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Enfermedad de Alzheimer: reporte de caso

Alzheimer's disease: case report

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Palabras claves:
Enfermedad de Alzheimer; Disfunción Cognitiva; Trastorno Depresivo leve; Memoria.

Resumen

Introducción: La enfermedad de Alzheimer es un trastorno neurodegenerativo progresivo con cambios neuropatológicos característicos, es la forma más común de demencia. como un diagnóstico definitivo requiere un examen neuropatológico, se han establecido criterios clínicos para el diagnóstico de una probable enfermedad de Alzheimer, su prevalencia aumentará considerablemente en los próximos años, al ritmo del aumento de la proporción de personas mayores, las medidas para mitigar el riesgo en la mediana edad pueden potencialmente prevenir o posponer hasta el 40 % de los casos de demencia. **Objetivo:** Determinar el manejo y terapéutica de la enfermedad de Alzheimer en un caso clínico con el fin de establecer elementos novedosos e instructivos de la enfermedad. **Metodología:** estudio de caso clínico de tipo descriptivo, retrospectivo. La técnica empleada para la recolección de la información del caso será mediante la revisión de historia clínica y para la descripción de la patología será mediante la recopilación de artículos extraídos de bases de datos reconocidas como: Scopus, PorQuest, Pubmed, web of science, lilacs. Como criterio de inclusión: artículos publicados en los últimos 5 años, en español e inglés. El proceso ético legal se cumple con la firma del consentimiento del paciente. **Resultados:** paciente femenino de 40 años, que presenta sintomatología importante neuropsicológica, mediante exámenes de extensión catalogan como cuadro de Alzheimer moderado, con MOCCA 6/30, se implementó el tratamiento multidisciplinario y farmacológico con rivastigmina, sertralina y memantina, con posterior mejoría de MOCCA 11/30, y luego a 17/30, evidenciando una evolución clínica favorable. **Conclusión:** un diagnóstico preciso, mediante una adecuada historia clínica, en donde recabe los factores de riesgo es vital para aproximarse al diagnóstico, posterior a ello debe ser ubicado en su nivel de gravedad mediante estudios complementarios, finalmente, si el paciente recibe un abordaje multidisciplinario, tendrá una evolución clínica favorable, mejorando la calidad de vida del paciente como de su familia. **Área de estudio general:** medicina. **Área de estudio específica:** cardiología. **Tipo de estudio:** Casos clínicos.

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Keywords:
Alzheimer's disease; Cognitive dysfunction; Mild depressive disorder; Memory.

Abstract

Introduction: Alzheimer's disease is a progressive neurodegenerative disorder with characteristic neuropathological changes, it is the most common form of dementia.As a definitive diagnosis requires neuropathological examination, clinical criteria have been established for the diagnosis of probable Alzheimer's disease, its prevalence will increase considerably in the coming years, at the rate of increase in the proportion of older people, measures to mitigate risk in middle age can potentially prevent or postpone up to 40% of dementia cases. Objective: To determine the management and therapeutics of Alzheimer's disease in a clinical case to establish novel and instructive elements of the disease. Methodology: descriptive, retrospective clinical case study. The technique used for the collection of the information of the case will be through the review of clinical history and for the description of the pathology will be through the compilation of articles extracted from recognized databases such as: Scopus, PorQuest, Pubmed, web of science , lilacs. Inclusion criteria: articles published in the last 5 years, in Spanish and English. The legal ethical process is fulfilled with the patient's consent signature. Results: 40-year-old female patient, presenting significant neuropsychological symptoms, classified by subsequent extension tests as moderate Alzheimer's disease, with MOCCA 6/30, multidisciplinary and pharmacological treatment was implemented with rivastigmine, sertraline and memantine, with improvement of MOCCA 11/ 30, and then to 17/30, showing a favorable clinical evolution. Conclusion: an accurate diagnosis, by means of an adequate clinical history, where the risk factors are collected, is vital to approach the diagnosis, after which the patient should be placed at his level of severity by means of complementary studies, finally, if the patient receives a multidisciplinary approach, he will have a favorable clinical evolution, improving the quality of life of the patient and his family.

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Introduction

The increase in the frequency of dementia makes it important to recognize the factors involved, both genetic and environmental. It is estimated that by 2030 there will be a 35% increase in the number of individuals suffering from dementia, and this figure will triple by 2050 (1). The purpose of this clinical case report is to detail the situation of a patient suffering from Alzheimer's disease, for which the clinical, laboratory and therapeutic data of the patient were described. The patient presented some risk factors, and important clinical features with which she was diagnosed with this clinical picture, a treatment scheme focused on the phase in which she was found was applied, evidencing a satisfactory evolution (2).

Statistical projections for 2020 show considerably higher rates in developing nations with a young population than in Europe or the United States (3, 4). Less than one person in every 4,000 people under 50 years of age suffers from this disease, and factors such as demographics, changes in lifestyle, the profile of vascular diseases and the variety of diagnostic methods and criteria alter the statistical figures (5, 6).

It is crucial to identify the elements, whether of genetic or environmental origin, that are related to the increase in the frequency of dementia. It is estimated that by 2030 there will be a 35% increase in the number of individuals with dementia, and it is expected to triple by 2050 (7). According to the World Alzheimer's Report, the prevalence of Alzheimer's dementia doubles every 5 years in people over 65 years of age. In 2022, it is estimated that 6.5 million Americans aged 65 and older were living with this disease, of these 73% were over 75 years of age, at least two-thirds are women, the black race is almost twice as likely to suffer from this pathology, as well as Hispanics are 1.5 times more susceptible to suffer from dementia (8).

