the times of the recent automobile accidents. Remote memory was intact. Serial three's were performed well, and serial seven's were performed poorly. A suspicious atti-

Continued on page 204

Continued from page 201

tude was noted. Laboratory evaluations revealed a normal hemoglobin level, urinalysis, and electroencephalogram. Computerized tomography of the brain was normal except for "fullness of the ventricles." Consulting neurological and psychiatric evaluations revealed the impression of mild dementia, but he was declared competent to care for himself at home. After a reasonable recovery from the compression fracture, he was discharged from the hospital.

Two weeks after discharge, Mr. O. was readmitted to another hospital for diagnosis and treatment of "progressively worsening confusion, agitation, and violent behavior." Mental status examination at that time revealed disorientation to time, severely impaired recent memory, and impaired cognitive function. Agitation, paranoia, and hallucinations were noted. Laboratory evaluations during the admission, including complete blood count, SMA-22, serum B_{12} and folic acid levels, and thyroid function tests, were normal. He was treated with various psychotropic medications at different times including haloperidol, thioridazine, and loxapine succinate. After a 17-day hospitalization he was transferred to a local nursing home for continued care. The discharge diagnosis was senile dementia with a severe delusional syndrome.

On admission to the nursing home, Mr. O. was pleasant and cooperative. He was oriented to person, city, and year, but he did not know he was in a nursing home or why he was there. Short-term memory was impaired and stream of thought revealed some loose associations. Medications at that time included 90 mg per day of loxapine succinate in divided dosages, 1 mg of benztropine (Cogentin) twice a day, daily multiple vitamin, daily stool softener, and 500 mg of chloral hydrate at bedtime for sleeplessness. Observations by nursing home staff included periodic confusion, frequent drooling, limited social interaction, and occasional need for restraint to prevent wandering.

After 82 days in the nursing home, Mr. O. developed an acutely swollen and tender left leg. Phlebography revealed evidence of deep venous obstruction, and he was admitted to the local hospital for anticoagulant therapy. During this hospitalization he developed acute, bilateral, patchy pneumonia, which responded very slowly to penicillin and tobramycin. His mental status

Continued on page 206

Continued from page 204

declined markedly with this insult, and motor rigidity became significantly pronounced, despite discontinuation of his psychotropic medications.

Twenty-six days after admission his pneumonia and mental status improved, but he remained significantly more demented than on admission. Plans were then made for transfer back to the nursing home, but he subsequently sustained a large aspiration pneumonia, which led to a respiratory arrest and ventricular fibrillation. Although he was successfully resuscitated, he remained comatose and responsive only to deep pain. On the 48th hospital day he died from a respiratory arrest without further attempts at resuscitation. An autopsy was performed at the family's request. Dr. Powers will now present the pathological findings of the autopsy.

DR. JAMES POWERS *(Professor, Department of Pathology)*: The major findings at autopsy were largely restricted to the central nervous system. In both the gross and the microscopic examination of the brain, we noted the classic changes of Alzheimer's disease. In this disease one finds diffuse atrophy of the cerebral hemispheres, most prominently in the frontal lobes and in the medial portions of the temporal lobes. Microscopically, with silver staining, we recognized the two classical histopathologic changes, senile plaques and neurofibrillary degeneration.

The cause of Alzheimer's disease is still unknown, but possibilities have included aluminum toxicity, a slow viral illness, or an immunologic disorder. Studies during the last ten years have revealed a reduced concentration of the neuronal enzyme choline acetyltransferase. These have raised the treatment possibility of effectively increasing acetylcholine at the synapse, but clinical trials have not been promising. Five to 10 percent of patients with Alzheimer's disease have a positive family history for it.

Differential Diagnosis of Dementia

DR. PAPADOPOULOS: In discussing the differential diagnosis of dementia, it is useful to think in terms of the acute vs chronic nature of the illness. Acute dementias are referred to as acute confusional states or acute organic brain syndromes (Table 1). The characteristic feature is sudden onset, frequently associated with clouding

Table 1. Causes of Acute Confusional States[1]

Cause	Examples
Infection	Pneumonia Urinary tract Central nervous system Others
Circulatory	Congestive heart failure Dysrhythmia
Psychiatric	Depression Sensory deprivation
Neoplasia	Primary Metastatic
Drugs	Alcohol Psychotropics Cardiac
Vascular accidents	Myocardial infarction Stroke Pulmonary embolus Gangrene
Metabolic	Hypoglycemia, hypothyroidism Hepatic failure Uremia
Trauma	Subdural Concussion Intracerebral hemorrhage
Homeostatic failure	Dehydration Electrolyte disturbance Fecal impaction Postural hypotension
Anemia	B_{12} deficiency Folate deficiency Hemorrhage
Collagen-vascular	Giant cell arteritis Periarteritis

of consciousness, muddled thinking, and perceptual abnormalities. Approximately 25 percent of patients with acute dementias will die, and another 25 percent will go on to have a chronic dementing illness.

