Case Report

Risperidone-induced Leukopenia and Neutropenia

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Background: Risperidone tends to have a lower risk of hematotoxicity. Here, we report a woman patient who developed risperidone-induced neutropenia. Case Report: A 64-year-old female patient with a diagnosis of bipolar disorder had received several antipsychotics previously, without a history of neutropenia or leukopenia. During a depressive episode with psychotic feature, she received risperidone 3.5 mg/day, lamotrigine 100 mg/day, and valproic acid 1,000 mg/day. Four weeks later, she had leukopenia (white blood cells [WBC]: 2900/mm$^3$) and neutropenia (1,131/mm$^3$) were noted in the regular laboratory test. Initially we suspected the lamotrigine was related to the neutropenia and discontinued it, and increased risperidone to 5 mg/day. Five days later, the neutrophil was further decreased to 1,015/mm$^3$, so we discontinued risperidone and switched risperidone to 5 mg/day to sulpiride 600 mg/day. Twelve days later, the WBC and differential count were returned to normal limits. Conclusion: This is the first report of risperidone-induced leukopenia and neutropenia in Taiwan.

Key words: risperidone, leucopenia, neutropenia, blood dyscrasias

Introduction

Almost all the major classes of psychotropic medications have been reported to be associated with hematological side effects, including leukopenia, neutropenia, agranulocytosis, thrombocytopenia, and anemia. But routine hematological monitoring is only required for clozapine, due to its high risk of agranulocytosis. Among the antipsychotics drugs, risperidone tends to have a lower risk of hematotoxicity. King et al. reviewed the antipsychotic-related hematological side effects and reported in the UK monitoring system between 1963 and 1996. They concluded that among 16 antipsychotics agents, clozapine and remoxipride have the highest risk of inhibiting hemopoietic production related to the aliphatic phenothiazine derivatives, and that no evidence of increased risk is noted with high-potency drugs such as haloperidol, pimozide, sulpiride, or risperidone [1]. Furthermore, Mahmood et al. suggested that risperidone may be considered as an alternative when blood dyscrasias occur with the first generation classic antipsychotics drugs. Two cases were reported to develop neutropenia and thrombocytopenia with the use of phenothiazine and butyrophenone, but the hematological condi-

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tion was improved after the antipsychotic drug was switched to risperidone [2].

Eight possible cases of risperidone-induced leukopenia and neutropenia have been noted in a literature review. But the causal relationship between risperidone and blood dyscrasias is debatable in seven cases, because five of them had a previous history of other antipsychotic-induced leukopenia [3-6] or were under concomitant clozapine treatment [3,5,6]. The sixth case was a 90-year-old man who developed leukopenia, neutropenia and pneumonia after a six-month treatment with risperidone 2 mg/day. The authors admitted that the six-month interval and the patient's age to have the causality of risperidone are questionable [8]. The seventh case was a 24-year-old female schizophrenic patient who developed leukopenia after a nine-day risperidone treatment (2-6 mg/day), but she suffered from influenza B virus infection at the same time. Therefore, the causality of a virus infection cannot be excluded [9]. Only the last case had a higher possibility of causality. In another report, an African adolescent was found to develop leukopenia 10 days after receiving risperidone therapy (4 mg/day), and leukopenia was found again with rechallenge of risperidone at 2 mg/day [10].

In summary, the case reports of risperidone-induced leukopenia and neutropenia are still limited in number. Here, we describe the first reported case in Taiwan of a patient who developed risperidone-induced leukopenia and neutropenia without previous history of blood dyscrasias.

