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Case Report / Olgu Sunumu

Neutropenia Related to Sertraline Treatment: a Case Report

Rukiye Ay[1]

[1]Malatya Training and Research Hospital, Department of Psychiatry, Malatya - Turkey

ABSTRACT

Neutropenia related to sertraline treatment: a case report

Sertraline is a selective serotonin reuptake inhibitor (SSRI) with antidepressant and anxiolytic properties. Hematological adverse effects related to sertraline are rare. Drug-induced neutropenia is a rare but fatal condition. Patients may present with non-specific symptoms like fever, shivering, sore throat, or muscle and joint pain. Even though the condition is hard to diagnose, an early detection is essential. In this article, we present a male patient with neutropenia related to sertraline treatment.

Keywords: Antidepressant, neutropenia, obsessive compulsive disorder, sertraline

ÖZ

Sertralin kullanımıyla ilişkili nötropeni: Bir olgu sunumu

Sertralin, antidepresan ve anksiyolitik özellikleri olan seçici serotonin gerialım inhibitörü (SSGI) grubundan bir antidepresandır. Sertraline bağlı hematolojik yan etkiler nadirdir. İlaca bağlı nötropeni gelişimi nadir ancak ölümcül bir tablodur. Hastalar ateş, titreme, boğaz ağrısı, kas ve eklem ağrısı gibi nonspesifik semptomlarla başvurabilir. Tanı koymak zor olsa da zamanında tanınması çok önemlidir. Bu yazıda sertralin kullanımı sonucu nötropeni gelişen erkek hasta sunulmuştur.

Anahtar kelimeler: Antidepresan, nötropeni, obsesif kompulsif bozukluk, sertralin

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Address reprint requests to / Yazışma adresi:
Rukiye Ay,
Malatya Training and Research Hospital,
Department of Psychiatry, Malatya - Turkey

Phone / Telefon: +90-422-326-1569

E-mail address / Elektronik posta adresi:
rukiyeayy@gmail.com

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INTRODUCTION

Sertraline is an serotonine reuptake inhibitor (SSRI) antidepressant with antidepressant and anxiolytic properties. It is indicated in the treatment of several psychiatric disorders such as major depressive disorder, obsessive-compulsive disorder (OCD), and post-traumatic stress disorder (1). Sertraline causes a highly selective and potent serotonin reuptake inhibition and has a minimal effect on the reuptake of noradrenaline and dopamine. Sertraline is a preferred antidepressant due to its low adverse effect profile. The most common adverse effects are nausea, headache, dry mouth, diarrhea, insomnia, and dizziness (2). Hematological adverse effects related to sertraline are rare.

In this article, we present a male patient with neutropenia related to sertraline treatment.

CASE

We report a 45-year-old male patient who had been under follow-up due to OCD for nine years. A complete blood count was performed by the department where the patient was admitted with complaints of a sore throat, muscle pain, and fatigue. As the white blood cell (WBC) was 1260/mm^3 and neutrophil count was 150/mm^3, the patient was referred to the outpatient department of psychiatry. The anamnesis revealed that the patient had been using sertraline (150mg/day) for eight months and he

was in remission. According to his medical history, he had used antidepressants like fluvoxamine, paroxetine, and clomipramine and he had to discontinue these drugs because of adverse effects such as fatigue, constipation, and dry mouth but he had not suffered from neutropenia during these treatments. There was no physical disorder, tobacco and alcohol consumption, nor any other legal or illegal drugs in his medical history except sertraline. The dose of sertraline was reduced to 50mg/day and the patient was referred to the hematology department, where physical and laboratory examinations did not detect any physical disorder, liver damage, infection, or blood dyscrasia that might have caused the condition. As the only drug used was sertraline, we concluded that it was the causal factor. The score on the Naranjo adverse drug reaction probability scale for our case was 5 points, indicating a probable association between neutropenia and sertraline treatment. In order not to interrupt a high-dose treatment suddenly, we decided to drop the dose first to 50mg/day and to discontinue it completely if neutropenia were to persist. A blood analysis carried out on the 3rd day after dose reduction found a WBC of 2230/mm^3 and a neutrophil count of 350/mm^3; the analysis on the 8th day resulted in a WBC of 7780/mm^3 and a neutrophil count of 5190/mm^3. As the neutrophil level was increased and continued within normal levels in spite of the continuation of the sertraline treatment with a dose of 50mg/day, we did not recommend the discontinuation of the drug. Given that the patient had no fever, we also did not initiate antibiotic therapy. The patient continued to use sertraline with a dose of 50mg/day in the last month and he is still in remission with no detected neutropenia in the blood examinations.

DISCUSSION

Neutropenia is defined as a neutrophil count of less than 500/mm^3 or a drop from an initial count of less than 1000/mm^3 to less than 500/mm^3 within 24-48 hours (3). Neutropenia is a condition commonly encountered during the use of chemotherapeutic agents. Drug-induced neutropenia is rarely fatal except in chemotherapy. The prevalence in the population is 2.4-15.4%. It develops within weeks to months after the initial administration of the drug and the mortality rate is approximately 5.0% (4).

