

Caso clinico

THE IMPORTANCE OF EARLY DIAGNOSIS OF ALZHEIMER'S DISEASE AND SPECIFIC TREATMENT OF ASSOCIATED DISEASES. CASE REPORT

N. SILVESTRI¹, G. CASTELLANO², A. DI PALMA³, M. SCOGNAMIGLIO³, F. CASERTA³

¹ Scuola di Specializzazione di Geriatria e Gerontologia Università degli Studi di Napoli Federico II.

² Dipartimento di Emergenza e Primo Soccorso Ulss 22 Bussolengo (Ve).

³ Unità Operativa Complessa Tutela della Salute dell'Anziano ASL Napoli 1 Centro.

Abstract

Alzheimer's disease develops in three stages: 1) pre-clinical Alzheimer's disease in which the patient is completely asymptomatic, but alterations are already present in the brain and in the cerebrospinal fluid ; 2) mild cognitive impairment due to Alzheimer's disease when patient have mild deficits in one or more cognitive domains which does not cause impaired ability to perform activities of daily living; 3) dementia due to Alzheimer's disease when impairment of memory, thinking, behavior compromise the performance of activities of daily living. Early diagnosis should be made with an accurate medical history, a battery of psychometric tests that assess more cognitive areas, the use of neuroimaging and the identification of any coexisting pathological conditions and their treatment. The diagnosis should be followed by a neuropsychological rehabilitation and drug medication as soon as possible. The clinical case described is an example of an early diagnosis can allow the patient with Alzheimer's disease long survival (17 years).

Keywords

Alzheimer, mild cognitive impairment, treatment.

In June 1997 a woman, E.P., of 72 years old came to geriatric assessment for memory disorders, accompanied by her husband. She had difficulty in remembering names, appointments, things to do and that created problems in the management of the home and in social relations.

Her schooling was 17 years of which 4 at the University of Medicine, and had always played the role of housewife.

The family history was positive for dementia (mother and sister).

In medical history: hypertension in treatment for several years with Quinapril 20 mg /day and Pott's disease.

Physical examination showed nothing of significant if not a functional limitation of the spine for Pott's disease, aortomiocardiosclerosis, signs of arthrosis in more districts and senile osteoporosis. Therefore it was considered appropriate to initiate therapy with bisphosphonates (Clodronic Acid), Calcium carbonate and Cholecalciferol.

The neurological examination was entirely negative. The laboratory tests were all normal, and MRI of the brain without contrast showed a moderate bilateral parietal atrophy.

We submitted her to psychometric tests using enlarged battery. She appeared alert and cooperative, oriented in space and time; speech was spontaneous, flowing, without anomie, nor neologisms, nor paraphrase, with morphological and correct syntax, good prosody, preserved understanding. The Mini Mental Status Examination (MMSE) score was 30/30, Geriatric Depression Scale score 5/30.

Deficit appeared to Rey Auditory Verbal Learning Test (score: 32/75 to immediate recall, and score: 6/15 to delayed recall); Cube Test and Clock Drawing Test were altered. The patient was autonomous in basic and instrumental activities of daily living (IADL 6/8, 6/6 ADL).

Based on all data collected, we made a diagnosis of "Mild Cognitive Impairment with constructional apraxia" and so decided to start therapy with Donepezil 5 mg/day. Following our instructions, she began neurocognitive rehabilitation with the support of her husband.

Was re-evaluated after a month of starting therapy and, as was well tolerated, we confirmed the same therapy.

The next check was nine months after the first visit and on that time the MMSE score was 30/30 and Rey Auditory Verbal Learning Test had improved (score: 40/75 to immediate recall, score: 8/15 to delayed recall). The patient continued to take Donepezil 5 mg/day.

Regularly she came to visit, accompanied by her husband, and in November 2000 showed initial signs of disorientation in time and worsening of amnesic disorders (MMSE score: 25/30, MMSE correct score: 23.3/30). Therefore for the first time she was diagnosed "Degenerative Dementia of probable Alzheimer's type" and was included in the protocol of the CRONOS project by increasing the dose of Donepezil to 10 mg/day given to her by National Health System.

The clinical situation was more or less stable in the time, with no adverse events to Donepezil, nor further deterioration in psychometric tests, until January 2002 when, as a result of an accidental fall, she procured a subcapital fracture of the right femur with meshed fragments and was treated with immobilization in bed. In fact she showed a worsening of cognitive status (to MMSE, in addition to disorientation and

memory disorders, presented also calculation and language deficits with circumlocutions and synonyms. MMSE score: 23/30, MMSE correct score: 21.3/30). She presented an initial no autonomy in instrumental activities of daily living (IADL 4/8, 6/6 ADL).

Over the years, the patient developed mild gradual deterioration of cognitive functions as well as some kind of internal medicine diseases such as dyslipidemia type II A treated with Lovastatin 20 mg/day and then ischemic heart disease with increase blood pressure treated with Carvedilol 25 mg/day.

In October 2004 she came to visit geriatric and showed deficits in the long term memory, total disorientation in time and space, ideomotor apraxia, acalculia, impairment of language in perceptive component, state of psychomotor agitation (MMSE score: 14/30, MMSE correct score: 12.3/30) and was now reliant in instrumental activities of daily living (IADL 2/8, 6/6 ADL). So we was added to existing treatment Memantine 10 mg/day.

