

Sertraline induced severe neutropenia: An adolescent case with the Guillain-Barre Syndrome

Sertralin kullanımı sonrası şiddetli nötrojeni: Guillain-Barre Sendromu olan bir ergen olgu

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SUMMARY

Neutropenia, which is defined as a neutrophil count below 1500/ml, is a rare but potentially life-threatening side effect of psychotropic drugs. Neutropenia associated with sertraline, which is a selective serotonin reuptake inhibitor (SSRI) antidepressant, has been reported in only five case reports so far. We report a 16-year-old adolescent male diagnosed with Guillain-Barre Syndrome who developed severe neutropenia during treatment with sertraline for his depressive and anxious symptoms.

Key Words: Neutropenia, Agranulocytosis, Sertraline, Antidepressants, Drug-Related Side Effects and Adverse Reactions

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ÖZET

Psikotrop ilaçların nadir fakat potansiyel olarak yaşamı tehdit eden bir yan etkisi olan nötrojeni, 1500 /ml altındaki nötrofil sayısı olarak tanımlanmaktadır. Seçici bir serotonin geri alım inhibitörü (SSRI) antidepresanı olan sertralin ile ilişkili nötrojeni, şimdiye kadar sadece beş vaka raporunda bildirilmiştir. Guillain-Barre Sendromu tanısı olan, depresyon ve anksiyete belirtilerine yönelik sertralin tedavisi kullanımı ile şiddetli nötrojeni geliştiren 16 yaşında bir ergen olgu sunulmuştur.

Anahtar Sözcükler: Nötrojeni, Agranülositoz, Sertralin, Antidepresanlar, İlaç ilişkili Yan Etkiler ve Advers Reaksiyonlar

INTRODUCTION

Neutropenia, defined as a neutrophil count below 1500/ml, is a relatively common disorder most often due to chemotherapy, adverse drug reactions, or autoimmune diseases (1). Severe neutropenia or agranulocytosis, defined as an absolute neutrophil count of less than <500/ml, is uncommon but can cause morbidity and mortality from infections. Drug-induced neutropenia is a rare but potentially life-threatening side effect of psychotropic drugs such as clozapine, the phenothiazines, and the tri- and tetracyclic antidepressants (2). Selective serotonin reuptake inhibitors (SSRI) have been rarely associated with possible neutropenia. There are limited case reports of neutropenia due to sertraline in the literature (3-7). The Guillain-Barre syndrome (GBS) is an acute monophasic illness causing a rapidly progressive polyneuropathy with weakness or paralysis. Guillain-Barre syndrome is thought to result from an immune response to a preceding infection that cross-reacts with peripheral nerve components because of molecular mimicry (8). We report here an adolescent male patient in the chronic phase of the Guillain Barre Syndrome who developed neutropenia possibly related to sertraline treatment.

CASE REPORT

A 16-year-old boy diagnosed with Guillain-Barre syndrome two years ago was hospitalized for physical rehabilitation and decubitus ulcer treatment. He was treated with teicoplanin 400 mg/day and ceftriaxone 1000 mg/day to treat decubitus ulcers for three weeks. He was consulted with us from the physical medicine and rehabilitation inpatient clinic for increased fatigue, anxiety, and depressive symptoms. Given psychiatric symptoms, sertraline was started at 25mg/day, which was increased to 50 mg/day after five days. When sertraline treatment started, he had not been on the antibiotic treatment for three days. Before sertraline treatment was initiated, complete blood count parameters were within the normal range as follows: TLC (Total Leukocyte Count) was 4610/ml, DLC (Differential Leukocyte Count) showed 53.7 % neutrophils, 28.9 % lymphocytes, and 11.7 % monocytes. After eleven days of sertraline treatment initiation, his TLC was found to be 2760/ml, DLC showed 34.4 % neutrophils, 36.2% lymphocytes, and 20.3 % mono-

