

RESISTANT LATE-ONSET SCHIZOPHRENIA WITH PROMINENT NEUROCOGNITIVE DEFICITS -DIAGNOSTIC DILEMMA AND THE ROLE OF ELECTROCONVULSIVE THERAPY: A CASE SERIES

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Dear editor,

Late-onset psychosis (LOP) denotes a distinct group of psychosis that begins after 45 years and can manifest as paraphrenia, schizophrenia-like psychotic disorder, or affective psychosis in the absence of any attributable cerebral pathology or dementia (Tampi et al. 2019). It commonly denotes late-onset schizophrenia (LOS), which predominantly presents with paranoid delusions, less negative symptoms, formal thought disorder, and variable neurocognitive deficits. (Vahia & Cohen 2009) A higher incidence of this disorder is seen in females, particularly with sensory deficits and social deprivation. (Tampi et al. 2019) Unlike the classical Kraepelinian description of dementia praecox, LOS usually responds well to low doses of antipsychotics (Vahia & Cohen 2009), with rare reports of severe pharmaco-nonresponsive symptoms and prominent neurocognitive deficits. (Tampi et al. 2019)

Furthermore, in elderly patients at risk of extrapyramidal symptoms (EPS) and tardive dyskinesia (TD), the emergence of antipsychotic resistance can create further treatment hurdles necessitating somatic therapies. (Tampi et al. 2019) ECT is a safe and effective somatic treatment option across all age groups, with interestingly higher response rates in the elderly compared to the younger age group (73% vs 54%). But, medical comorbidities and the risk of neurocognitive deficits can frequently interfere with the decision to use ECT in the elderly population. However, ECT may be considered in the context of medication resistance or intolerance or acute exacerbations of illness. (Wilkins et al. 2008) In this report, we intend to reflect on the diagnostic and treatment challenges in the elderly presentation of severe psychosis with prominent neurocognitive deficits while emphasising on the beneficial role of ECT in such scenarios.

Table 1 summarises the case study of two elderly females developing schizophrenia-like psychosis after 45 years with intermittent catatonia against a background of neurocognitive deficits. Unlike the usual presentation of LOS, our patients had severe symptoms with poor response to psychotropics and high neuroleptic sensitivity. The prominence of neurocognitive deficits at presentation further produced diagnostic dilemmas

about whether the presentation was a resistant LOS with secondary neurocognitive deficits or a primary organic brain disease / neurodegenerative disorder manifesting as the described clinical picture. However, the relevant investigations could not explicitly indicate any specific organic aetiology for the presentation. Moreover, the neurocognitive deficits in our patients started after the onset of the psychosis and resolved with successful treatment of the psychosis thereby, indicating its development consequent to the psychotic process. Therefore, we conceptualised the clinical picture of our cases as resistant LOS presenting with recurrent catatonia and secondary neurocognitive deficits. The subtle MRI-Brain findings (Table 1) could either be incidental or maybe "interacting with some poorly understood vulnerability factors, contributing to the atypical phenotype and treatment resistance" in our cases. (Sachdev & Brodaty 1999) Elderly schizophrenia-like psychosis with otherwise no identifiable organic aetiology may have 'somewhat different specific' structural brain damages contributing to their unusual presentations (Vahia & Cohen 2009).

The evidence of clozapine use in LOS is sparse. Moreover, its use in the elderly is limited by its adverse effects. (Howard et al. 2000) as noted in both cases. The recurrence of benzodiazepine-non-responsive catatonia, treatment resistance to psychotropics, and neuroleptic sensitivity weighed our decision favouring ECT despite marked cognitive deficits at presentation. Both our cases showed significant improvement in psychopathology, catatonia, and overall functionality, which was sustained for months. In the advent of recurrence of psychotic symptoms, monthly maintenance-ECT (M-ECT) proved beneficial in maintaining the treatment benefits and consequent functional improvement. The literature on the therapeutic effects of M-ECT in TRS is limited to a few anecdotal reports and retrospective studies, more so in the elderly population. (Choi et al. 2018) In our cases, M-ECT was found to be an effective treatment option to maintain treatment gains in preventing relapses and improving the overall functionality.

