Clozapine Continuation in a Patient Requiring Chemotherapy for Lymphoma

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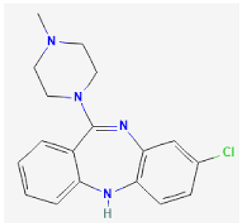
BACKGROUND

Due to risk of agranulocytosis, questions remain about clozapine (see Figure 1) management in patients requiring myelosuppressive chemotherapy even when these regimens include granulocyte colony stimulating factors (G-CSF) to support cell counts. Clozapine dose adjustment or discontinuation to avoid agranulocytosis risks psychiatric decompensation, which may limit adherence with recommended cancer treatment, especially if other medical complications arise.

Figure 1. Chemical structure of clozapine



CASE

ID/CC: A 56-year-old patient with history of schizophrenia, and >30 years of psychiatric stability on clozapine 375mg PO daily, was medically admitted for workup of new abdominal pain/distention, trouble breathing, and decreased urination. A large intra-abdominal mass was discovered, and pathology confirmed a diagnosis of aggressive non-Hodgkin B-cell (Burkitt) lymphoma.

Psychiatric Hx: Clozapine monotherapy was well-tolerated without neutropenia. It led to extended period of psychiatric symptom remission, enabling patient to live independently and maintain full-time employment.

Hospital Course: Clozapine level on admission was 132 ng/ml and initial absolute neutrophil count (ANC) was 6000 cells/µl. Qtc (Bazett) on admission was 496msec. Patient was planned for chemotherapy with hyperCVAD protocol: cyclophosphamide (CTX), vincristine, doxorubicin, and dexamethasone.

Given the history, a risk-risk discussion was facilitated to explore the risks of psychiatric decompensation and the risks of agranulocytosis (see Figure 2). The interdisciplinary team and patient decided to continue the clozapine at home dose throughout the recommended chemotherapy course.

After administration of first CTX dose, patient experienced supraventricular tachycardia. Wolff-Parkinson-White syndrome was diagnosed and patient required cardiac ablation prior to resumption of chemotherapy. Patient tolerated CTX re-induction and first cycle of protocol. ANC nadir reached 1000 and improved to 8900 with filgrastim (see Figure 3). Patient discharged with plan to return to the hospital for cycle 2 as per protocol.

Figure 2: RISK-RISK ANALYSIS HIGHLIGHTS

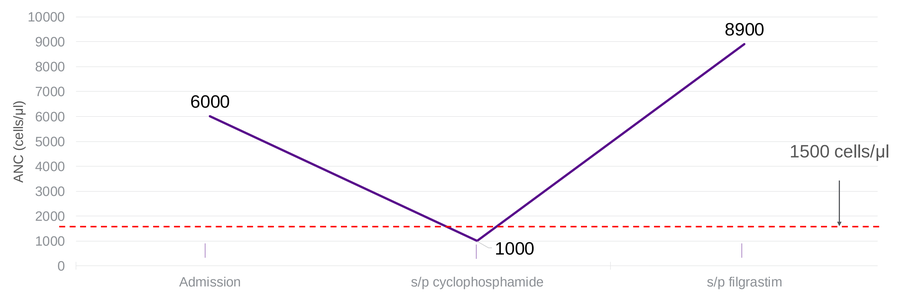
Clozapine Continuation During Chemotherapy

- ✓High likelihood ongoing psychiatric symptom stability
- ✓Protection against psychotic decompensation during significant acute stressors
- ✓Maintain structure & routine in setting of acute cancer treatment
- ✓No known significant drug-drug interactions with hyperCVAD regimen
- Theoretical increased risk of neutropenia/agranulocytosis (not observed for pt in >30yrs)

Clozapine Discontinuation During Chemotherapy

- High risk re-emergent psychotic symptoms
- Risk of treatment-interfering behavior, incl. nonadherence, agitation
- Risk breakdown in rapport with patient
- ✓Theoretical less risk of neutropenia/agranulocytosis

Figure 3. ANC through HyperCVAD Cycle 1



DISCUSSION & CONCLUSION

- Clozapine may be continued during chemotherapy with close clinical and laboratory monitoring.
- Clozapine continuation can be used to maintain psychiatric stability through acute stressors of new cancer diagnosis and chemotherapy initiation.
- Patients taking clozapine can demonstrate appropriate ANC response to G-CSF agent, such as filgrastim.
- **CL psychiatrists serve an important clinical & liaison role in advocating for patients with severe mental illnesses to continue clozapine treatment in the interest of promoting psychiatric symptom stability and quality of life, especially when faced with the potentially life-altering implications of cancer.**

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