

## A Case of Major Depression due to Interferon $\alpha$ Therapy

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**ABSTRACT.** Interferons have potential therapeutic applications in viral infections and cancer, but they cause many side effects including influenza-like symptoms, bone marrow suppression, bacterial infections, and psychiatric symptoms. The spectrum of psychiatric side effects is wide and includes irritability, anxiety, depression, and frank delirium. We report here a case of major depression due to interferon  $\alpha$  therapy. The patient was a 48-year-old man who had acute type-C hepatitis. After three months of interferon  $\alpha$  therapy (first two weeks 3 MU daily and the remaining weeks 3 MU every other day) he experienced major depression. Though the interferon  $\alpha$  therapy was discontinued, his psychiatric symptoms remained. We suggest that when treating patients with interferon, physicians should be alert to symptoms of major depression and that study of the biological characteristics of interferons may help explain the mechanisms of major depression. And we have to take care of psychiatric side effects on treatment of interferon therapy.

**Key words:** interferon  $\alpha$  — major depression

The interferons are a family of proteins that share antiviral, immunomodulatory, and antiproliferative actions. They appear to play important roles in resistance to and recovery from viral infection. However, their role in metabolism, growth, and homeostasis is unclear. In recent years, interferons have been used in the treatment of acute and chronic viral illnesses, malignant diseases, and immunologic deficiency states.

It is known that psychiatric side effects are caused by interferon therapy.<sup>1,2)</sup> However, there are little reports of major depression due to interferon. We describe here a case of interferon therapy which caused a major depression.

### CASE REPORT

The patient was a 48-year-old married man and a computer expert who had acute type-C hepatitis and a history of alcoholic hepatitis. He visited a clinic and received interferon  $\alpha$  therapy. After eight weeks of interferon  $\alpha$  therapy (first two weeks 3 MU daily and the remaining six weeks 3 MU every other day), he suffered insomnia. He was taking benzodiazepines before sleeping, but they were not effective. However, the interferon  $\alpha$  therapy was continued for four more weeks (3 MU every other day). After interferon  $\alpha$  therapy was stopped, he became depressed and agitated, and experienced a decreased appetite and inhibition of thoughts. He could not continue working

and his psychiatric symptoms became worse. He expressed the desire to commit suicide. He visited Kawasaki Medical School Hospital and was immediately admitted to the psychiatric ward.

On admission, the patient slept only a few hours a night and often woke up in the early morning, unable to get back to sleep. He had little appetite, and he had lost perhaps 5 kg in weight over the past few months. He reported a profound loss of energy and severe agitation. He complained of feelings of self-reproach or guilt, and mentioned thoughts of death or suicide. He did not speak except to give occasional monosyllabic answers to the interviewer's questions. His physical examination and liver function were normal (GOT 11, GPT 29,  $\gamma$ -GTP 8). He was diagnosed as suffering from major depression due to interferon  $\alpha$  therapy. He was started on a regimen of antidepressants, maprotiline 75 mg/day and trazodone 150 mg/day. Benzodiazepines, alprazolam 1.2 mg/day and bromazepam 15 mg/day, were used to treat his severe agitation and anxiety.

During his first four weeks in the hospital, the patient showed severe agitation and virtually no interest or pleasure in any activities and he spent most of the time sitting on his bed. At the end of the fourth hospital week, he was sleeping and eating well, and able to watch television and read a newspaper. However, he still displayed anxiety and loss of energy. During the eighth hospital week, the patient began to experience improvement in his energy level, and by the end of twelfth week, he was gradually smiling and talkative.

During the fifth month after admission to the hospital, the patient was discharged and returned home. After discharge, he visited a psychiatric clinic, on a maintenance regimen of some tricyclic antidepressants, because a slight loss of energy continued. On questioning he did not mention thoughts of death or suicide. However approximately one year after his discharge, the patient suddenly committed suicide by hanging.

## DISCUSSION

Interferons cause so-called "bone marrow suppression" with leukopenia, thrombocytopenia, and anemia, and also influenza-like symptoms including fever, chills, fatigue, lethargy, and headache.<sup>3,4)</sup> A previous paper reported that psychiatric side effects of interferon therapy occurred in less than 20% of patients.<sup>1)</sup> The spectrum of psychiatric side effects is wide and includes irritability, anxiety, depression, and frank delirium. Previous papers reported that psychiatric side effects including depressive mood of interferon therapy were caused by organic brain disturbance. Hirota *et al*<sup>5)</sup> reported that two cases of transient psychotic symptoms observed during interferon therapy for chronic hepatitis and Chikasawa *et al*<sup>6)</sup> also reported that two cases of chronic active hepatitis accompanied with psychiatric symptoms during interferon therapy. These reports said that psychiatric symptoms were exogenous reaction type. Mattson *et al*<sup>7)</sup> observed severe but reversible psychiatric symptoms that were also documented by characteristic alterations in EEG after iv infusion of interferon in patients with lung cancer. Smedley *et al*<sup>8)</sup> reported that ten patients with breast cancer showed psychiatric side effects and had increasing slow wave in EEG during treatment of interferon. Thus, psychiatric side effects

were considered due to organic brain disturbance.

The depression associated with interferon therapy represents a more severe form of the symptom complex described in previous papers.<sup>1,2)</sup> It is difficult to fit "depression" pathophysiologically into the context of organic mood syndrome or major depression because many of the other criteria for depression are commonly seen in patients receiving interferon who do not show depressed effects, such as fatigue, sleep disturbance, decreased appetite, weight loss, decreased libido, inhibition of thoughts, and memory loss. Nonetheless, the patient may become profoundly depressed, even suicidal, while receiving interferon. When interferon  $\alpha$  therapy was discontinued, our patient had all of the characteristic symptoms of major depression of the DSM-III-R criteria.<sup>9)</sup> He was persistently depressed, felt worthless, had trouble concentrating, had lost weight, had difficulty sleeping, and had thoughts of death or suicide.

Thus, on admission he was diagnosed to be suffering major depression. In the present case, the patient's major depression was due to interferon  $\alpha$  therapy. The mechanisms of depression have not been clarified. Interferon  $\alpha$  is a depression inducing substance, like reserpine.<sup>10)</sup> Therefore, study of the biological characteristics of interferons may help explain the mechanisms of depression in the not too far distant future. And we have to take care of psychiatric side effects on treatment of interferon therapy.

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