Drugs that most commonly cause neutropenia are mesalamine, ticlopidine, prednisone, methimazole, sulfasalazine, clozapine, carbamazepine, chlorpromazine, and mirtazapine (5).

Although certain SSRI antidepressants (fluoxetine, paroxetine, and sertraline) are selected in clinical use as they cause fewer side effects, neutropenia cases are nevertheless reported also during the use of these agents.

A 45-year-old female patient was under the treatment of fluoxetine (60mg/day) with a diagnosis of OCD and presented at the hospital because of a respiratory tract infection in the 6th month of therapy. Following the determination of neutropenia in the blood count, fluoxetine was discontinued. Neutrophil count recovered in the first week after the discontinuation of the drug (6). Similarly, neutropenia developed in our patient with OCD in the 8th month of the sertraline treatment.

Paroxetine with a dose of 20mg/day was initiated in a 38-year-old patient 6 months previously, and as the complaints of the patient did not improve, the dose was increased to 40mg/day. However, the dose was dropped again to 20mg/day because of the emergence of hypomania. Paroxetine treatment was discontinued due to the emergence of neutropenia in the 6th month of the therapy. The neutrophil count increased to the normal level after 6 weeks (7). Although the duration of the dose of 40mg/day was not stated in this case report, it can be considered as a case of a high-dose SSRI administration. Similar to our case, this case also developed neutropenia in the 6th month after the initiation of the paroxetine treatment.

In another case report, sertraline treatment (50mg/day) was initiated in a 73-year-old female patient due to a diagnosis of depressive disorder. The treatment was discontinued in the 4th week due

Table 1: Literature on drug-induced neutropenia

Author	Age	Gender	Drug name	Potion	Time in therapy when neutropenia developed	Time after discontinuation of the drug until neutropenia recovered
Bavle (2012) (6)	45	F	Fluoxetine	60mg/day	6th month	1 week
Moselhy and Conlon (1999) (7)	38	F	Paroxetine	40-20mg/day	6th month	6 weeks
Trescoli-Serrano and Smith (1996) (8)	73	F	Sertraline	50mg/day	4th week	1 week
Ozcanli et al. (2005) (10)	44	F	Mirtazapine	30mg/day	3rd week	2 weeks

to the emergence of agranulocytopenia. Following treatment with a granulocyte stimulating factor, the blood count recovered on the 7th day (8). With aging, the metabolism of the drugs may change as a result of an impairment of the liver tissue, liver functions, and hepatic blood flow. Furthermore, regarding the renal functional capacity, the glomerular and tubular functions decrease also with aging (9). Although neutropenia emerged in this patient with a low-dose sertraline treatment, considering her age, a high-dose effect of sertraline might have occurred due to the impairment of the drug metabolism.

A 44-year-old female patient received mirtazapine treatment (30mg/day) with the diagnosis of a depressive disorder. The treatment was discontinued due to the emergence of neutropenia in the 3rd week of the treatment. The blood neutrophil levels recovered to the normal level in two weeks. As the patient's complaints related to the depressive disorder did not improve, sertraline was initiated with a dose of 50mg/day and no adverse effects were observed during the follow-up. The investigators of that case discussed the different mechanisms of the antidepressants from different classes affecting the bone marrow (10).

Several mechanisms have been suggested for the emergence of neutropenia during drug treatment. These mechanisms include the immunological destruction of granulocytes or granulocyte precursor cells, dose-dependent suppression of granulopoiesis, and toxic effects on myeloid precursor cells or directly on the bone marrow. Several hematologists suggested that different mechanisms act together (11). Although the effects of the drugs on the neutrophils could not yet be elucidated, mechanisms being considered are the direct triggering of antibody production due to a hapten-like action of the drugs and the destruction of neutrophils because of auto-antibody production against the proteins attached to neutrophils or against the metabolites of the drugs (12). With current methods, these antibodies cannot be detected, as these drug-induced antibodies against neutrophils have a complex structure and the sensitivity of the available tests is low. Patients may present with fever, shivering, sore throat, or muscle and joint pain. Although diagnosis is difficult, early detection and timely management are essential for the reduction of mortality (4). In our case, we carried out a complete blood count due to complaints of sore throat, muscle pain, fatigue, and common cold and determined neutropenia.

Treatment of drug-induced neutropenia includes immediate discontinuation of the drug, initiation of a broad-spectrum antibiotic, and giving granulocyte colony-stimulation factor in high-risk patients (13). In our patient, we reduced the dose of the drug and referred him to the hematology department. As the patient had no fever, we did not initiate antibiotic treatment.

During sertraline treatment, which is commonly selected by clinicians, the patient should be closely monitored especially during high-dose treatments. The possibility of the development of neutropenia, even though it is a rarely encountered adverse effect, should be considered, detected at an early stage, and treated immediately in order to decrease mortality.

Contribution Categories		Author Initials
Category 1	Concept/Design	R.A.
	Literature review	R.A.
	Data analysis/Interpretation	R.A.
	Case follow-up (if applicable)	R.A.
Category 2	Drafting manuscript	R.A.
	Critical revision of manuscript	R.A.
Category 3	Final approval and accountability	R.A.
Other	Technical or material support	R.A.
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