

Interferon-Alpha Induced Obsessive-Compulsive Disorder in a Patient with Hepatitis-C

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ÖZET:

Hepatit-C'li bir hastada interferon-alfa ile tetiklenen obsesif kompulsif bozukluk

Interferon alfa (IFN- α) immün yanıt üzerindeki uyarıcı etkileri nedeniyle viral hepatit tedavisinde yaygın olarak kullanılmaktadır. Literatürde interferon alfa tedavisinin neden olduğu depresyon, mani ve psikoz gibi psikiyatrik yan etkiler oldukça iyi belgelenmiş olmasına rağmen interferona bağlı obsesif kompulsif bozukluğa dair çok az veri bulunmaktadır. Bu yazıda Hepatit C için interferon tedavisi almakta iken obsesif kompulsif bozukluk ve depresyon geliştiren 59 yaşında bir kadın olgu sunulmaktadır. Bu yazı interferon tedavisinin erken periyodunda psikiyatrik belirtilerin düzenli izlemi ve erken tedavi girişimi için disiplinlerarası işbirliğinin önemi vurgulanmaktadır.

Anahtar sözcükler: Interferon-alfa, obsesif kompulsif bozukluk, hepatit C enfeksiyonu, psikiyatrik ters etkiler

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ABSTRACT:

Interferon-alpha induced obsessive-compulsive disorder in a patient with Hepatitis-C

Interferon alpha (IFN- α) is commonly used in the treatment of viral hepatitis because of its stimulating effects on the immune response. While psychiatric adverse effects such as depression, mania or psychosis that arise during interferon alpha treatment have been well documented in the literature, the data regarding interferon-induced obsessive-compulsive disorder is rare. The case of a 59-year-old woman, who developed obsessive compulsive disorder and depression during interferon treatment for hepatitis C is presented here. This paper emphasizes the importance of regular monitoring and early treatment intervention for psychiatric symptoms and interdisciplinary collaboration during the course of interferon therapy in the early treatment period.

Keywords: Interferon-alpha, obsessive-compulsive disorder, hepatitis C infection, psychiatric adverse effects

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INTRODUCTION

Interleukin 2 (IL-2) or a combination therapy with ribavirin and pegylated interferon- α (IFN α) are currently used as standard treatment regimens in selected patients with chronic hepatitis C. Neuropsychiatric side effects such as depression, anxiety and mania are especially common with regimens that include IFN α or pegylated IFN α and they contribute to the morbidity and mortality associated with these therapies for hepatitis C. Because 10-20% of patients discontinue the

treatment due to neuropsychiatric side effects, there is a growing interest for a better understanding of possible pathogenic mechanisms¹. A dysfunction of serotonergic neurotransmission is discussed as an essential pathogenic factor of obsessive-compulsive disorder. Interestingly, there are few data in the literature concerning the possibly increased occurrence of obsessive-compulsive symptoms in the course of treatment with interferon. As far as we know, there exist only two case studies by Mavrogiorgou² and DeRosse et al.³. DeRosse

describes the initial manifestation of obsessive-compulsive disorder in a 53-year-old hepatitis C patient undergoing treatment with interferon. Mavrogiorgou describes the development of obsessive-compulsive symptoms in a 23-year-old malignant melanoma patient for the first time during interferon therapy after excision of the cancer tissue.

We present here the case of a 59-year-old female, who developed obsessive-compulsive disorder and major depression induced by interferon treatment for chronic hepatitis C.

CASE

This is the case of a fifty-nine year-old female patient, suffering from hepatitis C for 12 years. In 2001, during an admission to the department of internal medicine due to fatigue and widespread body pain, chronic hepatitis C was diagnosed. Interferon-alpha (3x5 IU once per week) was started. Although a one year treatment with interferon-alpha was planned, after 8 weeks treatment was stopped due to fever and fatigue. The patient had also psychiatric complaints such as intrusive thoughts about sacred values. After stopping the interferon therapy all these symptoms disappeared. The patient has been followed up twice in a year at Uskudar State Hospital since 2001. In 2012 September, 1st grade hepatic steatosis was identified in a routine hepatobiliary ultrasound. Abdominal tomography and the examination of a liver specimen showed diffuse parenchymal coarsening and interferon-alpha therapy was planned. During the first two months therapy for the patient included a total of peginterferon-alpha 2a (180 mcg/week) treatment administered subcutaneously. Initially the patient experienced undesirable effects such as headache, chills, nausea, emesis, fatigue and myalgia which could be relieved by antiemetic and analgesic medication. At the beginning of the interferon treatment neuropsychiatric status of the patient was normal. There were no indications of obsessive-compulsive disorder. In the second week

of treatment, the patient began to experience uncomfortable thoughts intruding on her about swearing to God and the prophet. In order to get rid of the fear coming along with these thoughts, she had repented and read prayers several times, all day long. She eventually told her primary clinician about her complaints after having additional sleep problems, sadness, passive thoughts of death, a general feeling of being a sinner, and an increasing anxiety of not being able to do household chores anymore. The patient was referred to the psychiatry outpatient clinic of Uskudar State Hospital after cessation of two month-long interferon therapy. A milnacipran HCl 25 mg/day treatment regimen was started and was increased up to 100mg/day after one month. While the depressive symptoms had subsided in two months, the obsessive compulsive symptoms resisted. Sulpiride 50 mg/day was added to the treatment regimen but the symptoms remained unresolved. In the last month preceding admission to the Erenkoy Training and Research Hospital for Psychiatric and Neurological Disorders, despite continued treatment, complaints of inability to do household chores, weight loss (6-7 kg) and fear of loneliness and insomnia were added. There was no characteristic event in her psychiatric history. She has had diabetes mellitus type 2 for 1 year and has been used insulin. There was no other drug use and no history of head injury or seizure disorder.