**Case Report**

Ms. A, a 64-year-old woman patient, was admitted to the acute psychiatric ward in January 2007 with a depressive episode and mood-congruent psychosis. The admission routine blood examination showed normal white blood cell (WBC) (5,800/mm\(^3\)) and neutrophil (2,726/mm\(^3\)) counts. At admission, her medication included valproic acid 1,000 mg/day (which had been maintained for three years), and quetiapine 200 mg/day (which had been maintained for one year). Because of severe psychotic symptoms, the antipsychotics were switched to risperidone, and lamotrigine was added and gradually titrated up to 100 mg/day. Six weeks later, she was discharged in stable mental condition, and followed up at the outpatient clinic regularly with risperidone 3.5 mg/day, lamotrigine 100 mg/day, and valproic acid 1,000 mg/day. Unfortunately, four weeks later, a manic episode with psychotic features developed. She was admitted to the psychiatric acute ward again. Neutropenia and leukopenia were noted in a routine blood examination, with WBC of 2,900/mm\(^3\) and absolute neutrophil of 1131/mm\(^3\). Lamotrigine was first suspected to be related to the neutropenia because it was newly added, so it was discontinued and risperidone was increased to 5 mg/day due to the severe manic symptoms. Two weeks later, the WBC count was still at 2,900/mm\(^3\), but the neutrophil count was further decreased to 1015/mm\(^3\). Risperidone was then suspected to be related to the hematologic side effects, and was switched to sulpiride 600 mg/day. Twelve days later, the WBC count was increased to 4000/mm\(^3\), with the absolute neutrophil count up to 1680/mm\(^3\). Nineteen days later, the WBC count was further increased to 4200/mm\(^3\) and the absolute neutrophil count continued at around 1638/mm\(^3\). Throughout the course, Ms. A was clinically asymptomatic without fever, sore throat, or any infectious sign.

Tracing her past history, Ms. A had the first depressive episode when she was 22 years old, and she was admitted to the acute psychiatric unit for the first time then. Thereafter, she suffered
from the residual symptoms of dysphoric mood, pessimistic thinking, and intermittent headache off and on, causing her to be frequently absent from work, but she didn’t not require hospitalization. Her second and third hospitalizations occurred at the ages of 37 and 44 years, due to irritability and persecutory delusions regarding her colleagues. Delusional disorder was diagnosed and she received haloperidol 15 mg/day and paroxetine 20 mg/day for depressed mood. The patient had the first manic episode when she was 58 years old, with symptoms of irritability, pressured speech, decreased need for sleep, racing thoughts, increased activity, and delusions of reference. The diagnosis was revised to bipolar disorder. She had recurrent depressive or manic episodes with mood-congruent psychosis thereafter and was admitted to acute wards three times. All blood examinations during her past hospitalizations showed normal results, with WBC around 5,000 to 6,000/mm³. She had previously received several antipsychotics drugs, including haloperidol 15 mg/day for 12 years, sulpiride 600 mg/day for 10 years, flupenthixol 3 mg/day for one year, quetiapine 200 mg/day for one year and risperidone 1 mg/day for one year. Her blood routine data were not available when she received flupenthixol and risperidone previously.

The patient is still regularly followed up at our outpatient clinic. Due to the extrapyramidal side effects, her antipsychotic drugs were switched to quetiapine 600 mg/day and aripiprazole 15 mg/day. All the follow-up blood tests in 2008, 2009 and 2010 showed normal results.

**Discussion**

The patient’s leukopenia and neutropenia could be attributed to concomitant use of lamotrigine and valproic acid, which had been reported to cause blood dyscrasias [11,12]. But she had received valproic acid for more than three years with normal WBC data at that time, and discontinuation of lamotrigine did not normalize the white blood cell differential count. After discontinuing risperidone, patient’s WBC and neutrophil counts returned to normal range within 12 days. Therefore, the leukopenia and neutropenia were highly suspected to be related to risperidone.

The best way to confirm the causality of risperidone with regard to the blood dyscrasias would be to rechallenge with risperidone. But since Ms. A was a geriatric patient, it would have been inappropriate to do so for ethical reasons. However, this case report has the clinical value of reminding clinicians of the possibility of the causal relationship of risperidone and leukopenia or neutropenia, because risperidone is a continuously prescribed antipsychotic drugs.

**References**

7. Qureshi SU, Rubin E: Risperidone- and aripiprazole-