The five most common causes of acute confusional states are pneumonia, urinary tract infection, congestive heart failure, neoplasia, and depression. Drugs are a common cause, and one must think of both prescribed and nonprescribed medications. Some examples include major and minor tranquilizers, hypnotics, digitalis, diuretics, anti-inflammatory agents, oral hypoglycemic agents, and alcohol. Under the vascular accident category, it should be noted that in the elderly a myocardial infarction or stroke may present only as an acute confusional state.

Table 2. Causes of Chronic Brain Failure

Alcoholism
Alzheimer's dementia
B_{12} or folate deficiency
Cerebral tumor
Depression
Drug toxicity
Giant cell arteritis
Huntington's chorea
Hypercalcemia
Hypoglycemia
Hypothyroidism
Infection
Jakob-Creutzfeldt disease
Malnutrition
Multi-infarct dementia
Normal pressure hydrocephalus
Pick's disease
Trauma

The aging brain is very sensitive to its internal environment. Metabolic problems, such as hypoglycemia and thyroid, liver, or kidney diseases, can cause acute confusional states. Falls are very common in the elderly, and often trauma is not reported to the physician. Intracranial problems from trauma include subdural hematomas, concussions, and intracerebral hemorrhages. Impaired homeostasis commonly occurs with aging and may result in dehydration, electrolyte disturbances, postural hypotension, and fecal impaction from chronic constipation. The classical vitamin deficiency anemias, B_{12} and folate deficiency, are easily diagnosed and easily treated. Finally, collagen-vascular diseases should also be considered in the differential diagnosis.

Fifty to 60 percent of the chronic dementias fall in the category of senile dementia of the Alzheimer's type (Table 2). Approximately 10 percent are vascular or "multi-infarct" dementias. Unfortunately, only 10 to 20 percent of the dementias are reversible. One can see from the table that many of the disease states that cause chronic brain

Continued on page 210

Continued from page 207

failure can also cause acute confusional states.[2,3]

DR. POWERS: In the pathologic differential diagnosis for our patient presentation, we should consider Pick's disease, which is a rare neurodegenerative disease. We probably see Pick's disease once for every 100 times we see Alzheimer's disease. In comparison with Alzheimer's disease, a much more extensive atrophy of the gyri and widening of sulci are seen in Pick's disease, reflecting a tremendous amount of neuronal and astrocytic loss in the brain. The nerve cells in Pick's disease also accumulate within their cytoplasm material that is argyrophilic, or silver positive, in staining, but the material is completely different from that seen in Alzheimer's disease.

Another diagnostic possibility in our patient would be Jakob-Creutzfeldt disease. For 40 or more years this disease was considered a "neurodegenerative" disease until pioneering studies from the National Institutes of Health showed that it was transmissable. Brain tissue from an affected patient can be implanted into monkeys, and within a certain period of time, similar clinical and identical histopathologic findings can be induced in the animals. In this disease the cortical grey matter does sometimes show a thinning, but not so much of a loss compared with Alzheimer's or Pick's disease. The most noteworthy pathologic feature of the Jakob-Creutzfeldt disease patient is spongiform degeneration of neurons and astrocytes, which is felt to be dilatation of the cellular processes at the ultrastructural level. A certain degree of spongiform degeneration was noted in the patient presented today, and specimens of his brain have been sent to the National Institutes of Health laboratory for inoculation into laboratory animals.

In multi-infarct dementia, clinically one should have historical and neurologic findings consistent with what the name implies. Pathologically one notes subcortical degeneration of the white matter, which may manifest as patchy areas of myelin loss or may actually progress to evidence of frank infarction. Arteriosclerosis and arteriolosclerosis are also noted.

In the patient with normal-pressure hydrocephalus, there is marked dilatation of all ventricles with normal or nearly normal pressure of the cerebrospinal fluid. The problem is felt to be in the subarachnoid space where the cerebrospinal fluid is absorbed at the pacchionian granulations. There

seems to be an inability to absorb a sufficient amount of fluid; therefore, large accumulations are found within the ventricles or in the subarachnoid space. A surgical shunting procedure may reverse the clinical findings of dementia, ataxia, and incontinence.

