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Introduction

The November 2007 quetiapine package insert carries the warning "leukopenia, neutropenia, and agranulocytosis (including fatal cases) have been reported related to atypical antipsychotics, including quetiapine" [1]. There are, however, few case reports that document this problem, including in children [2-7]. The authors are not aware of any reports describing medication interactions with quetiapine that produced sudden onset neutropenia. We are reporting a case of leukopenia following the introduction of erythromycin in a woman who had tolerated 300 mg quetiapine/day for over two years to treat successfully her bipolar depression. Both the quetiapine and erythromycin were stopped due to her declining absolute neutrophil count and white blood cell count. Her absolute neutrophil count and white blood cell count (WBC) promptly recovered. A re-challenge was done with quetiapine without erythromycin and her absolute neutrophil count and white count remained within the normal range.

and agranulocytosis [10,11]. In the case, even after re-starting prochlorperazine there was no changes in the hematologic parameters suggesting that prochlorperazine had no probable link to the neutrophil drop. This patient also tolerated quetiapine in the absence of 3A4 inhibition without hematologic sequelae. The rapid drop and recovery of the neutrophil count is a finding consistent with 6-10 hours intra-vascular life of neutrophils [12]. Without the blood drug levels, it is difficult to quantify the increase in quetiapine level. Still the findings in this case report, point to a likely toxic etiology arising from the interaction of the erythromycin and quetiapine given to the patient [3,14]. The chronological sequence of events leads us to think that erythromycin by inhibiting the cytochrome P450 3A4 isoenzyme led to a sudden increase in the quetiapine levels and thereby its substrates

Case Report

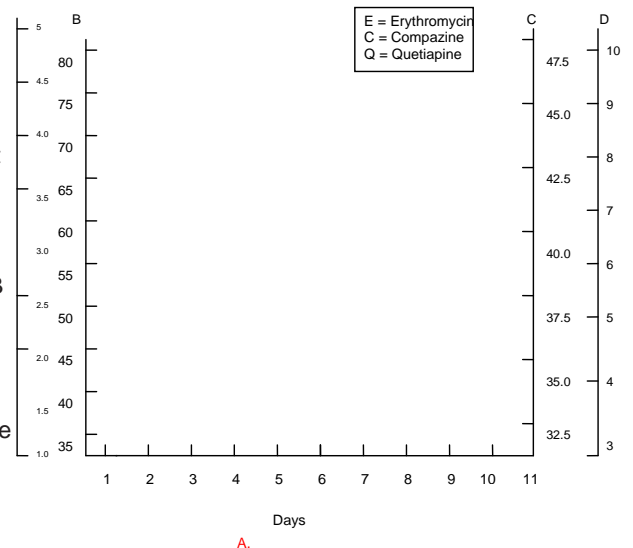
Ms. B, a 37-year-old female with a history of bipolar disorder was stable on quetiapine 300 mg/day for more than 2 years. There was no history of any blood dyscrasia, neutropenia or leukopenia. At the time of admission, patient was admitted for severe upper respiratory tract infection and routine blood counts were normal.

On day 3, Ms. B was started on erythromycin for treating her helicobacter pylori infection and metoclopramide for the nausea. The patient was getting prochlorperazine from a day earlier. Day 4, Ms. B was noted to have a decline in her white blood cell count. The total white count dropped to 3.8 K/ μ L from her baseline of 6.3 K/ μ L. The neutrophil count dropped to 42% from a baseline around 68%, with a drop in the absolute neutrophil count from baseline 4.8/ μ L to 1.2/ μ L. A psychiatry consult was called to consider quetiapine being a possible cause for the neutropenia and leukopenia. Immediately erythromycin, quetiapine, metoclopramide and prochlorperazine were stopped.

Her WBC returned to normal, with normalization of the absolute neutrophil count, on the next day. On day 5, prochlorperazine was re-started on the gastro-enterology consult service recommendation. On the same day, quetiapine was also added, at the initial dose of 300 mg/day at the bedtime. Erythromycin was not re-started. On subsequent days, the total white count, neutrophil count, absolute neutrophil count and other laboratory values stabilized and remained within the normal range. Within next 3-5 days, absolute neutrophil count came back to between 3-3.5/ μ L. The white count also, normalized to 5.3 K/ μ L. Patient's recovery was uneventful given rapid intervention and stopping of medications. During a 2 month follow-up out-patient visit, patient was still on quetiapine and had normal hematologic levels (Figure 1).

Discussion

Clozapine, olanzapine, and quetiapine can cause dose dependent myelotoxicity leading to neutropenia [8,9]. Erythromycin and prochlorperazine have also been associated with neutropenia



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Conclusion

Quetiapine and erythromycin are commonly used medications. The likely toxic interaction between them led to sudden onset neutropenia. This is further estimated to be likely based on the Naranjo probability test [15]. In this case drug interaction and adverse effects could be discovered through daily WBC monitoring which is clearly not an option in outpatient practice. In that setting only vigilance for gingivitis, fever, and sore throat would have alerted doctor and patient to the threat of neutropenia.

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