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Editorial Commentary

The Finding of a 19-years Old Patient with Probable Alzheimer's Disease: What is the Implication?

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Abstract

Alzheimer's disease (AD) is a major cause of disability and death. Nowadays, it does not only affect the older population, but also occurs at a very early age (<50 years). Recently, there has been a case finding of the youngest probable AD patient, at the age of 19 years. This calls for a prompt intervention in order to prevent the development of early onset AD in the wider population. Public health measures, accompanied by research projects on the basic, translational, and clinical aspects of the disease, are of crucial importance and must be undertaken and implemented within the global community.

KEYWORDS: Alzheimer's disease; early-onset; public health; research; young.

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Alzheimer's Disease (AD) is one of the leading causes of disability and death in people over 65 years old. More than 57 million people worldwide were estimated to have dementia – a severe decline in cognitive function – by 2019 [1], with AD as the leading cause of it (60-80%) [2]. With an aging population, the number of people with AD is expected to triple by 2050, leading to increased disability, disease burden, and healthcare costs. The broadening of AD's multifaceted pathophysiology parallels the changing nature of our modern lifestyle. The prevalence of many metabolic conditions, considered as risk factors for AD, is increasing globally. Furthermore, exposure to psychosocial (depression, stress, sleep disturbances) triggers during pregnancy and early life and environmental pollutants hamper normal brain developmental processes [3]. These factors could potentially contribute to an increase in the incidence and prevalence of Alzheimer's disease along with a shift to a younger age of onset.

1. Early and Very-early Onset Alzheimer's Disease

Early-onset AD affects an estimated 41.1 people per 100,000 population aged 30-64 years [4]. Young-onset dementia, particularly AD, is reportedly more common in middle-income countries than in high-income countries, primarily attributable to disparities in healthcare system development, lack of risk prediction research, and socioeconomic disparity [5]. However, further research has to be done on the available evidence due to data scarcity [4]. This AD subset has conflicting results in terms of the disease characteristics, particularly in relation to the course and rate of advancement of the illness, which requires additional investigation to identify any potential confounding variables such education stage, initial cognitive impairment, and vascular risk factors [6].

Additionally, there is an emerging subset of very early-onset AD i.e., occurring in people ≤50 years of age, that is of potential concern to the community (Figure 1). However, the number of young-onset Alzheimer's disease cases appeared to be increasing related to the intensification of screening efforts and quality improvement of healthcare facilities, particularly related to active screening programs [4]. According to a study, there has been a rise in the number of insured people between the ages of 30-64 who have been identified as having early-onset AD, with a 131% increase in diagnoses recorded from 1.3/10,000 adults in 2013 to 3/10,000 adults in 2017 [7]. Figure 1 depicted the three youngest patients diagnosed with AD, including the most recent case from China (19 years old).



Figure 1. Example of Findings of Youngest Alzheimer's Disease Patient

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2. Are Genetic Factors the Sole Contributors?

Researchers and practitioners do not yet have a complete understanding of why the majority of older individuals go on to develop AD, which contributes significantly to the unavailability of effective therapeutics to treat this global issue [8]. However, they have determined several risk factors that may impact AD development, such as age-related changes in the molecular structure of the brain, genetic regulation, environmental triggers, baseline cognitive reserve, medical and social support, and cerebrovascular pathologies [2,9]. In addition, an increase in global metabolic diseases, such as cardiovascular disease and diabetes mellitus, modulates the risk of AD in all sections of the population [10]. Nonetheless, it is pertinent to note that the individual characteristics associated with the multifactorial basis of AD largely determine the final outcome of AD. A portion of the early-onset Alzheimer's disease cases (approximately 13%) have strong relations to family history and/or genetic mutations in Presenilin-1 (PSEN-1) gene. De novo allelic configurations in the PSEN-1 gene and death of the transmitting parent before the onset of AD are considered the leading causes (premature death excluding a family history of AD) [11]. Furthermore, a key genetic revelation in early-onset AD occurred 30 years ago with the recognition of a missense mutation in the amyloid-β protein precursor (AβPP) that segregated with the disease in an autosomal dominant early-onset AD family [12]. This subsequently had a profound impact on the research journey into all forms of AD. Until recently, many pathogenic mutations, such as those in PSEN-1, PSEN-2, and apolipoprotein E (APOE) genes, which share the same autosomal dominant inheritance pattern as AβPP, were thought to significantly influence AD's progression [13,14].

