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Review on Alzheimer Disease

Akash Popatrao Kale, Ms. Pooja Bhonde, Dr. Gajanan Sanap
LBYP College of Pharmacy, Pathri, Chh. Sambhaji Nagar, Maharashtra, India
akkikale3302@gmail.com

Abstract: *The most frequent cause of dementia, Alzheimer's disease, is a major global health concern that affects both individuals and society as a whole. This overview first discusses the current state of knowledge regarding the epidemiology, genetics, pathology, and pathophysiology of Alzheimer's disease before moving on to the disease's clinical manifestation and available treatments. Lastly, the article explores how novel therapeutic approaches are being developed with the goal of shifting from treatment to prevention in light of our growing understanding of Alzheimer aetiology, which includes the identification of a prolonged preclinical phase.*

Keywords: EHR system.

I. INTRODUCTION

The primary cause of dementia, Alzheimer's disease, isswiftly rising to the top of the list of this century's mostcostly, fatal, and debilitating illnesses (1).

Understanding the underlying pathology, identifying multiple protective and causative genes, discovering new blood-based and imaging biomarkers, and seeing the first tentative signs of the beneficial effects of disease-modifying therapies and lifestyle changes haveall advanced significantly since the Seminar was
published in 2016. The aim of this new Seminar is to provide the reader with up to date insight into the field of Alzheimer's disease(2,3).

Clinical Signs and Symptoms

Panel 1 (also see picture 1) shows three cases that demonstrate the range of symptoms associated with Alzheimer's disease. According to the current international endeavours of the Dominantly Inherited Alzheimer Network, the Alzheimer Prevention Initiative, and the related clinical studies, Case Aillustrates how Alzheimer's disease is decided genetically. Case B is an example of a linguistic variation of Alzheimer's disease, which typically manifests at a younger age (less than 70 years of age). This illustrates how difficult it is to diagnose Alzheimer's disease in people whose memory issues arenot the primary symptom. Case **C**, a typical amnestic variety that is more frequently observed in patients over 70, exemplifies the expanding demographic impacted by dementia and Alzheimer's disease: elderly people who are frequently living alone and becoming more andmore reliant on others for care.(3)

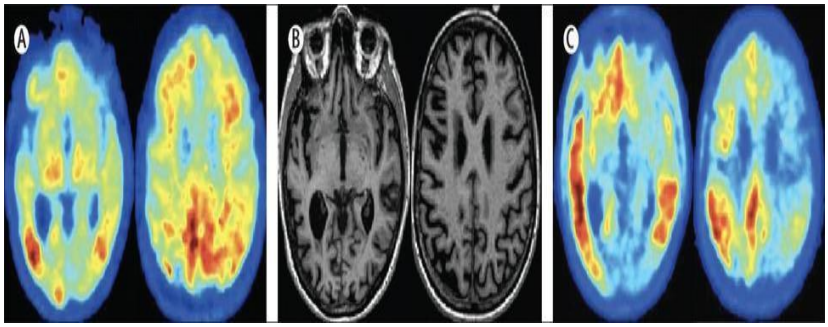

Figure 1: Imaging findings of a case similar to patient B's case in panel 1 (A) Amyloid Pittsburgh compound B-PET scan showing amyloid deposition predominantly in the posterior cingulate region. (B) T1-weighted MRI images showing generalised cortical atrophy, left to right. (C) Tau-PET image using AV1451 tracer, showing left-sided inferotemporal lobe, parietal, and mild posterior cingulate deposition of tau. Image courtesy of Rik Ossenkoppele and Gil Rabinovici.

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Epidemiology and Risk Factors

With Alzheimer's disease accounting for 50–60% ofcases, it is the most prevalent type of dementia.

Dementia prevalence is less than 1% in people 60–64 years of age, but it increases virtually exponentially with age, reaching a prevalence of 24%–33% in the Western world in those 85 years of age or older (4).

Although there is a dearth of representative data from developing nations, it is believed that 60% of dementiasufferers worldwide reside in these regions. Due to its high prevalence, Alzheimer's disease represents a significant public health issue. Over 24 million personssuffered from dementia in 2001; this figure is projectedto double every 20 years to reach 81 million in 2040 due to an estimated increase in life expectancy (4).

