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(CASE REPORT)

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Cognitive Impairment in Aging Bipolar Disorder: Clinical Profile, Risk Factors, and Differentiation from Neurodegenerative Dementia - A Case Report and literature review

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Abstract

Introduction: Bipolar disorder (BD) in older individuals is frequently associated with cognitive impairment; nevertheless, the attributes, trajectory, and specificity of this deterioration remain contentious. The investigation into a bipolar disorder-specific dementia pattern is hindered by confounding variables, including comorbidities, polypharmacy, and concomitant neurodegenerative processes.

Methods: We describe a detailed case study of a 64-year-old patient with a 17-year history of bipolar disorder, characterized by persistent cognitive impairments. Along with this, there is a long narrative overview of the literature on cognitive trajectories, risk factors, pathophysiological mechanisms, and differential diagnosis in bipolar disorder in older adults.

Results: The index case demonstrates a unique cognitive profile marked by pronounced psychomotor retardation, executive dysfunction, attentional impairments, and memory impairment, in contrast to relatively preserved Mini-Mental State Examination (MMSE) scores. Literature synthesis reveals that cognitive decline is contingent upon age, intensifying post-45 years, with a rapid advancement subsequent to 65 years. Several risk variables were identified: recurrence of mood disorders, frequency of hospitalization, early-onset mania, late-onset depression, psychotic characteristics, suicide attempts, and medical comorbidities. Neuropathological hypotheses include the decrease of frontal gray matter, altered Brain-Derived Neurotrophic Factor (BDNF) signaling, and the activation of inflammatory pathways.

Conclusions: Currently, the factors explaining, or even predicting, a "dementia-like" progression in aging bipolar patients are uncertain. Screening and preventing cognitive impairment therefore seem all the more important, as it is crucial to offer tailored and patient-specific care.

Keywords: Bipolar Disease; Aging; Cognitive Decline; Dementia; Executive Function; Neuropsychology; Differential Diagnosis; Neuroprogression

1. Introduction

The question of the occurrence of cognitive impairment, and particularly dementia, in the course of psychiatric illnesses is widely debated. Recent data support the idea of a possible dementia-specific progression in aging bipolar disorder, but the difficulty lies in the presence of several factors that can alter the cognitive profile in aging bipolar individuals, such as the emergence of neurodegenerative disease, psychiatric and somatic comorbidities, and iatrogenic effects.

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This article aims to elucidate cognitive impairment in aging bipolar disorder via a comprehensive case presentation and an extensive literature review, examining clinical and neuropsychological profiles, identifying risk factors, exploring pathophysiological mechanisms, and proposing differential diagnostic criteria distinct from traditional dementias.

2. Case presentation

Mr. C. B., aged 64, who had been followed for bipolar disorder for 17 years, was admitted to the psychiatric ward after a stay in intensive care for a deterioration in his general condition with confusion following a suicide attempt by medication overdose. A detailed physical examination revealed no major organic disorders. Neurologically, the confusion resolved, but memory impairment persisted. His medical and surgical history included COPD, which he was treating. The course of his bipolar disorder over these 17 years has been marked by alternating depressive and manic episodes, including five suicide attempts. In terms of his socio-professional life, the patient has been unemployed for several years, having lost almost all his possessions, in contrast to his family's rejection of him.

On admission, the examination revealed a depressive-type presentation with severe anhedonia, abulia, and significant impairments in memory and executive functions. These cognitive impairments partially improved with treatment of the acute episode. It should be noted that the EEG and brain MRI were unremarkable. After resolution of this episode, memory problems persisted (slowed information processing speed, mild deficits in episodic and working memory, and attentional deficits), with a Mini-Mental State Examination (MMSE) score above 24 in four out of five cases.

3. Discussion

The start of cognitive impairment and the probable development of dementia in the course of bipolar disorder (BD) has emerged as a critical focus of study attention [1]. Recent studies indicate a unique cognitive trajectory in aging bipolar disorder, potentially differentiating it from typical cognitive aging and traditional neurodegenerative dementias.

3.1. The Neuroprogression Hypothesis

several pathophysiological and neurodegenerative hypotheses are being explored to explain this specific cognitive evolution, such as the decrease in grey matter in the frontal lobe, the role of brain-derived neurotrophic factor (BDNF), and the inflammatory pathway. [2]

The concept of 'neuroprogression' in BD has become increasingly significant, indicating that the cumulative burden of the illness leads to progressive abnormalities in the brain and cognitive decline [3].

3.2. Cognitive Profile in Aging Bipolar Disorder

In older individuals with bipolar disorder, MMSE scores often remain relatively stable, similar to our case description [2, 3]. Spatial-temporal disorientation and pronounced episodic memory losses, indicative of early Alzheimer's disease, are typically absent in the initial phases of cognitive decline associated with bipolar disorder.

The cognitive profile is characterized by significant psychomotor retardation, with processing speed impairments identified as a primary feature [2, 3]. Executive functions show a wider range of problems, such as trouble with planning, moving sets, and being flexible in thinking. Sustained attention deficiencies seem to worsen as individuals age [2, 3].