According to a recently published case report from China, no known gene mutations were identified by whole genome sequencing in a patient with suspected very early onset AD. The patient, 19 years old, presented with progressive memory and concentration impairment for two years. This person has unremarkable past medical history and trauma nor consume any specific medication. Examination using the World Health Organization-University of California, Los Angeles Auditory Verbal Learning Test also revealed a significant memory impairment. Furthermore, the patient's examination revealed bilateral hippocampal degeneration (brain magnetic resonance imaging), hypo metabolism of the temporal lobe (18-F fluorodeoxyglucose positron emission tomography/FDG-PET scan), elevated p-tau181 concentration, and reduced Aβ42/ Aβ40 ratio (cerebrospinal fluid assessment), all of them were claimed to be the features suggestive of AD by the authors [15]. This research still needs further clarification because of the in availability of gold standard examination, namely pathological examination, which can only be made postmortem [16]. This finding calls for further research into the underlying causes of the very early onset AD, be it the identification of external risk factors or the search for novel genetic mutations that can cause AD at such a young age. Nevertheless, such an anecdotal occurrence may not significantly impact AD incidence, rather it must be used to increase our awareness of possibility of developing AD (or at least memory impairment) at such a young age, even without specific mutation.

3. Need for Public Health Interventions

Advocates such as the Alzheimer's Association and the Alzheimer's Impact Movement work with volunteers to influence federal and state Alzheimer's and dementia legislation. Through their advocacy efforts, these organizations help to raise awareness of the issue and encourage decision makers to act [17]. Public health authorities need to ensure that resources are made available and understood, that cognitive health and risk reduction are promoted across all ages, and that health professionals and general public are made aware that early detection and management are important. For the young adults, it is really applicable since basic healthy lifestyle principles, such as maintaining regular physical exercise and sound nutrition, applying weight management, and not smoking cigarettes are commonly announced to reduce

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the occurrence of many diseases, including AD [18]. This is particularly important to reduce the occurrence of modifiable AD risk factors, such as insulin resistance and hypertension [19]. In order to increase public concern and recognition of forms of dementia, there must be an increase in public awareness of the widespread impact of dementia. Policy makers, advocacy organizations, health care systems, social service agencies and providers, and many other stakeholders must work together to ensure that Alzheimer's disease and dementia issues are at the forefront of public attention. Dementia awareness campaigns have focused on topics as improving recognition of dementia, dementia care, decreasing public stigma and dementia risk reduction, mainly implemented to help in improving the lives of people with dementia. It is only through these collaborative efforts and the combined contributions of different sectors that legitimate and sustainable change can be achieved - improving the lives of people with Alzheimer's disease, their caregivers, and the institutions that support these communities [17,20]. One of the most comprehensive programs in this particular situation is the Alzheimer's Disease and Healthy Aging Program declared by the Centers for Disease Control and Prevention (CDC) (https://www.cdc.gov/aging/index.html). This CDC program provides a comprehensive overview of Alzheimer's disease, from early diagnosis and assessment to health promotion and prevention, public and workforce education, and research to generate population-level data to guide AD interventions [21]. It can serve as an example for all countries, especially in the developing world, where the majority of Alzheimer's cases occur. Furthermore, regarding the young-onset AD, there are several main focus of intervention that must be addressed, such as financial planning, genetic counseling, depression management, counselling and/or psychological therapy, support group, community care program, respite care, and national disability insurance scheme [22]. Strengthening research capacity on basic, translational, and clinical issues is paramount. These include the pathophysiological process, precise drug targets (no specific and effective treatment has yet been identified), and the analysis of risk factors (epidemiological, environmental, genetic, and comorbidity). The integration of medical technology is crucial in this regard, especially in the application of regenerative medicine for a more effective prevention strategy and as a means of communication between the general public and health care providers. Additionally, modern technology-including the internet and mobile apps—allows for the quick transmission of knowledge to a large audience. People may quickly get reputable health information, educational materials, and updates concerning Alzheimer's disease because of the popularity of cell phones and internet connectivity. With reliable information, the general population is better equipped to decide on illness management, early identification, and prevention [23]. The ability to practice telemedicine and promote early diagnosis for AD patients using better diagnostic tools and methods are further features of medical technology's significance in this regard [24].

"The shift of Alzheimer's disease to younger populations is worrisome, a multidisciplinary approach is needed to address this situation."

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