Over the past century since the original publication of Alzheimer's, we have witnessed an explosion of work in the neuropsychology of dementia, and we still have much work to complete. Borrowing from another prominent psychologist who discussed his perspective on better understanding schizophrenia nearly 2 decades ago, Irving Gottesman pointedly suggested that no discipline committed to understanding any of the major disorders has a monopoly on the amounts of uncertainty that remain for present and future generations of researchers (9). By joining forces across disciplines and gathering the most certain and important facts, researchers can launch new initiatives never imagined, such an effort will be necessary to solve the complex puzzle about Alzheimer's (10).

It refers to a common mental problem in people over 65 years of age, which increases a lot and needs to be detected in time through a good medical evaluation, physical examination and additional tests (11). Alzheimer's is a very complicated brain disease that gets worse over time. It is a major health problem today, despite the advances in

research on this disease, the main cause is still unknown, but the relationship with more than one environmental factor is known and there is no cure despite the available treatments (12).

In Ecuador there is no precise data on how many people have Alzheimer's, but a study in Cuenca indicated that there are at least 24 cases per 1000 older adults and of these 42.84% suffered from AD (Alzheimer's disease) with an age between 85 to 90 years and predominantly in women (13). There are two known and histopathologically evidenced alterations on which the characteristic progressive symptoms of this pathology are based. The presence of accumulation of neurofibrillary tangles, dystrophic neurites, amyloid plaques, among others; also called positive lesions. Cerebral atrophy marked by loss of neural mass and synaptic function is known as negative lesion (14).

Neuropsychology has been very important in identifying how mental abilities change in Alzheimer's disease and other similar disorders. This has helped to better diagnose Alzheimer's disease and distinguish it from other memory problems, to detect mild changes in thinking in the early stages of the disease, and to follow how the disease progresses as a person ages. New advances in creating biological signals to detect Alzheimer's disease will change this role. In the future, doctors and scientists will need to use different biological signals to discover the neurological causes of mental changes in a person and to detect problems in the brain before they affect the mind (15).

Methodology

This article presents a descriptive, retrospective clinical case report with a bibliographic review describing the disease sinoatrial nodal block. To collect information on the case, the clinical history was verified and analyzed. Regarding the writing, the Vancouver style was used to reference; for the description of the pathology, the structure was applied: definition of the pathology, pathophysiology, risk factors, diagnosis, prognosis, signs and symptoms, consequences, nursing care plan and medical treatment. For the description of the pathology, the work was done through the collection of articles extracted from recognized databases such as: Scopus, Porquest, PubMed, Web of Science, Lilacs, etc.

A systematization of the clinical case information was carried out. The data was obtained according to the patient's clinical history (secondary database). To obtain the information, the informed consent was requested and the following structure was taken into account in the writing: reason for consultation, current illness of the patient upon admission, diagnostic impression (IDX), personal history, family history, medications commonly used by the patient, physical examination, initial laboratory tests taken from the patient, therapeutic management plan, complementary examinations, outcome (improvement, lack of response, or death).

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In the last part, a discussion and synthesis of knowledge was carried out on the particularities that holistically affect the patient's outcome. Finally, the data obtained were compared with those from other investigations in order to structure the clinical case article in the discussion.

Results

An elderly patient comes to the doctor's office with her daughter, who reports that she has memory loss and episodes of depression. The patient has slow thinking, and sometimes she loses her mind completely. She also mentions that she had a complicated childhood, where her mother treated her children very badly. During the Covid 19 pandemic, she developed major depression, having to resort to psychological therapy, under the diagnosis of Alzheimer's. In her initial assessment, a score of 6/30 is evident according to the MOCCA scale, cognitive behavioral and pharmacological treatment is started with rivastigmine, sertraline and memantine.

Additional tests showed normal blood, electrolyte, liver, thyroid, glucose and urine results, metabolic profile was hypercholesterolemia, and renal profile was normal; MRI showed temporal atrophy and decreased hippocampal size, with predominance on the left side (Figures 1 and 2).

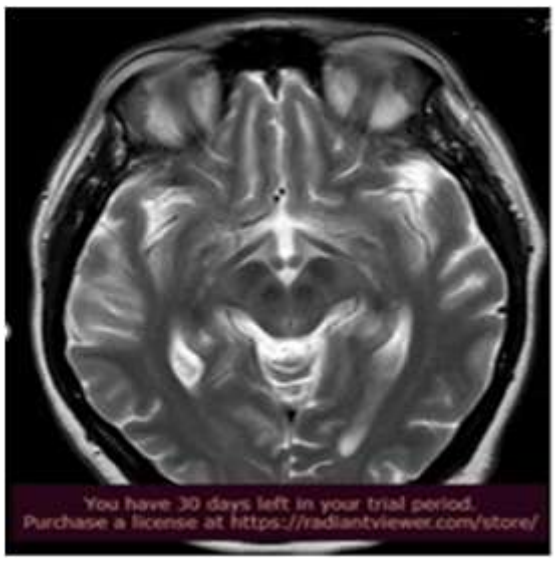

Figure2.-*Axial section T2 sequence*

Description 1.-*The Sylvian fissures and subarachnoid sulci are deep, note the hippocampi, which are thinned and have slight hyperintensity.*

Figure1.-*Sagittal section T1 sequence*

Description 2.-*marked decrease in overall brain volume, with deep subarachnoid sulci.*

Later, in his second psychiatric control, a slight clinical improvement is evident, the assessment shows the patient with bradypsychia, MOCCA with a score of 11/30, in the neuropsychological test executive functions are reported with severe alteration in

processing speed, cognitive flexibility, planning, problem solving and reasoning; In addition, severe cognitive impairment is observed, low working memory, Weschler memory scale 3, considered very low and very inferior in all its items; extremely low executive level, very low Luria test, ADAS test 27 thus confirming a moderately severe early-onset Alzheimer's disease dementia, compromising his daily life tasks, becoming semi-dependent.