Workup of Dementia

DR. PAPADOPOULOS: The diagnosis and cause of dementia are obtained from a complete history, the physical examination, and appropriate laboratory investigations. Because of the nature of the disease, the history is often not available from the patient and is usually obtained, therefore, from family members or friends and past medical records. One should differentiate an acute process from that which is chronic or of insidious onset. Alcohol and other drug information should be noted. History of trauma, previous psychiatric disease, pertinent medical problems, and a complete review of systems are also very important. The findings should be well documented on the medical record to compare with future changes.

The laboratory workup of dementia must be thorough. Routine laboratory tests should include a complete blood count; blood urea nitrogen; serum electrolytes, including calcium and phosphorous; and blood glucose. Liver function tests, chest x-ray examination, and electrocardiogram should also be routine. Specific tests that may pinpoint the cause include the folate level, vitamin B_{12} level, thyroid function tests, serologic tests for syphilis, serum drug levels, and screening for toxins. Finally, the physician is always faced with whether computerized tomography of the brain, an electroencephalogram, or a lumbar puncture should be performed. Many physicians believe that these should be done early in the workup of all persons with dementia. Others, however, prefer the simpler and less costly laboratory tests to establish the cause first. Certainly computerized tomography of the brain is very useful in pinpointing focal intracranial neurologic disease, but it should be noted that it is not useful in confirming the diagnosis of Alzheimer's disease.[4]

Social Assessment

DR. VINCENT BUCHINSKY *(Third-year resident in family practice)*: It is very important for the primary physician to undertake a social assessment of the patient with senile dementia. The first area to be assessed is the home environment. We need to determine whether the patient is able to ambulate well at home. For example, stairs may prevent patients from getting about, and small hallways or door openings may interfere with the use of a wheelchair. The toilet and bath facilities should be accessible and should have support bars for those who are unsteady. Adequate cooking facilities and good lighting are necessary. Furthermore, it should be determined whether there are accident hazards present in the home, such as loose rugs or open flames.

The assessment of domestic arrangements should include information about who does the cleaning, cooking, and shopping. The transportation assessment should determine whether the patient is able to drive or use public transportation. Assessment in self-care includes determining the abilities to feed, dress, and groom oneself without aid. Problems with bowel or bladder function are very common and should be carefully evaluated. The financial status assessment involves determining the sources and amount of income, as well as monthly bills and the degree of indebtedness. Most patients with senile dementia qualify for Medicare, and many qualify for Medicaid and other financial or medical assistance programs available in the community.

The final aspect of social assessment concerns the family, which includes three areas of consideration. First, one should identify the significant family members and where they live and determine who has primary responsibility for the patient. Second, family patterns of relating and coping should be assessed by observing interactions among various family members and determining how they are dealing with current problems. Finally, one should have knowledge of the family resources, including an understanding of how much time family members are willing to make available for the patient, how much financial support is available, and how much emotional support can be offered.

Counseling

It is ultimately desirable to maintain these patients in familiar surroundings, preferably in their

Continued on page 214

Continued from page 211

own homes, for as long as possible. As the patient develops progressive deterioration of memory, intellect, and self-care, he or she will increasingly need the supportive care of relatives and other care providers. The physician can play an important role as counselor.[5,6]

Information Giving

Physicians need to provide information to relatives about the progressive nature of Alzheimer's disease as well as the character changes, intellectual limitations, and behavioral problems caused by it. The response of family members can range from expecting too much to being overly protective of the patient. For example, the caregiver may expect the affected person to perform functions that he is no longer capable of doing, such as paying the bills. The opposite problem occurs when relatives wrongly assume that the patient's functioning must be restricted in all areas because he is no longer competent in a few areas.

Relatives can find it difficult to relate such character changes as emotional instability, impulsiveness, irritability, and lack of initiative to the disease process. Also, caretakers with inadequate information about the effects of the disease on intellectual function can become angry and hostile when the patient is seen as consciously choosing to have his symptoms. For example, they may angrily insist that the patient could remember better if he tried harder, or that she could stop asking the same question if she wanted to.

Behavior Management

The second area of counseling involves helping family members deal with disturbing types of behavior. Examples include potentially harmful behavior to self or others, poor self-care, restlessness, paranoid reactions, and sleep disturbances. Reactions of family members vary from feeling personally responsible for and inappropriately guilty about the behavioral problems to experiencing anger, resentment, and frustration.

Caregivers will often express concern about potentially dangerous behavior. Activities such as driving a car or wandering off will in fact need to be limited if the patient is at risk to himself and others. Unnecessary restriction of the individual,

however, will increase dependence and take away areas of competent functioning. Thus, it is wise to encourage the family to tolerate, when possible, harmless incompetencies or inefficiencies such as somewhat sloppy dressing or poor housekeeping.

