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Case Report

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Late Life Psychosis with Alzheimer's Biomarkers Successfully Treated with Electro Convulsive Therapy: A Case Report

Jacob P. Feigal[1,2*] and Kim G. Johnson[1,3]

[1]*Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine, Durham, USA*
[2]*Department of Medicine, Duke University School of Medicine, Durham, USA*
[3]*Department of Neurology, Duke University School of Medicine, Durham, USA*

Abstract

Introduction: Biomarkers for Alzheimer's Disease (AD) are available for use and are part of current clinical practice, yet little is known about the prognostic implications for psychiatric symptoms and treatment.

Case report: A 65 year old man with mild cognitive changes and normal functioning who developed psychosis and rapid functional decline. He was discovered to have Cerebro Spinal Fluid (CSF) biomarkers consistent with an AD pathologic process. He underwent Electro Convulsive Therapy (ECT) to treat worsening psychosis symptoms and demonstrated improvement in functioning back to his baseline with resolution of psychotic symptoms.

Discussion: This patient had benefit from ECT despite the presence of AD biomarkers and a severe presentation of late life psychosis. More research is needed to understand the neurobiology of late life psychosis, and the interaction between AD biomarkers and response to psychiatric treatments such as ECT.

Keywords: Biomarkers • Alzheimer's disease • Tau • Amyloid • Electroconvulsive therapy

Introduction

In patients aged 65 and over, new onset psychosis is correlated with neurodegenerative diseases such as Alzheimer's Disease and Related Dementias (ADRD) [1]. Traditionally, Electro Convulsive Therapy (ECT) has been avoided in patients with cognitive impairment, and research on ECT in patients with dementia focuses on treating depression and agitation in advanced disease [2,3]. ECT is known to be an effective treatment for psychosis in depression, however few studies examine the effectiveness of ECT for psychosis in neurodegenerative disease. There is a lack of effective treatment options for psychosis in ADRD with no Food and Drug Administration (FDA) approved medications. We present a male patient with mild cognitive changes who developed psychosis followed by rapid functional decline and was discovered to have CSF biomarkers consistent with an AD pathologic process. He underwent ECT to treat worsening psychosis and demonstrated resolution of functional impairments and psychotic symptoms.

Case Presentation

The patient, aged 65 with no significant psychiatric history and a family history of dementia (father and paternal grandmother), was hospitalized in a psychiatric hospital for three weeks in 1/2020 with a first episode of psychosis consisting of delusions and paranoia. Prior to the hospitalization, he was semi-retired (4 year professional degree), performed all independent Activities of Daily Living (iADL's) and engaged in hobbies. He had mild memory changes with trouble remembering names but no formal evaluation. Delusions consisted of beliefs that he was a pawn in a scheme, someone was stealing from him and watching him and his family through the Television (TV) or phone. Patient and his wife denied current, or history of, depression symptoms. He was treated with two antipsychotic medications, quetiapine and thiothixene, but had persistent psychotic symptoms including delusions, paranoia, disorganized thought process and thought blocking.

At a follow up outpatient evaluation in 2/2020, Montreal Cognitive Assessment (MoCA) was 23/30. All labs were normal including vitamin B12, thyroid, infectious exposures, inflammatory markers, and autoimmune encephalopathy panel. Electroencephalogram (EEG) showed low normal background frequency at 8.5 Hz. Magnetic Resonance Imaging (MRI) showed mild generalized atrophy and mild small vessel white matter changes but was otherwise normal for age. CSF studies showed elevated phosphorylated-tau (p-tau) and decreased amyloid beta-42 to total-tau (t-tau) index (Athena Diagnostics), consistent with Alzheimer's Disease pathology as shown in Table 1. Genetic testing showed *APOE* 3/3 (Apolipoprotein E) genotype. Provisional diagnosis of Alzheimer's Disease was made.

Table 1. CSF biomarker test results for Alzheimer's Disease.

	Company, Test name	Sample	P-tau (pg/mL)	T-tau(pg/mL)	A-beta 42 (pg/mL)	A-beta 42 to T-Tau Index (ATI)	p-tau/A-beta 42 ratio	Interpretation
Pre-ECT	Athena Diagnostics, ADMark	CSF	82.65(reference <54)	492.2	425.95	0.52 (reference >1.2)	n/a	Alzheimer's Disease

***Corresponding Author:** Jacob P. Feigal, Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine, Durham, USA, E-mail: Jacob.feigal@duke.edu*

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Post-ECT	Mayo Laboratories, ADEVL	CSF	41 pg/mL (reference <21.7) *specifically p-tau181	472 (reference <238)	815 (reference >1026)	n/a	0.05 (reference <0.023)	Consistent with the presence of pathological changes associated with Alzheimer's disease