Her progress has shown adequate rehabilitation, with an improvement in her memory work; she has become independent in many of the assigned tasks; she has stabilized emotionally, and has not even had any relapses for 15 days when she was told to stop taking the medication; she sleeps adequately; her MOCCA classification score is 17/30; in the 10 months of follow-up, the patient is stable, performs all her daily activities independently, however, she maintains mild apraxia, and integrates effectively into her social and family environment.

Discussion

Alzheimer's is the leading cause of memory loss worldwide. The number of cases will increase greatly in the coming years as more elderly people become older. At this time, there is no disease-changing treatment available. Risk-avoiding actions in midlife can help prevent or delay about 40% of dementia cases in a group of people (16, 17). In this case, it can be seen that it is important to follow the treatment with medications and other recommendations, it has been of great help in avoiding flare-ups or complications.

Kvello-Alme et al. (18), in their study explain that, dementia is a problem caused by diseases that affect the ability to think, behavioral alteration and poor self-care. Age is the main factor that increases the risk of dementia, in fact our patient presents this risk factor. The elderly usually have multifactorial causes of dementia due to comorbidity. Among the younger, mixed pathology is less common. Approximately 2% to 5% of those who develop dementia develop the condition before the age of 65 (18). Livingston et al. (19), in their research indicate that, in approximately 40% of cases, the risk increases due to potentially modifiable conditions such as low educational level, hypertension, obesity, reduced hearing, depression, diabetes, reduced physical activity, smoking and social isolation (19).

According to McKhann et al. (20), in the case of Alzheimer's disease (AD), there is a progressive emergence of signs linked to the decrease of cortical capacities. From a clinical point of view, two types of manifestations of the disease can be identified: the amnestic variant and the non-amnestic variant (20). In its amnestic manifestation, the disorder begins with a decrease in the ability to remember recent events or dialogues (episodic memory) and difficulties in locating oneself in time. As time passes, signs such as a decrease in the ability to understand, reason, think and communicate appear. In its

non-amnestic presentation, the disease begins with alterations in behavior, sadness, speech disorders, disorientation or visual complications. In the case of our patient, it is observed that she presents the amnestic variant, since she has shown bradypsychia (20).

Strand et al. (21) indicate that, over time, everyone develops a global cognitive deterioration, various behavioral and psychological symptoms, and presents a notable decrease in their life expectancy in contrast to other individuals of the same age, a situation that has not been confirmed in our patient since she is still alive (21). In their research, Bertram et al. (22) indicates that most cases are isolated, that is, they have no identified family history. According to Kern et al. (23), the APOE-ε4 genotype is the allele with the highest risk probability for suffering from the disease and is present in approximately 15% of the population in the Nordic region (23). Scheltens et al. (31) states that hereditary Alzheimer's disease that manifests at early ages due to mutations in the amyloid precursor protein (APP), presenilin-1 (PSEN1) or presenilin-2 (PSEN2) is rare (24, 25).

According to Lukiw et al. (24), in the clinical setting, the diagnosis of Alzheimer's disease is established from the characteristic symptoms and the evolution of the disease, and this is precisely the initial approach that was given to our patient, by evaluating everything collected in the clinical history. The development of new diagnostic biomarkers has increased the biological understanding of the disease, but has also made visible that there is often a mixed pathology (24). Research to develop new diagnostic biomarkers has been intense in recent decades in areas such as genetics, epigenetics, blood, fluid in the brain and spinal cord, and urine. In addition, advanced structural and functional imaging is being investigated (24).

The Helsedirektoratet (25) states in its research that, the detection of dementia is based on a mixture of data collected from the clinical history (also from relatives), presentation of symptoms, cognitive tests, somatic examination and structural and functional examinations of the brain. In our patient, CT studies were even performed to determine organic damage (25). Nasjonal et al, comment that, the evaluation tools and the guidelines for their use in both the basic and extended evaluation should be used for a better comprehensive approach (26).

According to Jack et al. (27) and his team, abnormal processes in the brain may begin 10 to 20 years before symptoms become apparent. Thanks to the creation of innovative biomarkers, it is possible to identify transformations related to Alzheimer's disease at a stage when no symptoms are present (27). The disease begins with the formation and extracellular deposition of insoluble amyloid plaques, which is what was found in the patient's CT scan, deposits of important amyloid matter. Intracellularly, tau proteins are phosphorylated, resulting in the formation of neurofibrillary tangles. Neurons are damaged, the immune system is activated, and vascular changes occur. Receptors in nerve

synapses are damaged, and the production of several neurotransmitter substances is reduced (24).

Jansen et al. (28) indicate that it is possible to quantify the levels of soluble amyloid, phosphorylated tau and total tau in the cerebrospinal fluid for use in diagnosis. There is an inverse relationship between cerebrospinal fluid amyloid and amyloid plaques in the brain organ. In individuals suffering from Alzheimer's and in those who are APOE-ε4 carriers, a decrease in soluble amyloid levels is observed, but they also decrease somewhat with age. In our patient, cerebrospinal fluid studies were not chosen, which is an important consideration to take into account for future cases (28).

Schoonenboom (29) explains that people suffering from Lewy body dementia, vascular dementia and frontotemporal dementia might also present slightly lower levels of amyloid (29). Total-tau is a non-specific marker of neuronal damage and is increased in many conditions. Phosphorylated tau, on the other hand, is considered specific to AD (28, 31). When interpreting the responses of dementia markers, one should not emphasize individual results, but rather view them in context. At least two out of three markers must be pathological when a diagnosis of Alzheimer's disease is made, this marker was not possible to request from our patient due to the lack of such input (28, 31).