Epidemiological research have revealed numerous tentative correlations with the condition, in addition toageing being the most evident risk factor. Reduced brain size, low educational and occupational accomplishment, low mental aptitude in early life, and lower mental and physical activity during late life are some that are associated with a diminished reserve capacity of the brain (5,6).

Epidemiology

Incidence and prevalence

In 2018, Alzheimer's Disease International estimated a dementia prevalence of about 50 million people worldwide, projected to triple in 2050, with two-thirdsliving in low-income and middle-income countries.(7)The most recent data estimate that dementia prevalence in Europe will double by 2050. Accumulating evidence suggests that the incidence of dementia is declining in high-income countries(8). Although evidence for a decline in prevalence is lessconvincing(9).

Pathophysiology

Basic scientists designate the preclinical phase of Alzheimer's disease as the cellular phase. Alterations in neurons, microglia, and astroglia drive the insidious progression of the disease before cognitive impairment is observed(10).Neuro-inflammation alterations in the vessels ageing and dysfunction of the glymphatic system act upstream or in parallel to accumulating amyloid β in this cellular disease landscape. Amyloid βinduces, via an unknown way, the spread of tau pathology, which is associated with the appearance ofnecroptosis markers in neurons displaying granulovacuolar degeneration(11).

Stages of Alzheimer's disease

Early Stage (Mild Alzheimer's Disease):

- Memory lapses: Individuals may experience difficulty remembering names, recent events, orfamiliar words.
- Challenges with planning and organizing.
- Mild difficulties with tasks requiring attention andconcentration.
- Changes in mood or personality may be subtle.
- Individuals can usually perform daily activities butmay start having difficulty with more complex tasks.

Middle Stage (Moderate Alzheimer's Disease):

- Increased memory loss and confusion.
- Greater difficulty with tasks such as dressing,bathing, and grooming.
- Problems with language, including difficultyfinding the right words or forming coherent sentences.
- Personality and behavioral changes may becomemore noticeable.
- Wandering and getting lost may occur.
- Individuals may have difficulty recognizingfamiliar people, including family members.
- Assistance with daily activities becomes necessary.

Late Stage (Severe Alzheimer's Disease):

- Profound memory loss and cognitive decline.
- Inability to communicate effectively.

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- Total dependence on others for daily activities,including personal care.
- Loss of physical abilities, including mobility andability to swallow.
- Increased vulnerability to infections and othermedical complications.
- Individuals may become bedridden and requireconstant care.
- Death often occurs due to complications related tosevere cognitive and physical decline.(12)

Identification and biomarkers

A proper diagnosis of dementia helps identify conditions like depression, vitamin deficiencies, andhypothyroidism that may be treated and lead to cognitive impairment. It also helps patients and their families make plans for the future, including makingadvance directives and choosing the best course of action for their care. A prognosticator's capacity to deliver an early and accurate diagnosis is crucial given the potential for the development of disease-modifying medications. Since most dementia patients see family doctors, improving diagnosis in primary care is a top objective. Practical methods can increase dementia diagnosis and detection rates, such as practice-based workshops and decision help software(13).

Diagnosis

The medical history together with the clinical, neurological, and psychiatric examination serves as the basis in the diagnostic work-up. In very early cases, neuropsychological testing can help to obtain objective signs of memory disturbances. Laboratory studies, such as thyroid-function tests and serum vitamin B12, are necessary to identify secondary causes of dementia and coexisting disorders that are common in elderly people. (14)

Treatment

Knowledge of the neurotransmitter disturbances in Alzheimer's disease has led to the development of drugs with symptomatic effects, which are approved in many countries. Research advances in the molecular pathogenesis of Alzheimer's disease have also led to new drug candidates with disease- modifying potential, which have now come to testing in clinical trials. Epidemiological data have suggested additional drug candidates, some of which have been investigated in randomised trials.

Symptomatic treatments

Acetylcholinesterase inhibitors The cholinergic hypothesis in Alzheimer's disease states that degeneration of cholinergic neurons in the basal forebrain nuclei causes disturbances in presynaptic cholinergic terminals in the hippocampus and neocortex, which is important for memory disturbances and other cognitive symptoms(15).