Note: *reference range noted where provided by the lab
Key: P-tau = Phospho-tau; T-tau = Total tau; A-beta 42 = Amyloid beta 42 peptide

Over the following 5 months, delusions and paranoia worsened, with beliefs that food and water were contaminated and that his wife was an intruder. He paced at home daily with one episode of fleeing a restaurant in public. He also developed aphasia and functional decline, needing prompting to bathe, dress and groom, as well as anorexia with a 17-pound weight loss. Consideration was given to formal neuropsychological testing, but he was not capable of participating due to psychomotor agitation. In 10/2020, ECT was recommended due to concern that agitation represented an excited catatonia. Treatment was initiated with right unilateral electrode placement and ultrabrief pulse width. After 9 treatments he had a partial response with amelioration of hyperactive behaviors, but developed staring, mutism and withdrawal.

Treatment was changed to bitemporal electrode placement with brief pulse stimulus for an additional 13 index treatments. There were no noted adverse events. By maintenance treatment number 9, tapered to an interval of 4 weeks, his cognition, functioning and behavior improved to levels prior to hospitalization in 1/2020. He had 13 total maintenance ECT treatments and concluded ECT in 11/2021. By 1/2022, he resumed all activities including overseeing complex finances, managing medications, driving distances and hobbies. Repeat MoCA in 7/2022 was 24/30; he reported persistent difficulty recalling names. Repeat CSF testing in 9/2022 redemonstrated biomarker positive Alzheimer's Disease pathology including elevated p-tau/abeta 42 ratio, low abeta 42, high t-tau, and high p-tau 181 (Mayo labs).

Results and Discussion

Our patient had a robust response to ECT after presenting with late-life psychotic symptoms and receiving a diagnosis of AD due to CSF biomarker results. This case provides support for careful psychiatric assessment and treatment of patients with new psychiatric symptoms, even when AD biomarkers are present. Without ECT treatment, the deterioration of this patient might have been presumed due to a rapid course of AD. Several studies show that patients with neurodegenerative disease who experience hallucinations and delusions have a more rapid course of decline and possible early death [4]. It is possible that this patient's symptoms were best diagnosed as a major depressive episode with psychosis, a highly ECT responsive condition, but he never endorsed depressive symptoms prior to psychosis during treatment course and so diagnostic focus remained on the psychosis and biomarker status.

Patients with normal cognition or mild cognitive impairment can experience psychosis as the initial symptom of a neurodegenerative disease [1]. Identifying ADRD pathology as an organic cause of psychosis may be important for clinical course, prognosis and treatment. Biomarker analysis has increased the accuracy of diagnosis of ADRD, which can be identified by the A,T (N) classification system developed by the NIA-AA based in the presence of ☒Amyloid plaques (A), neurofibrillary Tau deposits (T) and Neurodegeneration (N) [5]. A☒42 and p-tau 181 are unique to AD and measurement of their presence differentiates AD from other neurodegenerative diseases affecting cognition [6]. More widespread biomarker analysis of patients with new onset late life psychosis will likely increase, especially as plasma biomarker measurement becomes more reliable [7] and new treatments become available.

Given the profound improvements seen in this case, we postulate that ECT could impact psychotic symptoms in AD through inflammatory or biochemical mechanisms. There is a known association between microglia/macrophage activated inflammation and the development of AD pathology [8] and ECT treatment could decrease markers of macrophage/microglia inflammation in the CSF [9]. Additionally, ECT increases levels of CSF Aβ-42 in depressed patients [10], reflecting a possible reduction in brain amyloid. It is unknown if ECT influences AD biomarker levels in patients with psychosis or cognitive disorders receiving ECT. Further study is needed to determine the safety, efficacy, and mechanisms of action of ECT for treatment resistant psychosis in individuals with AD pathology.

This case brings up several salient points about psychosis in the setting of confirmed AD pathology and its treatment, while having the limitation of lacking formal neuropsychological testing.

Conclusion

ECT was highly effective and without complication in this patient with late life psychosis and positive AD biomarkers reflecting AD pathology. As AD biomarkers become more widespread in clinical use, their presence should not represent a contraindication to ECT, and care is needed to ensure proper assessment and treatment of psychiatric symptoms in this population. More research is needed to understand the effects of ECT on the neuropsychiatric manifestations of neurodegenerative diseases.

Declaration

Author's contributions

Dr. Feigal and Dr. Johnson participated equally in the preparation and editing of this manuscript.

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Ethical publication statement

This paper has adhered to relevant ethical guidelines, and is considered to be IRB exempt given the retrospective nature.

Consent

The patient has provided consent for publication of this anonymized report.

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Conflict of Interest

The authors have no financial disclosures or conflict of interest.

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