Case Report

Concomitant Use of Topiramate Inducing Neutropenia in a Schizophrenic Male Stabilized on Clozapine

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This is a case of a 23-year-old African American male with a history of paranoid schizophrenia that developed neutropenia on a clozapine-topiramate therapy. Clozapine had well addressed the patient’s psychotic symptoms, while topiramate was used as a weight-lowering agent. The patient had fairly stable leukocyte counts for eight months on clozapine 300 mg and topiramate 100 mg daily. Doubling the dosage of topiramate led to severe neutropenia after two months. Reviewing the patient’s laboratory reports showed a gradual decline of neutrophils occurring at a lower dosage, followed by a rapid decline after an increased dosage. In this case, we report that not only did topiramate act as the neutropenic agent, but also it might have done so in a dose-dependent manner.

1. Introduction

Atypical antipsychotics have been preferred over first-generation or typical antipsychotics due to their decreased extrapyramidal side effects [1]. However, they are also associated with metabolic syndrome, particularly weight gain, and clozapine has been shown to have the greatest impact on weight gain among all atypical antipsychotics [2]. A common method of countering this effect is treatment with topiramate [3]. In a 12-week naturalistic, open study to understand the benefits of topiramate in individuals suffering from schizophrenia and treated with clozapine, topiramate augmentation led to a 2.5% decrease in body weight ($P = 0.015$). A meta-analysis of nine studies examining its use in nonpsychiatric patients for treatment of obesity found a 6.5% rate of weight loss at 6 months [4]. Clozapine has also been well known to cause leukopenia, particularly neutropenia. Regular laboratory interventions are mandated when a patient is started on clozapine as per guidelines [5]. Typically, topiramate is not considered a neutropenic agent, but the effects of cotherapy on decrease in leukocytes have not been thoroughly studied or reported.

2. Case Report

Mr. S, a 23-year-old African American male with the diagnosis of paranoid schizophrenia, was hospitalized in our inpatient psychiatric hospital approximately 15 months ago. The patient had failed trials of several typical and atypical antipsychotics. Leading up to the admission, he was having religious delusions, ideas of reference, and thoughts of cutting his arm (he had lacerated his arm prior to that admission). He was displaying thought blocking and poverty of speech. His laboratory data, including complete blood count, basal metabolic profile, and thyroid function tests, were within normal limits. His urine drug screen was negative except for cannabinoids and blood alcohol level was less than 5 milligram per deciliter. Based on that, he was started on clozapine. He was discharged with a dosage of 200 mg of clozapine daily and was instructed to return to outpatient psychiatry clinic in a week. During that appointment, the patient continued to exhibit psychotic symptoms and also had gained considerable weight (345.7 pounds, body mass index of 42.7 kg/m$^2$). Subsequently, clozapine was increased to 250 mg per day for one week and to 300 mg per day thereafter. In addition, topiramate was initiated at 25 mg per day for one week and 50 mg per day for the following two weeks and then finally increased to 100 mg per day until the following appointment. Mr. S continued clozapine 300 mg daily and topiramate 100 mg daily for the following eight months, during which his WBC and ANC were within the normal range. After eight months on this regimen, his weight continued to increase (370.2 pounds, body mass index of...
There is empirical evidence of leukopenia or neutropenia resulting from clozapine and from a combination of clozapine and other psychotropic drugs [7, 8], but a search of topiramate-induced leukopenia or neutropenia is scarce. The search produced two reported cases. In one case a patient with a two-year history of being on clozapine developed leukopenia after the addition of topiramate due to concerns about weight gain. Consequently, topiramate was stopped while clozapine was restarted. The patient’s leukocyte count then returned to the normal limits [9].

A second case report described a patient with intractable partial epilepsy who developed agranulocytosis after topiramate was added to a phenytoin and acetazolamide regimen. Topiramate was decreased and eventually discontinued causing WBC to return to the normal limits [10].

Our case suggests a dose-dependent effect of topiramate when used with another leukopenic agent. Mr. S showed an upward trend in WBC and ANC during the 6 weeks prior to reaching the combination of clozapine 300 mg and topiramate 100 mg. At these doses, WBC and ANC levels gradually declined and then decreased more rapidly after topiramate was increased to 200 mg. Clozapine is mostly metabolized by CYP1A2. However, drugs that inhibit CYP2D6 are reported to elevate clozapine plasma level. There is little data about the interaction between topiramate and antipsychotic drugs. It is worth noting that topiramate has no effect on CYP1A2 and CYP2D6, which are the main metabolizing enzymes of clozapine [11].

4. Conclusion

Care should be taken when considering adding topiramate concurrently with any neutropenic agent. While the benefits of weight control may be desired, patients and their families should be counseled that the addition of topiramate to clozapine might cause decreased leukocytes or neutrophils, even if the patient has not previously had neutropenia while on clozapine. Nevertheless, if topiramate is started, the dose should be increased slowly and laboratory values monitored carefully. As established in our case report, this may be a dose-dependent effect. Dosage changes should be spaced apart enough to monitor the trends in leukocyte counts and special care should be taken when considering an increase of topiramate to 200 mg daily. An increase in frequency of complete blood count tests might be considered to provide closer attention to and changes in trends.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Authors’ Contribution

All authors contributed equally to the preparation and writing of this case report.

References

[1] American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists,


