Leukopenia as side effect of paroxetine

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Leucopenia como efecto secundario de la paroxetina

Paroxetine is a selective serotonin reuptake inhibitor (SSRI) with a known side effects profile. Leukopenia may occur more with certain psychodrugs (clozapine, chlorpromazine, thioridazine, carbamazepine)[1] than with paroxetine. This side effect may sometimes be more likely found in the combination of two psychotropic drugs: i.e. clozapine plus risperiodone or haloperidol or paroxetine.

We present herein the case of a female patient who had leukopenia secondary to the use of paroxetine as treatment of her major depression. The patient is 35 years old, married, the younger of two sisters, who works as health care staff in a hospital. She came to the mental health center of Arganda in March 2002 due to uneasiness, concentration difficulty and repercussion in her professional work.

She was anxious, with depressive symptoms of sadness, apathy, lack of interest in life, hopelessness and suicide ideation. She was diagnosed of anxious-depressive disorder and treated with paroxetine (20 mg/d) and bromazepam 1.5 mg free times day

At two months, she still suffered anxiety, concentration deficit, low self-esteem and personal questioning. The paroxetine dose was increased to 40 mg/day and then in October to 50 mg. In addition, benzodiazepine was changed to alprazolam extended release 0.5 mg, 1 tablet every 12 hours. In January of the following year, leukopenia was discovered in a routine analysis. Evaluated by the hematologist, the possibility of paroxetine as causal factor was commented on. As this side effect is very rare, we waited for another evaluation by hematology. In March, this was confirmed and paroxetine was discontinued, maintaining alprazolam.

In May, the cause of the leukopenia was ratified when the leukocyte values became normal with the suspension of paroxetine (table 1). At the same time, the alternative diagnosis of chronic idiopathic leukopenia was ruled out.

The patient has no known drug allergies, no diabetes mellitus or HBP. She suffers hypercholesterolemia that is being treated by diet. Ex-smoker since 3 years ago. The physical examination showed no abnormality. She had

TABLE 1. Blood analyses performed in several periods

Date	*Red blood cells*	*Hb*	*Leukocytes*	*Neutrophils*	*Platelets*
Dec. 2002	3.92		3,500/mm^3	1.63 (46%)	
Apr. 2003	3.5	11.5 g/dl	3,800/mm^3	1.82 (48%)	174,000/mm^3
May 2003	3.93	13 g/dl	4,700/mm^3	48%	210,000/mm^3

no infections or morphological abnormalities in peripheral blood (MCV, ALT, AST, alkaline phosphatase, gamma-GT, glucose, Na, K and ferritin).

Other analysis performed were negative for: CMV, Epstein Barr, hepatitis C Ab, hepatitis B Ag, HIV negative, antinuclear Ab, C-reactive protein, rheumatoid factor, anti-DNA Ab, anti-ENA I Ab, antithyroglobulin and antimicrosomal antibodies and thyroid hormones.

Until March 20th of this year when the antidepressant was discontinued, her usual treatment was: paroxetine, 50 mg day; alprazolam, 0.5 mg extended release every 12 h, and omeprazole, 20 mg/day. Paroxetine was discontinued in 6 days.

It was possible to verify how leukopenia recovered after the discontinuation of paroxetine and the platelets increased, although thrombocytopenia had not previously developed.

Few references are found in the literature regarding the association of paroxetine with leukopenia, it being observed more when it was added to clozapine[2-4]. However, it seems that the increase of clozapine blood levels and its metabolite (that occurs in the interactions with SSRI, and with greater increase with paroxetine[3], does not affect the risk of agranulocytosis, but rather other side effects such as sedation, seizures and hypertension[5,6]. On the contrary, other authors do not associate paroxetine-leukopenia[7] and attribute the risk of suffering leukopenia to the interaction with clozapine and the consequent increase of its blood levels[4]. This was normalized with the withdrawal of the neuroleptic, maintaining paroxetine.

However, neutropenia was not observed in other studies in which these drugs were associated[8]. Two other cases of neutropenia were detected in the association of paroxetine with lamotrigine[9].

Leukopenia has also been observed with paroxetine without association with other drugs[10-13]. It was moderate in one case, with no involvement of the bone

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marrow and no clear relationship with paroxetine[10]. On the contrary, leukopenia and neutropenia were observed in two other cases with the use of this antidepressant, and there was early recovery of the white blood series with the interruption of paroxetine[12].

A severe hepatic reaction, with increase of hepatic enzymes and leukopenia was seen in a patient who took 60 mg of paroxetine combined with low doses of lithium and tricyclic trimethroprin as added treatment[12]. With the discontinuation of paroxetine, the hepatic reaction disappeared and the white blood series became normal.

The case that we present coincides with the literatures regarding the disappearance of leukopenia when paroxetine is discontinued. No symptoms associated to this leukopenia were detected, but rather the abnormality was discovered in a routine analysis. We ignore the latency period from the treatment onset to the establishment of the leukopenia and if this is dose-dependent. In our case, it occurred with a 50 mg dose and at 10 months of the onset of the treatment. However, the product's data sheet speaks about leukopenia as a side effect having a very low frequency, less than 1/10,000 (< 0.01 %)[14]. It also refers to thrombocytopenia as a very rare side effect. In this case, we observe how the platelet amount improves when paroxetine is discontinued, but without previously developing thyrombocytopenia.

In conclusion, we show a clinical case of leukopenia associated to paroxetine, that became normal after paroxetine was discontinued.

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