Unfortunately, the presence of paranoid delusions is relatively common in patients with Alzheimer's disease. Patients can be quarrelsome with and suspicious of their relatives, and may complain of being mistreated. Because it is often futile to reason or argue with these patients, the family needs to be counseled to respond to what the patient may be feeling when the accusation is made. For example, instead of explaining that an object had not been stolen, but only misplaced, the family could respond by saying that it must be confusing or distressing to have had the belonging disappear. Often, it is necessary to use major tranquilizers such as haloperidol or thioridazine in the management of paranoid reactions.

Improving Functioning

The third area of physician counseling deals with improving the functioning and abilities of the demented patient. Simple organizational strategies such as keeping a calendar of appointments and activities or using notepads to write down reminders can sometimes help compensate for memory loss. Because these patients often do not cope well with unfamiliar surroundings, it is advisable to avoid unnecessary moves. Safe and effective functioning in the home can be enhanced by good lighting, support bars in the bathroom, the lack of stairs or narrow doors for the wheelchair bound, and elimination of accident hazards. Also, it is necessary to deal with specific problems such as urinary incontinence, for which a bedside commode and adult diapers can be useful.

Families can be counseled about making the most of the abilities of and interactions with relatives with Alzheimer's disease. Because the behavior of these patients can fluctuate from day to day, the family can be advised to take advantage of good periods of functioning to engage in activities with them. Also, because some areas of functioning, but not others, are affected, the family can be encouraged to make a list of mutually pleasant or satisfying activities in which the patient is able to participate.

The functioning of patients with Alzheimer's disease can be aided by enhancing sensory input. Sensory deprivation secondary to poor vision or partial deafness is common, can aggravate existing confusion and disorientation, and can result in paranoia, delusions, and hallucinations. Appropriate eyeglasses and hearing aids, if necessary, should be provided to these patients. Light should be bright for daytime functioning, and a light in the patient's room should be left on at night. It is also helpful to look directly at a partially deaf person and speak clearly and slowly in a moderately loud voice.

Community Resources

The fourth area of physician counseling involves the effective use of community resources. With such help it is often possible to maintain the impaired individual in the home and thus prevent institutionalization. Although the patient with senile dementia will often receive help from friends or relatives, the burden of providing care may eventually become too great for these caregivers to manage alone. The physician can help by determining the patient's needs and then assist in finding appropriate community services.

A wide variety of community resources can provide needed services to the impaired elderly person. Home health agencies provide such services as skilled nursing care, physical therapy, and medical supplies. Home-delivered meal programs can play an important role in helping maintain good nutrition. Transportation services can allow the individual to do his or her shopping or keep medical appointments. Day-care centers can be valuable when the relative with whom the patient lives works during the day but is still able to provide care at night and on weekends. Homemaker services can provide help in housework, shopping, meal preparation, and personal care.

Counseling of Relatives

The fifth area in which the physician can play a significant role is in counseling the families of patients. Families are often severely stressed by the demands of caring for their demented relatives at home and may report feelings of depression, isola-

tion, and hostility. The great amount of time required for this care curtails their own independent activities and social contacts and further stresses those who already have major responsibilities to their family or job. Also, caregivers are often further isolated socially because of embarrassment about the patient's labile behavior and because of fear that if they should leave home, the patient may wander or become injured. Another source of stress and conflict results from changes in family dynamics such as role reversals and reactivation of unresolved parent-child conflicts.

In addition to empathic counseling, the physician can aid these stressed caretakers by encouraging some form of intermittent respite. Arranging for a friend or homeworker to stay with the patient for even a half-day a week can be very beneficial for the homemaker who is then freed to leave the house. There may be times when an intermittent temporary admission to a nursing home or hospital is warranted. Providing respite to caretakers allows them to maintain social contacts and personal activities. Thus, institutionalization may often be prevented or delayed because they are then able to better handle the burden of caring for the patient at home.

A valuable means by which families of patients with Alzheimer's disease can obtain support and information is through their involvement in support groups with other caregivers.[7] In these groups, members develop a better understanding of the disease and thus develop more appropriate expectations and fewer feelings of guilt, anger, and frustration. Through their participation, group members are able to share difficult feelings such as hostility and depression, and are then provided with a sense of support and acceptance by others who experience similar feelings. The group also functions as a practical reservoir of personal experiences and knowledge to help members deal with the diverse behavioral, self-care, social, and financial problems with which they are faced. For many members, the group serves as a social outlet to alleviate some of their isolation and loneliness and to encourage more attention to their own personal needs and interests.

