Clozapine in the Geriatric Patient With Neuropsychiatric Comorbidities

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Little is known about the development of cognitive changes or psychiatric symptoms in patients with intellectual disabilities as they age. Psychiatric symptoms with functional decline could be confused with or contribute to cognitive decline in patients experiencing neurodegeneration. The combination of intellectual disability with cognitive decline increases risk for behavioral manifestations including abnormal perceptions and agitation. There are little to no guidelines for treating these behavioral symptoms.[1–3]

Antipsychotics can be used in the geriatric population for primary psychosis and psychosis and agitation related to dementia. Data support the use of clozapine in this population, particularly for debilitating behavioral disturbances refractory to treatment with first-line antipsychotics, but with strong recommendations for low-dose initiation and slow titration.[4–6]

This case will explore the initiation of clozapine for a geriatric patient with intellectual disability who developed treatment-refractory behavioral disturbances and delusions.

Case Report

Ms A is a 68-year-old woman with diagnoses of Asperger syndrome (AS), social anxiety, and obsessive-compulsive disorder (OCD), which was successfully managed intermittently with quetiapine for many years.

She functioned and lived independently for most of her adult life. Then, at age 66 years, she experienced a subacute decline in her ability to care for herself secondary to an increase in obsessive thoughts, paranoia, and delusions requiring hospitalization. On neuropsychological testing, she displayed lack of frontal lobe function with utilization behavior, perseveration, and OCD-like qualities. She was presumed to have a frontotemporal lobar dementia (FTLD)–like process and was placed in a locked memory care facility. She continued to have prominent bizarre delusions triggered by anxiety. Her in-office cognitive testing and magnetic resonance imaging (MRI) of the brain were normal. Repeat formal neuropsychological testing indicated a frontal subcortical process with functional deficits thought most likely to be secondary to psychiatric causes. She was treated with risperidone and then switched to olanzapine. She developed a prominent hand tremor and oral tardive dyskinesia. Due to ongoing distressing bizarre delusions and movement symptoms, clozapine was started at low doses and titrated to 75 mg twice daily. After a period of 1 month of starting clozapine, the delusions, severe anxiety, tremor, and tardive dyskinesia resolved, and her functioning increased. The patient was able to move out of memory care into an assisted living facility.

Discussion

This patient, over the age of 65 years with multiple behavioral disturbances and paranoid delusions refractory to treatment with risperidone and olanzapine, did meet criteria for treatment with clozapine.[5] In particular, autism spectrum disorder (ASD) did not preclude use of clozapine.[7]

Complicating factors in this patient's treatment course include significant psychiatric comorbidities, comprising a historical diagnosis of AS and a possible FTLD diagnosis. Prior research with patients with ASD and AS has shown a relationship between earlier onset of cognitive impairments and dementia, especially FTLD, with anatomic differences on MRI and sustained impairments of executive function into later adulthood.[3,8–14]

Anxiety, such as this patient had, can serve as a prognostic indicator for future cognitive decline in dementia.[1,14,15] Patients with ASD and AS also have a higher incidence of comorbid psychiatric diagnoses with complex presentations.[16,17] Effective treatment of comorbidities in addition to multimodal treatment for dementia may augment management of patients already at a higher risk of early onset cognitive impairment due to AS and ASD.[12,14,18]

In conclusion, this case demonstrates how clozapine allowed a treatment-refractory geriatric patient otherwise limited by severe anxiety, OCD, possible FTLD, and AS to manage her symptoms, thereby giving her the ability to live independently once more.

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REFERENCES

1. Ismail Z, Gatchel J, Bateman DR, et al. Affective and emotional dysregulation as pre-dementia risk markers: exploring the mild behavioral impairment symptoms of depression, anxiety, irritability, and euphoria. *Int Psychogeriatr*. 2018;30(2):185–196.
2. James IA, Mukaetova-Ladinska E, Reichelt FK, et al. Diagnosing Aspergers syndrome in the elderly: a series of case presentations. *Int J Geriatr Psychiatry*. 2006;21(10):951–960.
3. Ruggieri V, Gómez JLC, Martínez MM, et al. Aging and autism: understanding, intervention and proposals to improve quality of life. *Curr Pharm Des*. 2019;25(41):4454–4461.
4. Farooq S, Choudry A, Cohen D, et al. Barriers to using clozapine in treatment-resistant schizophrenia: systematic review. *BJPsych Bull*. 2019;43(1):8–16.
5. Frankenburg FR, Kalunian D. Clozapine in the elderly. *J Geriatr Psychiatry Neurol*. 1994;7(2):129–132.
6. Rubio JM, Kane JM. How and when to use clozapine. *Acta Psychiatr Scand*. 2020;141(3):178–189.
7. Kaplan G, McCracken JT. Psychopharmacology of autism spectrum disorders. *Pediatr Clin North Am*. 2012;59(1):175–187, xii.
8. Ambery FZ, Russell AJ, Perry K, et al. Neuropsychological functioning in adults with Asperger syndrome. *Autism*. 2006;10(6):551–564.
9. Geurts HM, Vissers ME. Elderly with autism: executive functions and memory. *J Autism Dev Disord*. 2012;42(5):665–675.
10. Hill EL, Bird CM. Executive processes in Asperger syndrome: patterns of performance in a multiple case series. *Neuropsychologia*. 2006;44(14):2822–2835.
11. Luna B, Doll SK, Hegedus SJ, et al. Maturation of executive function in autism. *Biol Psychiatry*. 2007;61(4):474–481.
12. Midorikawa A, Kawamura M. The relationship between subclinical Aspergers syndrome and frontotemporal lobar degeneration. *Dement Geriatr Cogn Disord Extra*. 2012;2(1):180–186.
13. Raznahan A, Toro R, Daly E, et al. Cortical anatomy in autism spectrum disorder: an in vivo MRI study on the effect of age. *Cereb Cortex*. 2010;20(6):1332–1340.
14. Rhodus EK, Barber J, Abner EL, et al. Behaviors characteristic of autism spectrum disorder in a geriatric cohort with mild cognitive impairment or early dementia. *Alzheimer Dis Assoc Disord*. 2020;34(1):66–71.
15. Gulpers B, Ramakers I, Hamel R, et al. Anxiety as a predictor for cognitive decline and dementia: a systematic review and meta-analysis. *Am J Geriatr Psychiatry*. 2016;24(10):823–842.
16. Hollocks MJ, Lerh JW, Magiati I, et al. Anxiety and depression in adults with autism spectrum disorder: a systematic review and meta-analysis. *Psychol Med*. 2019;49(4):559–572.
17. Tarazi FI, Sahli ZT, Pleskow J, et al. Asperger's syndrome: diagnosis, comorbidity and therapy. *Expert Rev Neurother*. 2015;15(3):281–293.
18. Orgeta V, Qazi A, Spector A, et al. Psychological treatments for depression and anxiety in dementia and mild cognitive impairment: systematic review and meta-analysis. *Br J Psychiatry*. 2015;207(4):293–298.