In her mental state examination; decreased self-care and psychomotor activity, depressive affect, depressed mood, reduced speech rate, amount and graduation were noted. Her speed of thought was decreased and in her thought content there were intruding thoughts of rebellion against God and swearing and in the form of fears of inability to control her thoughts. She displayed compulsions in the form of continuous praying, Salawat had to bring and avoidance behavior.

Her primary personality showed cheerful and talkative traits. Laboratory parameters, except for AST (SGOT): 77 IU/L (5-34), ALT (SGPT): 112 IU/L (0-55) and GGT: 220 U/L (125-243), were within the normal range. The Porteus Maze test showed mild

mental retardation (IQ: 66). Brain magnetic resonance images were interpreted as normal.

Initially we evaluated the patient's clinical picture as interferon-induced severely pronounced obsessive compulsive disorder (Y-BOCS=32) and a moderately severe depressive episode (HAM-D score=26, CGI=5). We then started treatment with sertraline 25mg/day, milnacipran 50mg/day and lorazepam 2.5 mg/day. Milnacipran was stopped and sertraline was initiated in a cross-tapering manner and the dose of sertraline was titrated up to 100 mg/day by the 12th day of hospitalization. Because hyperglycemia was observed on follow-up of the patient in the ward, an internalist was consulted and insulin doses were reorganised. During the clinical interviews with the patient her affect was depressive, rate of speech was slow, tone of speech was low and she complained of guilt because of religious obsessions in her thought content. By the end of the second week, the HAM-D score was 22 and laboratory parameters, except for AST (SGOT): 79 IU/L (5-34), ALT (SGPT): 100 IU/L (0-55) and GGT: 194 U/L (125-243), were within the normal range. At the end of the third week, it was decided to implement ECT because of the patient's resistant depressive complaints. The patient underwent 6 sessions of ECT and the depressive symptoms decreased significantly. The HAM-D score was 14 and Y-BOCS score was 20 by the end of the fifth week. The obsessive thoughts of the patient had subsided, which enabled her to gradually stop her compulsive and avoidant behaviors. In the following 2 months, the patient showed no further deterioration of obsessive compulsive and depressive symptoms and continued sertraline treatment and behavioral therapy.

DISCUSSION

The underlying mechanism of action of interferon has not been fully explained, however, the relevant literature provides several clues that interferon affects tryptophan metabolism and serotonergic neurotransmission². Apart from changes regarding hormones as well as

neurotransmitters such as serotonergic deficits, an induction of immunological parameters including cytokines may be involved in the pathogenesis of the psychiatric side effects of IFN α . Since interferon cannot pass through the blood-brain barrier, it has been suggested that this is an indirect effect^{2,3}. Interferon treatment brings about anxiety symptoms in approximately 10-20% of patients. Anxiety often tends to develop in the first stage of a high dose parenteral alpha-interferon treatment and becomes more frequent and severe over time. The present case indicates that obsessive-compulsive symptoms in the form of obsessive thoughts and compulsive acts may occur with interferon treatment in viral hepatitis C as well as depressive symptoms. In the case study by DeRosse et al.³ obsessive thoughts with hypochondriac content (fear of falling ill with asbestosis) and excessive compulsion to wash and clean continued to exist after initial manifestation with varying degrees of severity even during longer interferon-free periods. Similarly, in the case of our patient obsessive-compulsive symptoms appeared for the first time soon after initiation of therapy with interferon (in the second week) and continued even after discontinuation of treatment, although we finally achieved almost complete remission of obsessive-compulsive symptoms. Our patient's obsessive-compulsive symptoms mostly recovered after 3 month-long antidepressant and cognitive behavioral therapy.

Mavrogiorgou² described a case of interferon treatment in malignant melanoma that demonstrated initial manifestation of obsessive-compulsive symptoms, which occurred in the first stage of a high-dose parenteral interferon-alpha treatment and achieved complete remission of obsessive-compulsive symptoms in the further course of treatment.

According to several studies psychiatric side effects of interferon alpha are reversible after cessation of therapy^{4,5}. In our case, at the beginning, depressive symptoms and obsessive-compulsive symptoms remained constant in severity despite discontinuation of interferon treatment. According to results of a prospective

study by Gohier et al. depression and anxiety show a high incidence both during interferon alpha therapy for hepatitis C and also after treatment is discontinued⁶.

Researchers have showed that interferon-induced anxiety and depression respond to serotonergic antidepressants, but other antidepressants might also be effective^{5,7}. It has been suggested that antidepressants might also be used as prophylactic agents⁵ but there is no standard practice in this regard. It has been reported that benzodiazepines may help manage interferon-induced anxiety, offering more rapid anxiolysis. However, use of benzodiazepines in

patients with a history of substance abuse (which is very high among hepatitis C patients) requires caution, owing to their addictive potential⁸.

This paper emphasizes the importance of regular monitoring and early treatment intervention for psychiatric symptoms during the early stages of interferon treatment, since occurrence of serious psychiatric symptoms may lead to termination of interferon therapy⁹.

In conclusion, interferon therapy has been increasingly used for several medical conditions and interdisciplinary collaboration should be established for these kinds of treatment modalities.

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