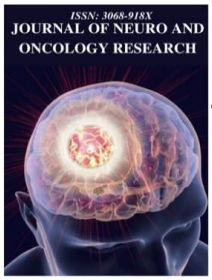

ISSN: 3068-918X
Journal of Neuro and Oncology Research

ATHENAEUM SCIENTIFIC PUBLISHERS

Short Communication

Gait Impairment as a Clue to Possible Future Dementia in Non-Alzheimer Older Patients

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Citation: Gallina P, et al. Gait Impairment as a Clue to Possible Future Dementia in Non-Alzheimer Older Patients. J Neuro Onco Res. 2025;5(3):1-3.

https://doi.org/10.46889/JNOR.2025.5311

Received Date: 08-12-2025

Accepted Date: 23-12-2025

Published Date: 31-12-2025

Abstract

The article discusses the possible role of motor dysfunction (particularly gait dysfunction) as a clinical marker for preclinical Alzheimer's disease and related dementias.

Keywords: Alzheimer's Disease; Dementias; Motor Dysfunction

Introduction

Motor dysfunction (particularly gait dysfunction) can precede the onset of dementia in older adults and has been proposed as a clinical marker for preclinical Alzheimer's Disease and related dementias (AD dementias) [1,2].

A recent study confirmed the association between gait dysfunction and subsequent cognitive decline, and established a decade as the relative time interval [3]. However, post-mortem brain pathology has shown neither indices of AD dementias, thus denying the role of gait impairment as predictor of AD dementias, nor evidence of other alterations explaining this clinical course, thereby questioning the existence of a common pathogenetic substrate for the two dysfunctions [3]. Extra-brain clinical factors unrelated to cognitive deterioration should be investigated to explain gait decline in subjects with dementias [3]. Conversely, we believe that in non-AD-dementia patients, gait and cognitive dysfunctions have a common pathological substrate, right lying into the brain, and that this association did not emerge in Oveisgharan, et al., as a consequence of methodological bias [3].

In their study, about 4% of the patients were diagnosed with possible/probable AD at baseline [3]. This percentage increased more than tenfold at the last visit, indicating AD as the most common disease in the study [3]. Because brain pathology denied this presumed diagnosis, it follows that a majority of the population had a disease clinically mimicking AD dementias [3]. Without imaging data, it is impossible to exclude that a number of the study's subjects had Normal Pressure Hydrocephalus (NPH), a neurodegenerative disease highly prevalent in older age related to Cerebrospinal Fluid (CSF) flow disturbances [3,4]. NPH typically presents with gait dysfunction, also preceding cognitive decline by years, sphincteric disturbances, that were not considered in the study and parkinsonism [3,4]. The brain of NPH patients, particularly in advanced disease, can show vascular damage, which is the main pathological data found in Oveisgharan, et al. [3,5]. The challenging distinction between NPH and AD dementias (particularly in those patients who present ventricular dilatation) becomes crucial for the individuation of candidates for CSF shunting to which the former are responsive and the latter are not [6]. The primary tool used for this purpose involves transient subtraction of CSF via external lumbar drainage with post-procedural improvement of gait and/or cognitive dysfunctions indicating that these impairments were principally related to the endoventricular accumulation of CSF [7]. Correction of this alteration of intracranial hydrodynamics by CSF shunting provides, in selected patients, a significant benefit not only in gait and urinary domains, but also cognitive, leading to consider dementia in NPH a treatable one [4].

We previously reported on few patients with signs/symptoms of NPH without ventriculomegaly [8]. The brain imaging pattern of these patients was the high burden of enlarged Perivascular Spaces (PVS), the result of accumulation of CSF in the PVS, possibly due to CSF flow disruption [9]. The association between CSF dynamics and PVS flow disturbances have been demonstrated [10]. Enlargement of PVS indicate failure of the Glymphatic System (GS), which is emerging as the common pathological substrate of neurodegenerative diseases [11]. If the GS fails, derangement of the interstitial neurotoxins clearance and ultimately neurodegeneration follow [11]. The patients in the above-mentioned study improved in both gait and cognitive functions after CSF shunting, which possibly ameliorated fluid movement into the PVS and subsequent GS functioning [8]. These results go in the direction of the real association between gait and cognitive dysfunctions based on a common pathogenetic substrate, again at the brain level [8].

Gait impairment can be associated to dementia in diseases in which extra-cranial pathological factors may trigger a cascade of events leading to neurodegeneration. Lumbar spinal stenosis, which is highly frequent among older adults, involves a narrowing of the spinal canal with compression of the nerve roots and vessels and consequent gait impairment [12]. The association of lumbar spinal stenosis and dementia has been reported in a limited Japanese experience and calls for demonstration on a larger scale [13]. We previously hypothesized that dementia in lumbar spinal stenosis develops as the consequence of an intra-extracranial hydrodynamic derangement resulting in disruption of the GS [14]. If this proposed model were demonstrated by further studies, gait impairment might represent a clue for the risk of developing dementia. Because lumbar spinal stenosis benefits from surgical decompression of the spinal canal, dementia in these cases might represent another preventable/treatable form [12].

Conclusion

Concluding, gait impairment in older non-AD-dementia patients should not lose relevance as a possible sign of oncoming cognitive decline as indicated by Oveisgharan, et al. [3]. Studies in this field should be not abandoned but rather drawn to explore other diseases in which the correction of their pathogenetic mechanism might change the natural course of some dementias.

Conflict of Interest

The authors declare no conflict of interest related to this study.

Funding

No source of funding for this study.

Author Contributions

PG and FL contributed equally in the conceptualization and preparation of the manuscript. Both authors approved the submitted version of the paper.

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