During acute mood episodes in older bipolar disorder patients, cognitive impairments resemble those seen in younger individuals, suggesting state-dependent consequences [1]. However, during euthymic stages, there exists substantial inter-individual variability, ranging from minimal cognitive deficits to significant deterioration approaching dementia criteria [1].

Recent meta-analyses demonstrate that cognitive deficiencies persist during euthymia, supporting a trait component that is separate from acute mood symptoms [5]. This discovery challenges prior beliefs that cognitive deficits in bipolar disease are exclusively episodic and reversible.

3.3. Age-Related Cognitive Trajectory in Bipolar Disorder

Longitudinal investigations reveal a unique age-dependent cognitive trajectory in bipolar disorder (BD) [2]:

- Before age 45: Cognitive performance comparable to the average populace
- Cognitive deterioration becomes more noticeable after age 45.

- After age 65: Rapid cognitive deterioration with substantial functional repercussions [2].

While chronological age clearly influences cognitive trajectory, recent research suggests a potential dementia pattern peculiar to bipolar disorder, exhibiting distinct traits from Alzheimer's disease [1]. The rate of cognitive decline in senior BD patients may exceed that of typical aging; however, it diverges from the progression observed in Alzheimer's disease.

3.4. Risk Factors for Cognitive Decline in Bipolar Disorder

There are numerous factors that can alter the cognitive profile of elderly BD patients:

- BD subtype: BD-I typically has greater cognitive impairment compared to BD-II.
- Episode recurrence: Recurrent mood episodes signify 'neurotoxicity,' marked by increasing changes in brain structure [4].
- Frequency of hospitalization: This shows how serious the illness is and is linked to cognitive decline.
- Age at onset: Early onset of mania (before age 40) and late beginning of depression (subsequent to age 50) are suggestive of inferior cognitive outcomes.
- Psychotic features: Associated with increased severity of cognitive impairment
- Suicide attempts: Multiple attempts correlate with executive dysfunction.
- Polypharmacy in senior bipolar disorder patients increases the likelihood of drug interactions and cumulative cognitive side effects [2]. Lithium, while neuroprotective at therapeutic levels, may cause cognitive slowness. Antipsychotics and benzodiazepines present particular issues related to anticholinergic load and sedation.
- Psychiatric and medical comorbidities substantially impact cognitive trajectories [2]:
  - Substance use disorders: Direct neurotoxic effects worsen BD-related impairment.
  - Anxiety disorders: Reduce verbal memory and attention span.
  - Cardiovascular risk factors: Hypertension, diabetes, and dyslipidemia increase the risk of cerebrovascular disease, leading to cumulative cognitive deficits.

3.5. Cognitive impairment linked to bipolar disorder compared to alzheimer's disease:

It is quite challenging to distinguish the difference between cognitive impairment connected to BD and cognitive impairment linked to AD, especially since both disorders become more common as people mature older. However, some distinguishing traits have been identified:

Table 1 Cognitive impairment linked to bipolar disorder compared to alzheimer's disease

Feature	BD-Associated Cognitive Impairment	Alzheimer's Disease
MMSE Performance	Relatively preserved (often >24/30) until late stages	Progressive decline, early impairment common
Primary Cognitive Domain Affected	Executive function, processing speed, attention	Episodic memory (early and prominent)
Episodic Memory Impairment	Mild to moderate, less severe initially	Severe, early, and progressive
Spatial-Temporal Disorientation	Generally, absent until advanced stages	Present early, especially temporal
Psychomotor Slowing	Prominent and early feature	Variable, less prominent initially
Course Pattern	Fluctuating with mood state, stepwise with episodes	Gradual, progressive, relentless
Insight and Awareness	Often preserved longer	Early anosognosia common
Neuroimaging Pattern	Frontal atrophy, white matter changes	Hippocampal and medial temporal atrophy
CSF/PET Biomarkers	Generally negative for AD pathology	Positive (reduced Aβ42, elevated tau)
Response to Mood Treatment	Partial improvement with mood stabilization	No response to mood treatments

3.6. Clinical Implications

These distinguishing features suggest that comprehensive neuropsychological assessment beyond simple screening tools is essential. While MMSE may remain preserved in BD-associated cognitive impairment, detailed executive function testing (Trail Making Test, Wisconsin Card Sorting Test, Stroop Test) reveals characteristic deficits. Advanced biomarkers (CSF analysis, amyloid/tau PET imaging) may definitively distinguish BD-associated cognitive impairment from concurrent AD when diagnostic uncertainty exists.

4. Conclusion

Currently, the factors explaining, or even predicting, a "dementia-like" progression in aging bipolar patients are uncertain. Screening and preventing cognitive impairment therefore seem all the more important, as it is crucial to offer tailored and patient-specific care.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflicts of interest related to this article.

Statement of ethical approval

All identifying information has been removed to protect patient confidentiality. The case report was conducted in accordance with the Declaration of Helsinki and local ethical guidelines

Statement of informed consent

Written informed consent was obtained from the patient for publication of this case report.

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