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Risperidone-Induced Leukopenia in a Patient with Epilepsy and Sjögren's Synd- rome: A Case Report

Yi-Chun Liu*

Taichung Hospital, Ministry of Health and Welfare, Taichung, Taiwan

***Corresponding author:** Dr Yi-Chun Liu, Taichung Hospital, Ministry of Health and Welfare, Taichung City 199,sec. 1,San-Min Road, Taichung, Taiwan Tel.: +886-4-22294411; Fax: +886-4-22229517 E-mail address: purpplewhale@yahoo.com.tw

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Abstract

A-39-year-old Taiwanese man with epilepsy for 30 years and Sjögren's syndrome for 3 years was admitted for newly diagnosed psychosis. He developed leucopenia after treatment with risperidone. After risperidone was discontinued, the white blood cell (WBC) count returned to reference values. For improved symptom control, he was rechallenged with a lower dose of risperidone under close monitoring, but the leukopenia redeveloped. After a shift to paliperidone use, the WBC count gradually normalized. When prescribing risperidone, physicians should be aware of its effects on leukopenia.

Introduction

Many second-generation antipsychotics (SGAs) are associated with weight gain, hyperglycemia, and dyslipidemia, and the American Diabetes Association consensus statement recommends regular metabolic monitoring. [1] However, blood dyscrasias is a relatively rare side effect, and a complete blood count and differential count are not routinely examined, except for clozapine. [2] Only a few case reports on other SGAs, such as olanzapine [3,4] quetiapine [5,6] and risperidone [7,8] have related SGAs to leukopenia and neutropenia.

We describe a case of leucopenia and neutropenia during treatment with risperidone, antiepileptics, and lowdose disease-modifying antirheumatic drugs (DMARDs). The neutropenia resolved after the discontinuation of risperidone.

Case report

A 39-year-old man was admitted to our psychiatric acute ward with a 1-month history of sudden onset auditory hallucinations, referential delusion, and persecutory delusion. He had a history of refractory epilepsy for 30 years and Sjögren's syndrome for 3 years. The Sjögren's syndrome was diagnosed on the basis of the American-European Consensus Criteria [9]. The seizures were mostly simple partial seizures and treated with oxcarbazepine (1500mg/d), topiramate (425mg/d), levetiracetam (2500mg/d), and clonazepam (3mg/d) for 2 months. For Sjögren's syndrome, he was treated with hydroxychloroquine (400mg/d) and meloxicam (15mg/d) for 3 months. He had not taken any antipsychotic medications before hospitalization.

On admission, the laboratory assessment showed a white blood cell (WBC) count of 4.00×10⁹/L(normal range: 4.0 to 11.0×10⁹/L)and a neutrophil count of 2.05 x 10⁹/L(normal range: 1.5 to 8.0×10⁹/L). The other cell counts were within the normal ranges. The patient received risperidone at 2mg on the first day, and the dose was raised to 4mg on the second day. On day 7, laboratory tests revealed a prominent decrease in the WBC (WBC: 2.61×10⁹/L, neutrophils: 0.99×10⁹/L). There were no signs or symptoms of any acute or overwhelming infections.

Additional laboratory tests were conducted for identifying possible causes of the leucopenia and neutropenia. Vitamin B12, lactate dehydrogenase, C3, C4, and reticulocyte counts were within the normal range. Based on the temporality and disease course, side effects of risperidone and oxcarbazepine were considered. We discontinued risperidone and lowered the dosage of oxcarbazepine from 1500to 1200mg/d. Three days after risperidone was discontinued and the oxcarbazepine dosage was reduced, the leukopenia improved (WBC:3.53×10⁹/L, neutrophils: 2.05×10⁹/L). On day 10, we raised the oxcarbazepine dosage back to 1500mg/d and administered aripiprazole (30mg/d). On day 12, the WBC continued to increase (WBC:4.20×10⁹/L, neutrophils: 2.66×10⁹/L), but the psychotic symptoms responded poorly to aripiprazole. On day 13, risperidone (2mg/d) was substituted for aripiprazole. On day 17, WBC and neutrophils decreased to 3.23×10⁹/L and 1.74 x 10⁹/L, respectively. Paliperidone (3 mg/d) was administered instead of aripiprazole, and the dose was raised to 9mg 3 days later. The patient's WBC gradually normalized after the antipsychotic switch and remained normal for the rest of the hospitalization period.

Discussion

In the present case, the patient had normal range of WBC count before antipsychotics treatment. Leukopenia developed after risperidone treatment, and redeveloped after rechallenging with a lower dose. No leukopenia or neutropenia was observed with paliperidone. Based on the chronology of the treatment and the result of the rechallenge, we hypothesize that risperidone induced leukopenia in this patient.

According to previous studies, patients with Sjögren's syndrome are more susceptible to hematological abnormalities than general population. [10-12] these hematological abnormalities are known as autoimmune cytopenia, possibly related with the degree of extra-glandular or glandular organs involvement. [10-12] in this vulnerable population, certain antipsychotics use, especially risperidone, may further elevate the risk of leukopenia.

Although oxcarbazepine is a structural analog of carbamazepine, its association with hematological adverse effects is extremely rare. Among DMARDs, several drugs affect the hematological system. Hydroxychloroquine has been widely used to treat Sjögren's syndrome and is associated with rare hematologic side effects. The oxcarbazepine and DMARDs were unlikely to control the leukopenia in this patient.

Certain mechanisms of neutropenia induced by psychotropic drugs have been proposed. They include direct toxicity on the bone marrow and the formation of antibodies against hematopoietic precursors and neutrophils [2]. A few cases of risperidone-induced leucopenia and neutropenia [7,8] [13-16] and a case of paliperidone-induced leukopenia and neutropenia [17] have been reported. These case reports, except for one, did not report the results of rechallenge. [14] in that one case, the patient had a previous history of clozapine-related leukopenia, and he redeveloped leukopenia after using risperidone for weeks.

A previous report proposed that risperidone-induced neutropenia may be the direct toxic effect of unstable drug metabolites on circulating neutrophils and/or the bone marrow. [18] Paliperidone, 9-OH-risperiodne, is the primary metabolite of risperidone. In our case, paliperi done following risperidone use was not associated with leukopenia or neutropenia, indicating that risperidone itself may have direct toxic effects on the hematological system. From this case, we recommend that clinicians be aware of the possible effect of risperidone on leukopenia, especially those with susceptibility to hematologic abnormalities.

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