Scheltens et al. (31) explains that brain changes begin in most people in the entorhinal cortex. In magnetic resonance imaging (MRI) of the brain (possibly computed tomography (CT) if there is a contraindication for an MRI examination), in classic cases atrophy of the hippocampus in the medial temporal lobes can be observed, classified from 0 (no atrophy) to 4 (pronounced atrophy); in our patient the atrophy was grade 2, due to the accentuated sulci observed in the CT scan (31). It is feasible to use the PET imaging technique with fluorine-18-labeled FDG to perform CT scans, which measures metabolic activity in the brain, especially when the MRI findings are less pronounced and there is no certainty about the diagnosis (31).

Amyloid PET with flutemetamol may be considered when spinal tap is not recommended. This test detects amyloid deposits in the cortex, and this is the protocol followed in our patient, but it was a simple CT scan. It is essential to consider that amyloid accumulation is common as we age, therefore, the results must be interpreted taking into account the patient's age and clinical situation (21). The APOE-ε4 genotype has a reduced penetrance, so this marker cannot be used at an individual level. Therefore, the use of genotyping in medical care is not advised. Genetic analysis is available and can be considered in cases of familial dementia accumulation.

Ossenkoppele et al. (32) mention that various 18F compounds have been created to identify tau-related Alzheimer's disease, however, PET technology for tau is not currently available in Norway. Research has found that PET-tau is more specific for Alzheimer's

disease than CSF markers and PET-amyloid (32). Palmqvist et al. (33) say that other markers in cerebrospinal fluid are also being investigated. Cullen et al. (34) further say that blood-based diagnostic tests would increase availability and reduce costs. Currently there are no blood markers with good validity, and these relevant markers are not yet available in our setting (34).

The pharmacological treatment available today in the Western world relieves symptoms with individual, moderate and limited-duration effects, in fact, our patient received rivastigmine, sertraline and memantine. In Norway, there are two distinct sets of drugs available: those that block cholinesterase and memantine, a non-competitive NMDA receptor antagonist. The national professional guideline on dementia recommends that all people with a mild to moderate degree of dementia be treated with a cholinesterase inhibitor, as our patient was (14).

Memantine is only recommended when cholinesterase inhibitors are not tolerated or have no effect in advanced AD dementia, but in our case it was considered as the onset was initially severe (14). Livingston G, comments that, the three cholinesterase inhibitors, rivastigmine, donepezil and galantamine, are considered to have similar clinical effects, but somewhat different side effect profiles (35). Birks J., says that, the effect in advanced dementia is more uncertain (36). According to Tan CC, it is also noted that cholinesterase inhibitors help to stabilize or decrease impairments in cognition, behavior and general functioning (ADL) (37). Tan ECK, says that, they also have some effect on visual hallucinations, especially in individuals suffering from dementia with Lewy bodies (38).

Common side effects include gastrointestinal disturbances (diarrhea, nausea and vomiting), and dizziness, headaches and sleep problems, including nightmares, are common; our patient did not report any of these side effects. As cholinesterase inhibitors can cause bradycardia, caution should be used in people with cardiac conduction disorders or when using other drugs that affect cardiac conduction (e.g. beta-blockers). Memantine inhibits the effect of glutamate by acting antagonistically on the NMDA receptor. The indication is moderate to severe AD dementia (38).

The development of innovative medicines can be classified into two categories: disease-altering drugs and palliative treatments that enhance cognition and behavioral and psychological symptoms (36). The development of innovative disease-modifying drugs has sought to transform the presence of amyloid or tau into the pathology (38). Most trials have aimed to prevent the formation of amyloid plaques (β-secretase inhibitors), counteract aggregation or enhance the breakdown of amyloid (anti-amyloid immunotherapy), and prevent phosphorylation of tau (anti-tau immunotherapy). Currently, five drugs are in the trial phase, but so far none have been able to document a safe clinical effect, however, it was used in our patient.

Both patients and their relatives are demanding the development of new drugs against Alzheimer's disease. The long early stage of Alzheimer's disease, on the other hand, makes the development of new drugs ethically demanding. Disease-modifying drugs should be started at a time when there are no or few symptoms in the context of changes detected by biomarkers, possibly many years before symptoms had developed, in this sense, our patient did not have the possibility to undergo such tests (36).

Various health promotion strategies have been proposed with the aim of reducing the possibility of suffering from dementia (19, 37). In line with the reduction of the personal risk of suffering from cardiovascular diseases, the potential positive influence of physical exercise, prevention of head trauma, quitting smoking, a healthy diet, moderate alcohol intake, weight and blood pressure management, adequate control of diabetes and resources to improve hearing loss are highlighted. In addition, we know that education increases cognitive reserve and, therefore, protects against cognitive decline; in our patient, physical exercise and recreational activities were dosed (35).

In the middle phase of Alzheimer's, patients may experience difficulties moving independently. They may have problems with balance and coordination, which increases the risk of falls. Gait may become slow and unsteady, and some patients may have difficulty standing upright. In addition, spatial disorientation can lead to patients getting lost even in familiar surroundings, which increases the risk of accidents, a fact that was addressed with the family, in order to limit eventualities (29).

In the critical phase of Alzheimer's disease, mobility can be severely compromised. Many patients become completely dependent on the help of caregivers to carry out fundamental tasks of daily routine, such as getting out of bed in the morning, walking or even moving from one chair to another. Muscle stiffness and loss of strength contribute to immobility, and some patients may experience involuntary muscle contractions that make movement even more difficult. This was initially the reality experienced by our patient, however, with the rehabilitation offered, she improved substantially (34).

Mobility sequelae in Alzheimer's disease not only have physical implications, but also emotional ones. The loss of the ability to move independently can be frustrating and demoralizing for patients, which can increase the risk of depression and anxiety. In addition, immobility can increase the risk of physical complications, such as pressure ulcers, aspiration pneumonia and deep vein thrombosis, such measures were adapted to our patient (30).

