Letter to the Editor

To the Editor,

Interferon alfa has antiviral, anti-proliferative and immunomodulatory effects. Treatment with interferon is related to many psychiatric side effects like depression, depressive mood, suicidal thoughts, irritability, tiredness, cognitive impairment, mania and psychosis\(^1\). These psychiatric side effects are related to duration and dose, and when severe, usually lead to discontinuation of interferon treatment.

CASE

Our case study is a 17-year-old male patient. Due to frequent crying, suicidal thoughts and feelings of guilt, he was hospitalized. He had been diagnosed with chronic hepatitis B four months previously, and had been receiving 30 MIU interferon alfa 2b three times a week plus 100 mg lamivudine. Depressive symptoms like lack of interest and mental dullness began after 8 weeks of treatment. On psychiatric examination, he showed slumped posture, dullness and slowed speech. Thought content included delusions of being harmed and guilt. His affect was depressed and sometimes dysphoric. He showed decreased appetite and sleep and slowed psychomotor activity. Routine hematological and biochemical test results were normal. His cranial MR and EEG revealed no pathology. On the first day of his hospitalization, interferon and lamivudine treatment were discontinued.

The patient was diagnosed with depressive disorder with psychotic features, and escitalopram 10 mg and risperidone 3 mg p.o. were started. When the patient developed incontinence and rigidity, the risperidone was discontinued and biperiden and lorazepam were started. During the first week of hospitalization, signs of parkinsonism disappeared and 5 mg olanzapine was started for psychotic symptoms while escitalopram 10 mg was continued. Due to extrapyramidal symptoms from the olanzapine, the drug was discontinued. In the second week of hospitalization, psychotic symptoms continued, and aripiprazole 5 mg per day was given. No side effects were observed during the 3\(^{rd}\) week of hospitalization. The escitalopram and aripiprazole doses were increased to 15 mg and 10 mg per day, respectively. In the 4\(^{th}\) week of hospitalization, the patient’s psychotic symptoms improved and his escitalopram dose was increased to 20 mg per day to treat continuing depressive symptoms. In the 7\(^{th}\) week of hospitalization, the patient was discharged with significantly improved depressive symptoms and normal liver enzymes.

It is known that interferon has direct effects on the central nervous system, especially on the microglia. Although some theories are being discussed, the exact mechanism that leads to depression associated with interferon utilization remains unclear. During treatment with interferon, a sudden increase in cortisol, epinephrine, norepinephrine, cytokines IL-1 and IL-6, and decreases in tryptophan levels have previously been observed\(^2\). Each of these changes is similar to mechanisms that lead to depression. From studies of psychotic depression, it has been observed that interferon modulates many neurotransmitters in the brain (serotonin,
Is interferon-induced psychotic depression associated with extra-pyramidal sensitivity?

In some cases, extrapyramidal side effects have been reported related to low dose atypical antipsychotic use for psychotic symptoms developed after the use of interferon\(^1\). Acute dystonia, parkinsonism, and psychomotor retardation occurring after interferon injections have been viewed as related to dopaminergic changes due to the interferon\(^1\). In this patient, interferon-induced extrapyramidal side effects may have occurred secondary to activation of hypersensitivity in his dopaminergic system. However, extrapyramidal side effects may also be associated with the complex structure of dopaminergic synapses\(^3\). Furthermore, in a study in rats, the effects of interferon on the dopaminergic system have been clearly demonstrated\(^5\). In our case, using risperidone 3 mg/day at the beginning of treatment could be considered a high dose for a young person. Consequently, the occurrence of extrapyramidal side effects might have been expected. Extrapyramidal side effects due to the use of olanzapine 5 mg/day are rare. In these cases, the use of aripiprazole, which has a partial agonist structure for dopamine, has an important place.

Our study indicates the importance of the use of low dose antipsychotics with minimal dopaminergic effects in the treatment of psychotic symptoms due to interferon therapy. This is because of the risk of extrapyramidal side effects, like parkinsonism related to the dopaminergic system, occurring despite the low dosage of antipsychotic drugs.

References:


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This letter was accepted for publication in November 6, 2014.

Declaration of interest:
I.T., S.S., B.B.G., A.I., O.D., R.A., A.N.B.: The authors reported no conflict of interest related to this letter.