cytes. Absolute neutrophil count (ANC) was 950/ml, suggestive of neutropenia. Hemoglobin level, platelet counts were normal, and peripheral smear did not reveal any other abnormality. After 24 days of sertraline use, his TLC was found to be 1210/ml, DLC showed 6.6 % neutrophils, 77.7 % lymphocytes, and 15.7 % monocytes. Absolute neutrophil count (ANC) was 80/ml, suggestive of severe neutropenia. In this period, he had no medication except sertraline. The hematologist did physical and laboratory examinations to find probable reasons that may cause neutropenia and not found any reason. Finally, consultation liaison psychiatry was consulted for the use of sertraline, a rare cause of neutropenia. It was hypothesized that neutropenia is due to sertraline, and it was stopped on the 24th day of treatment. When The Naranjo Adverse Drug Reactions Probability Scale (NADRPS) is applied to our case, the adverse event was 6 indicating a "probable" reaction to sertraline (9, 10). After three days of discontinuation of sertraline, his ANC was 176/ml. Given severe neutropenia and associated high risk of infection, he was prescribed subcutaneous Filgrastim (granulocyte colony-stimulating factor) 30 MIU/day for three days following which his cell counts recovered to a TLC was 6.130/ml and an ANC of 3770/ml. We applied cognitive-behavioral therapy (CBT) for his mild anxiety and depressive symptoms, and another antidepressant treatment was not started. After discharge from the hospital, we continued CBT sessions for internalizing symptoms.

DISCUSSION

Severe Neutropenia (Agranulocytosis) is a rare side effect of psychotropic agents that may cause morbidity and mortality. Amongst psychotropic drugs, antipsychotics, including clozapine, olanzapine, and phenothiazines such as chlorpromazine, barbiturates, benzodiazepines antiepileptics/mood stabilizers are the most common causes of neutropenia and agranulocytosis (1). Severe neutropenia due to the tricyclic antidepressants (TCAs) is a rare idiosyncratic reaction, with a lower frequency than is reported for antipsychotics. Agranulocytosis has also been reported in treatment with tetracyclic antidepressants such as mirtazapine (2,11). Neutropenia with SSRIs, commonly used in children and adolescents for psychiatric treatment, is a scarce adverse effect. This is the first case

report of sertraline induced neutropenia in adolescence to the best of our knowledge. An 11-year-old girl who was treated with sertraline and quetiapine was reported in the literature (3). There are only four published case reports of neutropenia due to sertraline in adult patients, and one of them describes neutropenia due to combined use of sertraline and quetiapine (4-7). Neutropenia has also been reported in treatment with fluoxetine and paroxetine in adult patients (12-14). Drug-induced neutropenia usually emerges after 1 or 2 weeks of exposure; the neutropenia level develops depending on the duration and dose of drug exposure. Several mechanisms have been proposed for hematological side effects of psychotropic agents. Idiosyncratic factors could be one of the major mechanisms. Other possible mechanisms could be direct toxicity and immune-mediated destruction of neutrophils, and their precursors in bone marrow (15-17). There are no precise mechanisms and approaches regarding hematological side effects to sertraline.

Treatment of drug-induced neutropenia involves stopping the drug immediately, initiating a broad-spectrum antibiotic, and granulocyte colony-stimulation factor in high-risk patients (18). In our patient, we stopped the sertraline treatment due to severe neutropenia and gave subcutaneous Filgrastim (granulocyte colony-stimulating factor)

for three days. Our patient had no fever, so antibiotic treatment was not given to him. Another antidepressant treatment was not planned, and CBT was applied to him for mild internalizing symptoms.

Sertraline is a preferred antidepressant agent with low side effects. The most common side effects are dizziness, drowsiness, dyspepsia, fatigue, insomnia, nausea, headache, diarrhea (19). Although hematological side effects related to sertraline are rare and more associated with an increased tendency to bleeding, neutropenia is a potentially life-threatening adverse effect of sertraline treatment (1,15). Our case may contribute to the limited existing knowledge about the hematological adverse effects of sertraline in children and adolescents. Drug-induced neutropenia must be considered in a patient with sertraline use who has unexplained neutropenia. Severe neutropenia induced by psychopharmacological agents may interfere and complicate the treatment process of people with chronic diseases.

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