In order to care for patients with advanced stages of Alzheimer's, it is essential to adopt a comprehensive approach that addresses both their physical and emotional needs. It is important to provide a safe environment to prevent falls and injuries, as well as to encourage gentle physical activity to maintain mobility as much as possible. Caregivers

must also be trained to assist patients with reduced mobility in a safe and respectful manner, preserving their dignity and autonomy as much as possible, which is why our patient's family members were trained (3).

The progression of Alzheimer's disease towards intermediate and advanced stages causes a notable effect on the quality of life of the affected individual. The progressive loss of memory and cognitive skills makes independence and autonomy difficult. Patients may experience difficulties in recognizing their loved ones, performing simple tasks such as dressing or eating, and may become aggressive or anxious due to the confusion they experience, which is why social and family inclusion activities are essential, as was done with our patient (4).

In addition to the physical and cognitive impact, Alzheimer's disease in advanced stages also carries emotional and social consequences. Patients may experience depression, anxiety and frustration when they realize their cognitive decline, a reality that our patient experienced, since she presented significant depression, and even worse with the stressor of the murder she witnessed. Families and caregivers face a considerable emotional burden when witnessing the progression of the disease and having to assume increasingly demanding caregiving roles (14).

In the final stages of Alzheimer's, it is essential to provide palliative care focused on raising the quality of life of the affected individual. This involves providing a safe and understanding environment, managing signs such as discomfort or restlessness, promoting non-verbal communication and ensuring comprehensive care that addresses both the physical and emotional needs of the patient, an important part of which is physical therapy, which was suggested to our patient and a relevant clinical improvement was observed (18).

Immobilization in patients with severe Alzheimer's is a crucial aspect that requires specialized attention and specific care in order to ensure the comfort and protection of the patient. Our patient did not initially receive this service, however, with the therapy a significant improvement was observed in the MOCCA scale. Immobility in patients with severe Alzheimer's can lead to serious complications, such as pressure ulcers, muscle stiffness, loss of bone and muscle mass, among others. Therefore, it is essential to implement adequate mobilization and immobilization techniques to prevent these complications and preserve the patient's well-being. (25).

It is essential to have a multidisciplinary team that includes professionals trained in the management of patients with dementia. Specific techniques must be followed for the transfer of patients in different situations, such as transfers to medical consultations, examinations or transfers to other services. Among the Specific techniques: there is the Chair-Stretcher Transfer: This transfer is carried out in various situations and requires the

presence of trained personnel to safely mobilize the patient, which was used in the evolution of our patient with good results. Specific steps must be followed and appropriate material used to ensure a risk-free transfer (28).

It is essential to maintain the head-neck-spine axis during mobilization to prevent additional injuries to the patient. In cases of limb injuries, the patient must be immobilized and properly aligned to avoid complications. Immobilization syndrome is common in geriatric patients and can aggravate existing health conditions. It is essential to know the methods of prevention and appropriate care to reduce the incidence of illnesses and deaths related to immobility in patients with severe Alzheimer's disease. In our patient, these exercises were adequately adapted since she did not present relevant musculoskeletal conditions (28).

Among the recommendations for patients with advanced Alzheimer's are physical containment techniques. Reality Focusing Method (MER): This method is used to guide patients in their environment and facilitate their location and to remember who they are and where they are. On the other hand, we have the reminiscence technique: This technique consists of reminders of past events, such as photos or objects that recall important moments in the patient's life. Sensory stimulation technique: This technique is used to stimulate the patient's senses, just like the senses of sight, hearing, touch and smell, they are used to capture their attention and maintain their interest in what surrounds them. In our patient, the latter was used to promote effective mobility.

The psychomotor therapy technique: This technique is used to maintain the patient's mobility and motor coordination, through physical and cognitive exercises. The specific functional rehabilitation technique: This technique is used to maintain and improve the patient's functional skills, such as walking, eating, and personal hygiene. The maintenance of daily living activities technique: This technique is used to maintain the patient's independence in basic daily living activities, such as personal hygiene, dressing, and eating. These techniques were partially adapted to improve the quality of life of our patient (19).

When immobilizing a patient with severe Alzheimer's, it is essential to take specific precautions in order to ensure their protection and happiness. Suggested preventative measures include: Avoiding the Formation of Pressure Ulcers: To avoid the formation of pressure ulcers, it is essential to alternate the patient's position frequently, using specific mattresses and pillows that help keep the skin healthy after prolonged periods of inactivity. Controlled Mobilization: It is important to mobilize the patient carefully and gently, avoiding sudden movements that may cause injury or discomfort; these preventative measures have been used by the patient for better adherence to treatment (32).

Maintain continuous supervision of the patient to prevent falls, bumps or risk situations that may arise due to immobility. To achieve effective and calm communication with the patient, it is essential to use a calm and comforting tone of voice, clearly detail the actions to be carried out and maintain an empathetic connection during the interaction. Ensure that the environment in which the patient is located is adapted for their safety, removing dangerous objects, keeping corridors clear and providing a calm and welcoming environment, and Emotional support: Provide emotional support to the patient during the immobilization process, showing empathy, patience and understanding of their needs and emotions. In our patient, the family was an important pillar since it promoted all the required support (32).

Among a group of 81 individuals diagnosed with Alzheimer's with an MMSE ≥ 15, followed for a mean of 5.53 years, Kraemer et al (1994) suggested that the rate of disease progression might be more important than disease severity in predicting clinical course (39). Similarly, Doody et al (2001) found that those who declined rapidly at inclusion would continue to decline more rapidly (reaching the threshold of 5 point loss on MMSE in 1.6 years) compared to those who declined slowly initially (threshold in 2.3 years); in our patient, MMSE was not closely followed, a recommendation that arises from these arguments (40, 41).

