



# Clozapine Induced Extrapyrasidal Symptoms in a Korean-American Woman

Christopher Villongco<sup>1</sup>, Stephen Lee<sup>1</sup>, Otega Edukuye<sup>1</sup>, Ann Schwartz<sup>2</sup>  
1 Morehouse School of Medicine, 2 Emory University School of Medicine



EMORY  
UNIVERSITY

## Abstract

Clozapine is unique from other antipsychotics as it has minimal risk for extrapyramidal symptoms (EPS)<sup>1</sup>. Within the Korean-American population, the risk of EPS with clozapine has not been established. We report a case of clozapine-induced oculogyric crisis and akathisia in a Korean-American woman and discuss cultural considerations for using clozapine in the Korean-American population.

## Case Description

Ms. L is a 37 year old Korean-American woman with a past medical history of schizoaffective disorder: unspecified type who presented with worsening depression. She denied poor sleep, poor energy, poor concentration, anhedonia, suicidal ideation (SI) or homicidal ideation (HI). Additionally, Ms. L had issues with her eyes where she always "has to look up." She denied any visual hallucinations (VH), change in vision, or pain with eye movements. She did not know if this had happened before but further clarified that this had started 2 days ago. The patient ended the psychiatric evaluation abruptly. She did not endorse any auditory hallucinations or any manic symptoms.

Collateral (per Ms. L's stepfather Mr. H):  
Collateral stated that Ms. L was doing fine until 1 week ago prior to her presentation. At that time, the patient was calling the police several times a week, reporting that someone was outside, trying to attack her. Additionally, she had disorganized behavior such as pacing around the and leaving in the middle of the night. She was talking to herself non-stop and did not sleep for the past 1 night. He also reported that Ms. L had complained of "her eyes going up" in the past, which has resolved with Benztropine. The patient had done well on Haldol in the past and that the family would like Ms. L to be started back on Haldol.

### Collateral from Ms. L's outpatient provider:

The patient was started on Clozapine 350mg at night (qhs) in a previous hospitalization. Since then, the patient has been titrated up to 400mg qhs and 3 days ago, her dose was again further increased up to Clozapine 500mg po qhs.

Ms. L was given Benztropine 1mg for her oculogyric crisis which resolved the issue and on physical examination 5 hours later had no extraocular muscle issue. She was continued on her Clozapine 500mg dose.

Overnight observations from the staff indicated that Ms. L did not sleep following her admission and was noted to be pacing on the floor. Ms. L complained that she had not been able to sleep for the past 3 days secondary to her legs being uncomfortable. She describes this as a crawling sensation that is only in her legs. This sensation is improved with walking. The patient was started on propranolol for akathisia. The following day, Ms. L reported to be sleeping well and her desire to walk constantly had resolved.

Collateral from Ms. L's stepsister:  
Mental Health is a point of shame for Ms. L's family and have limited understanding of the patient's illness. Ms L's family is concerned about weight gain for Ms. L. Ms. L's parents are concerned that she will not be able to get married if she gains too much weight.

## Clinical Findings

### Vitals (on admission):

BP= 130/84  
HR = 100  
Resp = 18  
Temp = 98F

### Labs:

A1c = 5.7  
Vitamin D = 27.9 (L)  
Alk Phos = 137 (H)  
Calcium (10.3)  
ANC = 10.6 x 10E3 (H)

## Discussion

- ◆ Korean-Americans have been found to have greater improvement of psychosis while having significantly lower clozapine concentration when compared to Caucasians<sup>2</sup>. They also have a higher propensity to develop anticholinergic side effects but no relationship with extrapyramidal symptoms (EPS) was found. Clozapine is metabolized in the liver by CYP1A2, which was found to be significantly lower enzyme activity in Koreans when compared to Swedish Individuals<sup>3</sup>. Poor metabolism of clozapine may increase the risk for side effects, including EPS, and a lower starting dose and slower titration should be considered in Korean-American patients.
- ◆ Despite concern from Ms. L's parents about her psychosis, the patient presented with depression and EPS. Discussion with extended family highlights the concern for weight and poor understanding of Ms. L's diagnosis which could have contributed to her depression and potentially medication non-adherence. Discussion with family regarding diagnosis and treatment is essential when treating Korean-American patients.
- ◆ Despite having a lower BMI, Asian patients on Clozapine have been seen to have higher total cholesterol, ALT, and AST, possibly predisposing them to metabolic syndrome. Koreans in particular were more likely to have adverse effects at lower doses of Clozapine.<sup>4</sup>
- ◆ Korean Americans with schizophrenia had comparable levels of self-esteem but reported lower satisfaction with life compared to other ethnic groups with schizophrenia. This may be due to immigrating from a society in Korea that placed a greater emphasis on collectivism and family involvement.<sup>4</sup>
- ◆ Discussion with Ms. L's step-sister (who is a medical doctor) highlights that her family has limited insight into her mental health issues and are more concerned with her weight gain.

- ◆ Mental Health is a point of shame for Ms. L and her family and so her father is not always the most forthcoming with Ms, L's symptoms. Driving this concern about the weight gain is the desire to have their daughter get married. Her father reports that the patient has done well on Haldol in the past and asks for the patient to be switched back to this medication. Given that Haldol is a typical antipsychotic with less cholinergic activity, it has less propensity to increase weight gain in Ms. L. Despite this, her family's support is a protective factor as they take care of Ms. L.

## Conclusions

- ◆ CL psychiatrists must utilize an approach of cultural humility when dealing with Korean-American patients who are prescribed clozapine.

## References

1. Miller D. D. (2000). Review and management of clozapine side effects. *The Journal of clinical psychiatry*, 61 Suppl 8, 14–19.
2. Matsuda, K. T., Cho, M. C., Lin, K. M., Smith, M. W., Young, A. S., & Adams, J. A. (1996). Clozapine dosage, serum levels, efficacy, and side-effect profiles: a comparison of Korean-American and Caucasian patients. *Psychopharmacology bulletin*, 32(2), 253–257.
3. Ghotbi, R., Christensen, M., Roh, H. K., Ingelman-Sundberg, M., Akillu, E., & Bertilsson, L. (2007). Comparisons of CYP1A2 genetic polymorphisms, enzyme activity and the genotype-phenotype relationship in Swedes and Koreans. *European journal of clinical pharmacology*, 63(6), 537–546. <https://doi.org/10.1007/s00228-007-0288-2>
4. Subramaniam, M., Ng, C., Chong, S. A., Mahendran, R., Lambert, T., Pek, E., & Huak, C. Y. (2007). Metabolic differences between Asian and Caucasian patients on clozapine treatment. *Human psychopharmacology*, 22(4),
5. Bae, S. W., & Brekke, J. S. (2002). Characteristics of Korean-Americans with schizophrenia: a cross-ethnic comparison with African-Americans, Latinos, and Euro-Americans. *Schizophrenia bulletin*, 28(4), 703–717. <https://doi.org/10.1093/oxfordjournals.schbul.a006974>