Over time the disease continued its course and since 2007 we had noticed a significant deterioration because even her husband fell ill with Alzheimer's disease and so she stopped neurocognitive rehabilitation with his support. Later patient developed an anxious-depressive syndrome, a bilateral visual acuity deficit of central type and stabilized incontinence of the sphincters and therefore severely limited in the activities of everyday life. Also in 2011, following a further fall, she has fractured ulna of the left arm and was treated with immobilization of the limb.

On monitoring of June 2014, the clinical situational appeared stable, blood pressure and heart rate were normal (110/60 mmHg, 82 beats per minute), the pulse was regular, the situation hemodynamic balance. Psychometric tests were not administered, had kept the verbal production though but not congruent to the context, wanders only if accompanied. The patient was completely not self-sufficient in basic and instrumental activities of daily living (ADL 0/6, 0/8 IADL).

In July 2014, the patient had an episode of acute heart failure treated to home with diuretics i.v. (Furosemide 60 mg in 250 ml of NaCl 0.9%) and Nitrate transdermal patch without success as she died after about ten hours probably for acute pulmonary edema.

In 2011 the National Institute of Age and Alzheimer's Association established the new

criteria and the new guidelines for Alzheimer's disease (AD). A fundamental change compared to the old 1984 guidelines is the identification of three new stages of Alzheimer's disease: 1) pre-clinical Alzheimer's disease; 2) mild cognitive impairment (MCI) due to Alzheimer's disease; 3) dementia due to Alzheimer's disease (1-4).

In the pre-clinical phase of the MA the patient looks completely asymptomatic, but alterations are already present in the brain and in the cerebrospinal fluid. This step reflects the now common idea that the MA is starting to changes in the brain as early as 20 years before the onset of symptoms. Unfortunately the new criteria and guidelines do not establish the diagnostic criteria to define this stage.

The MCI stage due to Alzheimer's disease in the past was identified as the period of transition between physiological age-related cognitive changes and early changes of dementia. Individuals with MCI have mild deficits in one or more cognitive domains, often the memory, which does not cause impaired ability to perform activities of daily living, nor deterioration of the social and job performance in the absence of other medical conditions that may explain the disorder.

The estimated conversion rate of dementia varies enormously, in fact it goes from 10-15% per year (5-6) up to 20-50% in 2-3 years (7) according to the clinical criteria and neuropsychological evaluations more or less accurate used for the selection of patients (8,9). However, not all patients with MCI convert to dementia. Some studies, in fact, report that about 60% of these patients remain cognitively stable over a period of about 2-3 years (6, 10, 11). In other studies however it was determined that 40% of MCI subjects returned cognitively normal at follow up (12,13).

Among other cognitive decline, it is more likely in people with memory impairment (MCI amnesic) than those without memory involvement (not amnesic MCI) and patients suffering from a multiple-domain MCI compared to patients with amnesic MCI (14).

The stage dementia due to MA is characterized by impairment of memory, thinking, behavior that compromise the performance of activities of daily living. It is possible to distinguish a stage in mild, moderate and severe stage.

According to these new guidelines, we can say that the patient's case described before was seen for the first time when the disease was in the stage of mild cognitive impairment due to Alzhei-

mer's disease. The success of the long-term of disease (17 years) was definitely due to the diagnosis made at an early stage of the disease. This was possible, first of all, because the patient underwent a careful medical history, targeted to the search of family predisposition, exposure to risk factors and clinical conditions that could favor the onset of MA, and secondly, because the patient was administered an enlarged battery of psychometric tests. In fact, compared with a MMSE score within normal limits, some tests used to study different cognitive domains resulted in deficit (episodically memory-Rey test, planning-clock drawing test, constructive praxis-cube test). Also already brain MRI in 1997 showed alterations in cortical structure of the parietal lobes.

The long duration of the disease was also permitted by the excellent management of the associated pathologies that as in all elderly patients may create difficulties. An early diagnosis of MA has allowed the equally early treatment, although numerous studies and meta-analyses demonstrate that the use of acetylcholinesterase inhibitors are not useful in preventing the conversion of MCI to Alzheimer's disease (15-17). The patient immediately began to take Donepezil 5 mg/day paying totally pharmaceutical expenditure and only after the inclusion in the project CRONOS the medication was dispensed by the National Health System. Essential for maintaining long-cognitive function was also demonstrated neurocognitive therapy performed by the patient's husband until 2007.

In conclusion, this case report shows us that an early diagnosis can allow the patient with Alzheimer's disease long survival. Early diagnosis should be made with an accurate medical history, with the aid of a battery of psychometric tests that assess more cognitive areas, the use of neuroimaging (PET, SPECT, MRI, CT) and the identification of any coexisting pathological conditions and their treatment. The diagnosis should be followed by a neuropsychological rehabilitation and treatment with medication as soon as possible.

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Corrispondenza:

Dott. Francescosaverio Caserta
ASL Napoli 1 Centro - Dipartimento delle Fragilità
f.caserta@libero.it