Nanomaterials for the Treatment of Alzheimer's Disease (AD)

Over 80% of instances of dementia globally are caused by Alzheimer's disease (AD), one of the most prevalent neurodegenerative illnesses in the aged population. It results in loss of learning capacity as well as gradual mental, behavioural, and functional deterioration [16].

One example of how NPS may enhance the effectiveness of AD therapy is lipoic acid, a substance found naturally in the mitochondria that has strong anti-inflammatory and antioxidant properties that can lower oxidative stress [17].

Their design ensures that they are safe, biodegradable, and tailored to a specific target [18].

These nanosystems have the potential to efficiently distribute and maintain medications and other neuroprotective substances in the brain during the treatment of Alzheimer's disease [19].

Bypassing the blood-brain barrier, the intranasal technique facilitates the delivery of drugs straight to the brain. The most common method for transporting nanoparticles is endocytosis, which includes receptor-mediated endocytosis, phagocytosis, and pinocytosis Receptor-mediated endocytosis is the most desirable method[20].

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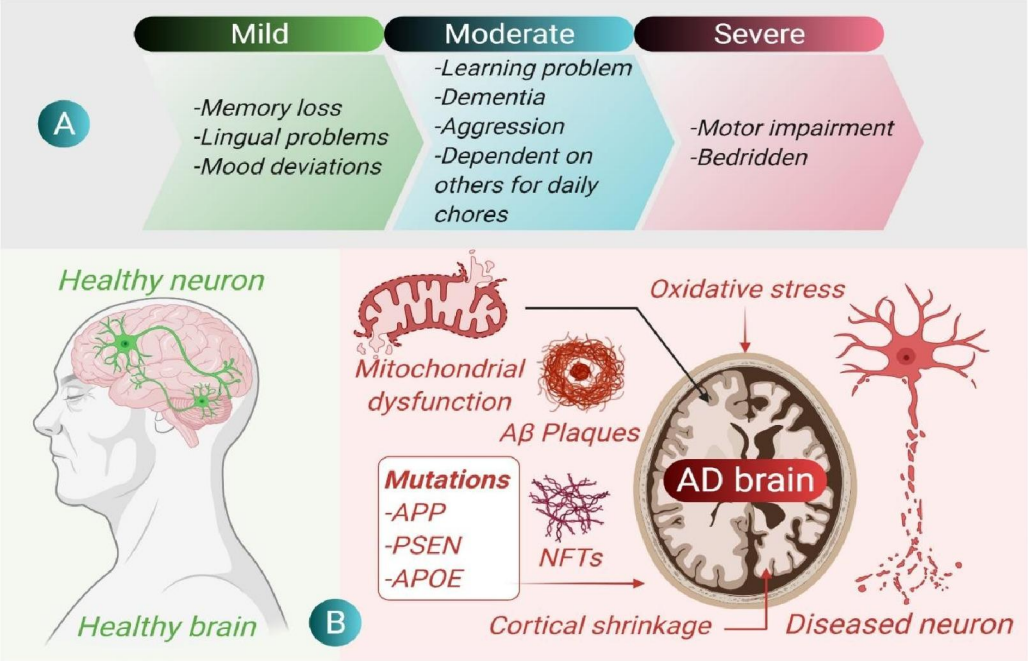

Medications:

- **Cholinesterase Inhibitors:** Drugs such as donepezil, rivastigmine, and galantamine are often prescribed to improve symptoms related to memoryand cognition.
- **Memantine**: This medication may be used in moderate to severe Alzheimer's disease to regulate glutamate activity and slow down cognitive decline

Behavioral and Cognitive Interventions:

- Cognitive Stimulation Therapy (CST): Engaging in activities and exercises designed to stimulate thinking, concentration, and memory.
- Reality Orientation: Helping individuals maintain awareness of their surroundings and circumstances.

Supportive Therapies:

- Occupational Therapy: Assisting individuals in maintaining independence in daily activities.
- Speech Therapy: Addressing communication difficulties that may arise.
- Physical Exercise: Regular physical activity has been associated with cognitive benefits.

Management of Coexisting Conditions:

Addressing other health issues such as diabetes, high blood pressure, and depression can help manage Alzheimer's symptoms.

Clinical Trials:

Participation in clinical trials may provide access to experimental treatments that are being tested for their effectiveness in slowing down or treating Alzheimer's disease.(12).

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