The use of ECT in LOP, has been reported with high risks of interictal delirium leading to premature discontinuation and non-response in many patients. (Wilkins et al. 2008) ECT is also known to cause temporary cognitive deficits, which is expected to be more prominent in the elderly population. (Choi et al. 2018) However, a recent study involving mixed-age population (15-69 years), interestingly found cognitions to improve significantly after a course of ECT. (Tor et al. 2017) Furthermore, we opted for bifrontal ECT to keep the cognitive side-effects minimal. In our cases, the improvement in cognition with ECT paralleled the resolution of psychotic symptoms encouraging ECT use in neurocognitive deficits secondary to psychosis. (Wilkins et al. 2008)

In conclusion, LOS can present with severe symptoms, catatonia, pharmaco-resistance and prominent cognitive deficits. In such cases, the clinical approach must emphasise understanding the evolution of cognitive decline along the course of psychosis to guide a rational therapeutic approach. ECT can be safely used, especially when cognitive deficits are secondary to the psychosis, and in resistant cases intolerant to clozapine. Also, M-ECT can help long-term maintenance of the treatment gains and functionality.

Table 1. Summary of the two cases of resistant late-onset schizophrenia with prominent neurocognitive deficits

Features	Case 1	Case 2
Age/Sex	54/F	68/F
Onset (DOI)*	51 (3)	65 (3)
Clinical presentation	Suspiciousness, muttering + intermittent catatonia (benzodiazepine-non-responsive) + prominent forgetfulness, inattention, and difficulty in ADLs ¹	Suspiciousness, muttering, disinhibited behaviour + intermittent catatonia (benzodiazepine-non-responsive) + prominent memory deficits and difficulty in ADLs ¹
MSE	Constricted affect, persecutory delusions, AHs (PANSS: 93), BFCRS 16	Constricted affect, persecutory delusions, AHs (PANSS: 108), BFCRS: 14
NPB [#]	Deficits in attention, new learning ability, planning, and visual-motor coordination	Deficits in attention, recent memory and constructional ability
Investigations	Thyroid profile, serology, vitamin-B ₁₂ , and anti-TPO antibody were normal	Thyroid function tests, serology, vitamin-B ₁₂ , and anti-TPO antibody were normal
MRI-Brain	Bilateral hippocampal atrophy with chronic lacunar infarcts in bilateral centrum semiovale	Non-specific white matter hyperintensities
Past failed trials	Risperidone 4mg/day, Amisulpride 600 mg/day (EPS on dose escalation), Clozapine: stopped due to intolerable giddiness	Olanzapine 15 mg/day, Amisulpride 400 mg/day (EPS on dose escalation), Clozapine: stopped due to alarming QTc prolongation
Acute ECT ²	Improvements in catatonia (BFCRS: 0), psychosis (PANSS: 38) and cognition (MoCA: 26)	Improvements in catatonia (BFCRS: 0), psychosis (PANSS: 32) and cognition (MoCA: 24)
M-ECT ³	Progressive improvement in cognition and functionality	Progressive improvement in cognition and functionality

Note: * in years; ADL: Activities of Daily Life; AH: auditory hallucinations, Mental Status Examination; PANSS: Positive and Negative Syndrome Scale; BFCRS: Bush Francis Catatonia Rating Scale; #: NIMHANS Neuropsychological Battery; anti-TPO: anti-Thyroid Peroxidase; 1: neurocognitive deficits appeared after the onset of the psychotic symptoms; 2: acute course of bifrontal ECT at frequency of thrice/week (8 sessions); M-ECT: Maintenance-ECT at frequency once/month; 3: M-ECT was given to prevent relapse; MoCA: Montreal Cognitive Assessment Scale

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MIXED STATES, PATHOPLASTICITY, AND THE BIPOLAR SPECTRUM

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Dear editor,

As a mood disorders psychiatrist, it was with great interest that I read the article by Prof. Tavormina on the clinical aspects and nosology of mixed states in bipolar disorder and its relationship with temperaments (Tavormina 2021). The author demonstrated a profound knowledge of the bipolar spectrum concept and offers valuable advice for the practicing clinician with regards to the identification and management of this condition. Nonetheless, as an academic exercise, I would like to bring up a few points that complement Prof. Tavormina's discussion on mixed states.

First, I missed a more direct reference to the concept of pathoplasticity (Widiger 2011), which can help us better understand the relationship between personality/temperament traits and mixed symptomatology. According to this model, an individual's baseline personality plays an important role in the clinical presentation of a certain psychiatric conditions, such as bipolar disorder. That may be the reason why two patients with bipolar disorder, despite suffering from the same condition, are never identical as for their psychopathological features during acute mood states and could potentially explain why some patients present with mixed symptomatology while others don't. In other