Medical Management

The final area I would like to discuss briefly is the role of the physician in enhancing the physical health and functioning of demented patients by treatment of physical disorders and by rational use of medications. The functioning of patients can be impaired by many physical disorders, ranging from congestive heart failure to urinary tract infections. The aggressive treatment of both chronic diseases and acute illnesses, therefore, can result in marked improvement of the patient's mental status. Because the elderly have an increased pharmacodynamic sensitivity to a wide variety of medications, it is important to review the patient's current medications and to monitor carefully the effects of any new medications that are introduced. This monitoring is particularly important for the tranquilizers and hypnotics that are sometimes necessary to help control the behavioral problems of restlessness, aggressive or paranoid behavior, and sleep disturbances.

Both vasodilators and drugs that improve cerebral metabolism have been used in the treatment of senile dementia. Despite more than 100 clinical trials of cerebral vasodilators in the treatment of dementias of old age over the past 25 years, there is no clearly proven effectiveness of this class of drugs. In another group of drugs being investigated are those that improve cerebral metabolism, of which ergoloid mesylate (Hydergine), a mixture of three ergot derivatives, is the most extensively studied. This drug and other similar drugs are said to improve neuronal cell metabolism and oxygen uptake. Although some of the double-blind control studies of Hydergine have shown variable improvement of some indices of mental function, significant defects in the design of many of these studies prevent us from drawing any firm conclusions. Most authors do not recommend using this medication routinely. However, a two-month therapeutic trial may be warranted in those patients with early dementia in whom small changes in cerebral metabolism may possibly result in significant functional improvement.

FAMILY PRACTICE RESIDENT: Many of these elderly people totally give up—they quit eating, and the family will demand that something be done for the patient. Do you ever use megadoses of vitamin B_{12} to stimulate the appetite, and, if so, do you get any response?

DR. PAPADOPOULOS: I personally do not use vitamin B_{12} shots, unless the vitamin defi-

Continued on page 218

Continued from page 216

ciency is present. I have not seen any evidence in the literature that vitamin B_{12} works any better than a placebo in the setting that you are referring to.[8] For me the issue of using Hydergine is the more common difficulty. I attempt to explain to the family that there is some literature that shows improvement with the drug.[9] I inform them of the high cost of the medication, and I then let them decide whether it will be used. Personally, I have not had much success using it. Has anyone in the audience had success with Hydergine?

FAMILY PHYSICIAN: I've tried Hydergine with geriatric patients in the nursing home, and I was disappointed with it. The family, again, was pressuring me to do something for the patient. If they did not object, I gave the patient small doses of wine. These patients became more active and happier. I have found it was a lot better than Hydergine.

FAMILY PRACTICE RESIDENT: What are the side effects of drugs like thioridazine (Mellaril) and haloperidol (Haldol)?

DR. PAPADOPOULOS: Although the toxicity of antipsychotic drugs is believed to be low, there are many neuropsychological adverse reactions that can occur, including sedation, paradoxical excitement, seizures, withdrawal reactions, dysphoric reactions, extrapyramidal effects, and tardive dyskinesia. Most of these, except tardive dyskinesia, can be controlled by reducing the dosage. It is important to emphasize that elderly patients require lower dosages than younger persons for a given desired therapeutic effect.[10]

References

1. Cape R: Aging: Its Complex Management. New York, Harper & Row, 1978
2. Task Force of the National Institute on Aging: Senility reconsidered: Treatment possibilities for mental impairment in the elderly. JAMA 244: 259, 1980
3. Wells CE: Diagnosis of dementia. Psychosomatics 20:517, 1979
4. Ford CV: Winter J: Computerized axial tomograms and dementia in elderly patients. J Gerontol 36:164, 1981
5. Zarit SH: The organic brain syndromes and family relationships. In Ragan PK (ed): Aging Parents. Los Angeles, University of Southern California Press, 1979
6. Kennie DC, Moore JT: Management of senile dementia. Am Fam Physician 22:105, 1980
7. Barnes RF, Saskind MA, Scott M, Murphy C: Problems of families caring for Alzheimer patients: Use of a support group. J Am Geriatr Soc 29:80, 1981
8. McCurdy PR: B_{12} shots. JAMA 229:703, 1974
9. Gaitz CM, Varner RV, Overall JE: Pharmacotherapy for organic brain syndrome in late life. Arch Gen Psychiatry 34:839, 1977
10. Inoue F: Adverse reactions of antipsychotic drugs. Drug Intell Clin Pharm 13:198, 1979