In their study of 91 patients with Alzheimer's disease, Capitani and colleagues (2004) explored the predictive power of the initial rate of progression of the disease on the course of later stages. They found that the course of decline tended to remain constant over time (42, 43). In a 5-year prospective study, Holtzer et al (2003) investigated how the rate of cognitive decline at the onset of the disease relates to the likelihood of reaching clinical milestones in later years. Their research included 236 patients receiving outpatient treatment with Alzheimer's disease, with an average age of 73 years.

Cox analyses showed that a rapid decline during the first year was associated with greater disability and with receiving a level of care equivalent to institutional care (44). In agreement with this finding, Dumont et al (2005) demonstrated in the ELSA cohort that patients with rapid decline, identified in the first 6 months of follow-up, became more dependent, as measured by the ADL scale, during the following 6 months than those who did not decline rapidly, a fact that highlights the importance of having scales that measure disability and evolution in a rapid and reliable way especially in places where there are no invasive inputs as in our patient (45).

In a group of 354 elderly people with Alzheimer's disease Hui et al (2003) (46) found that the death rate in Alzheimer's disease is closely linked to the speed of cognitive decline. Each of the patients underwent an annual clinical evaluation that included the administration of 17 cognitive function tests over a 4-year period. Cox models showed that compared with those with the least decline, the risk of death increased more than 3-

fold in the subgroup with mild decline, more than 5-fold in those with moderately rapid decline. In our patient, all comorbidities were controlled to improve her life prognosis.

Furthermore, RCD is often associated with a worse course of the disease, regardless of the endpoint chosen (death, mortality, loss of autonomy). Epidemiological studies of Alzheimer's disease have documented enormous variability (47), not only in the measures of progression rates, but also in factors associated with and predictive of rapid disease progression.

This reported heterogeneity likely reflects multiple phenomena, including 1) true differences in rates of disease progression across patients, such as pathologic lesions; 2) different properties, i.e., floor and ceiling, of the selected measures; 3) differences in the endpoints selected to represent progression (cognitive decline, functional decline, nursing home placement, or death); 4) other disparities in methodology including the number of patients, extent of follow-up, and time lapse between visits; 5) differences in medical comorbidities; and 6) differences in patient care.

There are several factors that may be involved in the evolution of the disease, including age. O'Hara et al (2002) found that age at clinic visit < 75 years was a predictor of rapid clinical deterioration, in this category our patient who is younger than 75 years falls (48). Patients with AD who began before age 65 years declined significantly faster than patients with late onset. The results revealed a trend of more than 2 years in the modified MMSE ($p < 0.001$) (49). In another comparison of 178 patients with AD, those who were 70 years or younger demonstrated greater and faster deterioration along with more severe pathology than patients over 70 years of age (50).

Similarly, the level of education may act as a "cognitive reserve" that must be used to a certain limit before dementia becomes clinically present and may affect the speed of cognitive decline. At higher educational stages, individuals with Alzheimer's disease may show a greater degree of progression at the time of experiencing the signs of dementia. Subsequently, these patients experience greater clinical progression. In support of this hypothesis, Stern et al (1992) reported a connection between the number of years of academic training and the development of Alzheimer's disease. Our patient had a basic education, so neurocognitive exercises have been implemented to improve this aspect in our patient (51).

For a given clinical severity, parietotemporal blood flow was further reduced in patients with higher levels of education, indicating more severe pathology. Several writers agreed with this idea, finding that higher educational level may be a risk factor for rapid worsening of Alzheimer's disease. In the case of our patient, who had a basic education, this may have contributed to her condition becoming severe (52, 53). Although advanced education may accelerate cognitive decline, it may postpone it in older individuals with

Alzheimer's disease (54). Disagreeing with these findings, Guk-Hee Suh et al (2004) did not find the duration of formal education to be a significant predictor of cognitive decline (55).

The influence of other elements on the rate at which cognitive decline progresses has been noted. In a recent paper, a connection was established between institutionalization and rapid short-term cognitive decline in 432 community-dwelling elderly people with AD (56). Higher levels of spirituality ($p < 0.05$) and private religious practices ($p < 0.005$) were associated with a slower rate of cognitive decline (57). Neither sex nor caregiver burden have emerged as risk factors for rapid clinical decline. This result has led to consideration of including our patient in a group of patients with the same diagnosis so that they can carry out their social activities.

Regarding nutritional status in the ELSA cohort, accelerated clinical deterioration was considered when a decrease of 4 points or more in the MMSE was observed within a 6-month period. Multivariate regression critical appraisal of 312 community-dwelling AD patients showed that optimal nutritional status, as measured by the Mini Nutritional Assessment (MNA), could delay DCR (58). In fact, a higher MNA score (indicating a lower risk of malnutrition) acted as a shield against rapid decline in the MMSE over a 6-month period (OR = 0.86; 95% CI: 0.75 to 0.99). Thus, it was found in a group of 160 patients with very early stage Alzheimer's that those with a lower MNA score and therefore a poorer nutritional status predicted faster cognitive progression at 1 year, in our patient the nutritional status was not optimal so nutrition was requested (59).

Several investigations have shown that individuals with Alzheimer's disease who showed extrapyramidal symptoms (EPS), such as tremor, rigidity and bradykinesia, suffered a subsequent faster cognitive decline. However, in a recent article, Capitani et al, attempted to verify whether EPS were associated with a high rate of mental decline in individuals with amnestic-onset dementia. The analysis of 1,082 patients found no relevant connection between socioeconomic status and a faster cognitive decline., our patient did not show extrapyramidal symptoms advantageously (60).

Manifestations of Lewy body dementia, extrapyramidal, psychotic and subcortical symptoms are common in patients with dementia with Lewy bodies (DLB), may be present in AD. Kraybill et al (2005) confirmed that AD patients with symptoms of DLB pathology are more likely to have a faster disease progression compared to patients with AD or LB pathology alone, in our patient confirmation by biopsies was pending. The rate of decline in AD patients with DLB symptoms was significantly faster on the Mattis Dementia Rating Scale over 18 months ($p < 0.03$) and on the MMSE over 6 months ($p < 0.04$) compared to patients with AD or LB (61).

At diagnosis, the patient's cognitive status might also be a useful predictor of disease course: Atchinson et al (2004) divided their AD population into rapid, intermediate, and slow decliners. Patients who showed significantly impaired performance on measures of attention and executive function at baseline had a more rapid decline over 1 year on the MMSE than those who did not, despite equivalent baseline MMSE scores for all groups. Our patient debuted with low levels of adaptability, poor knowledge, with strengthening her cognitive space being a fundamental pillar (62).

O´Hara et al found that patients at the first visit presenting moderate to severe aphasia and a MMSE > 7 were also risk factors for RCD (63). Marra et al (2000) found that mental control skills and attention-demanding tasks were predictors of RCD (64). In this study, fast and slow decliners were defined based on their rate of decline in MMSE score. Buccione et al (2007) showed freehand copying of geometric figures and word fluency as predictors of RCD (65). Accordingly, other different studies have analyzed the deterioration of performance at baseline on neuropsychological measures, these measures as in our patient were implemented, showing an improvement (66-68).

In a study of 43 patients with Alzheimer's disease who were followed for 2 years, signs of psychosis were found to predict a rapid decline in their cognitive abilities (69). In this study, slow and rapid decliners were defined on the basis of cognitive indices of disease progression. In controlled analyses, visual hallucinations were associated with more rapid global cognitive decline. Our patient showed obvious and significant signs of severe cognitive decline (70). Other articles also corroborated the predictive value of visual hallucinations in accelerating the rate of cognitive decline (71, 72).

A number of behavioural and psychological symptoms, such as aggressive behaviour, have also been assigned a predictive value for a faster rate of cognitive decline (73), agitation (74) or sleep disturbances (75). Recently, disruptive behaviour (wandering, verbal outbursts, physical threats/violence, agitation/restlessness and sundowning) was examined with the aim of assessing its ability to anticipate cognitive decline. The simplex included 497 patients with early-stage AD, followed for a mean of 4.4 years. It was found that having at least one disruptive behaviour is linked to an increased risk of cognitive decline (HR 1.45). In particular, sundowning and restlessness were linked to an acceleration in cognitive decline (76).

Although there is a wealth of epidemiological data indicating that cardiovascular risk factors (CVRFs) increase the likelihood of developing arterial disease (AD), few analyses have been devoted to investigating their impact on outcome once AD has been diagnosed. In a first article, Barghava et al (2006) followed 247 patients. Patients who progressed to the moderate stage (Clinical Dementia Rating (CDR) 2) were designated as rapid progressors, and those who remained in the early stage (CDR 1) were designated as slow progressors, our patient falls into the slow progressor category due to her

neuropsychological context. CVRFs, such as a history of heart problems, stroke, hypertension, diabetes, or current or past smoking, did not differ between the groups (77).

In agreement with these findings, the study carried out by Regan et al. in 2006, found after an 18-month follow-up that no relevant variations were observed in the speed of decline between 224 patients with Alzheimer's disease who had cardiovascular risk factors and those who did not, except for cerebrovascular events which were associated with a greater speed. Our patient evidently presented important periods of memory loss (78). Abellan et al. (79) studied 620 patients with AD from the REAL.fr cohort. The results found no differences in the rate of progression, neither in the MMSE nor in the ADAS-cog scales, when comparing the group with CVRF (presence of hypertension, diabetes, hypercholesterolemia at the beginning of the study) with the group without CVRF after 2 years of follow-up.

However, these findings are inconsistent with the study by Mielke et al (2007). A total of 135 individuals with incident AD, a population-based elderly sample, were observed for an average of 3.0 years. The MMSE and CDR were administered at each encounter. Atrial fibrillation, high blood pressure, and angina were associated with accelerated decline, whereas coronary bypass surgery, diabetes, and use of blood pressure medications were associated with a slower rate of decline. An age-related relationship was found linking high blood pressure, angina, and heart attack were associated with greater decline with increasing age at baseline, thus our patient is indicated to have good control of her risk factors (80).

A recent meta-analysis has evaluated the association of smoking with dementia and cognitive decline. Nineteen prospective studies with at least 12 months of follow-up were included with a total of 26,374 participants followed for dementia for 2 to 30 years. The mean age of the study was 74 years. In contrast to those who have never tried tobacco, at the beginning of the investigation, current smokers showed greater annual declines in MMSE scores during the follow-up period, our patient had a younger mean age (81).

Genetic factors may be one of the unknown underlying causes of the variation in the rate of decline in individuals suffering from Alzheimer's disease. A connection has been established between the rate of progression of Alzheimer's and two genetic elements, the apolipoprotein E protein (39) (ApoE ε4) and the butyrylcholinesterase (BuChE) genotype. The predictive value of the ApoE genotype in already diagnosed AD remains controversial. ApoE ε4 carriers with mild AD (MMSE score 22 to 26) declined faster on the ADAS-cog over 6 months compared to non-carriers, whereas moderate ApoE ε4 carriers with AD (MMSE score 10 to 21) declined more slowly than those without the allele (82). A recent study showed that ApoE ε4 may most significantly influence the rate of cognitive decline common in the early stages of Alzheimer's disease, therefore genetic research is essential in these situations (83).

However, many studies have failed to link the presence of ApoE ε4 with the rate of progression, possibly because disease severity is a determining factor (56). The rate of cognitive decline is best fitted to non-linear models (84). An increase in BuChE levels could be linked to a faster rate of cognitive decline in Alzheimer's disease. The K and A variants of BuChE encode a lower expression or a decrease in the activity of the BuChE enzyme in plasma. Therefore, patients who possess these variant alleles are less likely to experience an aggressive course of the disease, and this suggestion can be taken to access their genetic diagnosis and determine early morbidity and mortality (85, 86).

Some authors found that atrophy rates (hippocampus, entorhinal cortex, whole brain and ventricle) were higher among fast than slow AD progressors (87). According to this Kinkingnéhun et al. in 2008, set out to determine whether regional atrophy could predict the rate of decline in individuals suffering from mild Alzheimer's. At the end of 3 years of follow-up, patients were dichotomized into patients with declining correlation between the rate of morphological changes in the brain, as measured by magnetic resonance imaging (MRI) and the rate of cognitive decline.

Jack et al. (27) found slow or rapid decline based on their decline in MMSE score over time. Voxel-based morphometry analysis demonstrated that patients, who will have a faster decline at 3 years, already had more extensive cortical atrophy than slow-declining patients, especially in the medial occipitoparietal areas, which had not yet been detected by clinical and neuropsychological assessment. (88) These data support the use of rates of change in serial MRI studies in addition to standard clinical/psychometric measures as alternative indicators to follow the evolution of Alzheimer's disease.

Furthermore, white matter hyperintensity (WMH) volumes appear to be related to cortical atrophy and neuropsychological decline (89). Recently, the association between WMH severity and initial MRI brain atrophy measurements with the rate of decline on the Columbia-modified MMSE was assessed in 84 AD patients from the Predictors Study. General estimating equation models demonstrated that both the degree of brain atrophy and the severity of WMH are associated with the rapidity of cognitive decline. They suggest that atrophy and WMH may have a synergistic effect on future AD decline, in our patient specifically marked sulci were evident on CT (90).

Regional cerebral blood flow (rCBF) was measured in groups of patients with rapidly and slowly progressing AD using single-photon emission computed tomography and compared between groups. RCBF in the right posterodorsal, anterior and superior prefrontal cortices and in the inferior parietal cortex was significantly lower in rapidly progressing patients. Furthermore, lower perfusion in these regions was significantly correlated with rapid deterioration in the MMSE, blood flow could not be assessed in our patient (91).

Conventional markers present in cerebrospinal fluid (CSF), such as soluble amyloid beta 1-42 (Abeta1-42) and total tau protein (t-tau), may contribute to the accuracy of diagnosis of dementia subtypes. However, their sensitivity to assess different degrees of cognitive decline has not been clarified. One study showed that CSF markers are not related to different degrees of cognitive decline (92). Another study showed that CSF Abeta1-42 and ttau measurements by APOE genotype remained stable in AD. These findings may suggest that soluble Abeta1-42 and t-tau concentration in CSF has an insignificant correlation with clinical progression (93).

However, a more recent longitudinal study of 122 AD patients followed for a mean of 4.2 ± 2.6 years found a relationship between plasma biomarkers and rate of disease progression. Low plasma levels of Abeta40, Abeta42 and high-sensitivity C-reactive protein were associated with significantly faster cognitive decline, as indexed by the Blessed Dementia Scale, than high levels, these biomarkers have not been requested since they were not available in the hospital for our patient (94).

The lack of an agreed definition and tools used to assess cognitive decline in clinical settings is one of the main barriers to establishing appropriate care for patients experiencing rapid cognitive decline in clinical settings. Currently, the treatment of patients with rapid decline in AD remains a challenge pending a better understanding of the predictive factors of CKD. To date, there are no specific guidelines for the follow-up or treatment of patients with this condition, so our patient was primarily approached from a clinical perspective.

Two tested pharmacological therapies have shown possible efficacy in patients with RCD: rivastigmine (anticholinesterase drug with additional BuChE inhibition) (95, 96) and memantine (97). A protective effect of all AchEIs was observed in developing an RCD episode, which was defined as a loss of 3 or more points on the MMSE in one year (98). Therefore, it remains to be confirmed whether these beneficial effects are caused by the additional inhibition of BuChE by rivastigmine in contrast to other drugs that selectively inhibit the AChE enzyme. In our patient, the combination of pharmacological therapy was found to be very helpful, since the MOCCA scores improved significantly.

Conclusions

- A medical case was described of a female patient diagnosed with advanced stage Alzheimer's disease, who was recruited when the patient showed significant symptoms that even made her dependent on others. However, after applying the diagnostic and therapeutic measures that current evidence requires, the patient

evolved favorably, with an adequate integration into her family and social environment.

- In summary, advanced Alzheimer's disease poses a significant challenge for both affected individuals and their loved ones. The physical, cognitive, emotional and social consequences are profound and require a comprehensive approach that combines specialized medical care with emotional and social support. It is essential to raise awareness of this disease, promote research to find effective treatments and ensure dignified and respectful care for those who suffer from this debilitating condition.

Conflict of interest

The authors declare that there is no conflict of interest in relation to the submitted article.

Authors' contribution statement

Author 1: I actively participated in the planning and design of the literature review. I also carried out a critical evaluation of the selected studies, analyzing both the methodological quality and the validity of the results.

Author 2: Significantly contributed to the interpretation and discussion of the findings obtained in the clinical case. He/she also played an important role in the writing and revision of the content of the manuscript.

Author 3: Provided valuable input by providing comments that improved the clarity and coherence of the work. Actively participated in the development of the results and conclusions of the study.

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