Development of Different Psychiatric Manifestations during Antiviral Therapy for Chronic Hepatitis C

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Abstract:

Pegylated interferon and Ribavirin are the treatment backbone for chronic hepatitis C and may favour the development of psychiatric symptoms. These adverse events may reduce treatment adherence and are a risk factor for its failure. The recent experts' recommendations of European Association for the Study of the Liver, suggest monitoring psychiatric manifestations on a regular basis during the antiviral treatment but the frequency of psychiatric controls sometimes might be insufficient. We present a particular case of a young woman without psychiatric history, who developed different mood and behavioural disturbances during antiviral therapy, that required an intensive psychiatric monitoring and supportive psychotherapy.

Key words: Hepatitis C, Interferons, Antiviral Agents, Ribavarin, Psychotherapy.

Introduction

Psychiatric symptoms, among which depression, can occur during treatment with pegylated interferon-alpha (Peg-IFNα) and Ribavirin (RBV) in patients affected by chronic hepatitis C (CHC) [1,2,3]. In addition to mood change, this treatment can be also associated with a wide range of other psychiatric symptoms that are further complicated by emotional influence of stressful conditions [4,5]. These adverse events are the main reason for a poor adherence to treatment and early discontinuation [6,7]. It is generally accepted that patient's psychiatric and psychological condition should be monitored during peg-IFNα/RBV therapy to detect treatment related changes at they first appearance. The recent recommendations by the European Association for the Study of the Liver (EASL), suggest monitoring mood changes every 4 weeks for the first 3 months, then every 12 weeks until the end of therapy [8].

Here we present a case of a young woman, without any history of psychiatric disorders, who developed different mood and behavioral disturbances during antiviral therapy and required an intensive psychiatric monitoring and supportive psychotherapy.

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Received: January 14, 2014 | **Accepted:** March 27, 2014 | **Published Online:** April 25, 2014

Conflict of interest: None declared | **Source of funding:** Nil | **DOI:** http://dx.doi.org/10.17659/01.2014.0033

Case Report

This is the case of Mrs. F, a 26 year old Italian woman who was diagnosed as having chronic HCV infection in year 2000 with a positive family history of liver disease. She had a history of thrombocytopenia, atopic dermatitis as well as alimentary and inhalants allergies. She was a modest smoker. She had a negative history of hypertension, diabetes, drug addiction and alcohol consumption. No specific symptoms other than fatigue were referred. Her virological profile was characterized by HCV-RNA positive (169,000 IU/mL) genotype 1, subtype b. Hemoglobin level was 12.5 g/dL and body mass index 20.5. The liver biopsy showed mild necro-inflammatory activity and mild portal tract fibrosis (Ishak score: grading 4 and staging 2) [9]. Her personal history was negative for either psychiatric disorders or psychopharmacotherapy, but her mother had suffered from major depression. In October 2010, antiviral treatment was started with a weekly subcutaneous peg-IFNα at a dose of 180 µg along with a daily oral dose of 1000 mg of RBV.

After 4 weeks of treatment, she was evaluated by the hepatologist at the out-patient clinic when she complained of dyspepsia and irritability, but refused psychiatric counseling. After 12 weeks, she reported itching and worsening of fatigue; her psychological conditions seemed to get worse. In particular, she suffered from persistent irritability, growing anxiety and nightmares. These symptoms were no longer tolerable and she agreed to start a psychiatric counseling. The psychiatrist diagnosed a Not Otherwise Specified Personality Disorder and an interferon-induced psychiatric disturbance according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV TR) [10].

She started psychopharmacotherapy with alprazolam (0.25 mg in need) and weekly psychiatric surveillance. At the second psychiatric visit (13th week), the patient had a moderate depression with dysphoria, moderate to severe irritability, mild hostility and insomnia and abnormal sleep-wake clock cycle. Sertraline, 50 mg per day, was added at this point. As the psychiatrist believed that the symptoms induced by antiviral treatment were also influenced by psychological factors, psychotherapy was started. During the first session the patient referred a series of symptoms and concerns with insufficient acceptance of the situation.

She felt like a different person and didn't recognize herself any more. Family dynamics seemed to get worse, and F did not know how to manage the situation. Furthermore, she showed different emotional states, but cannot rationally explain what was happening. As a whole, she had no expectations on the effectiveness of psychotherapy.

At the 24 weeks control visit, asthenia was further deteriorated and nutritional disorders (loss of appetite and dysgeusia) also appeared. She referred a subjective perception of improvement in psychiatric symptoms.

During the psychotherapy sessions, F referred working difficulties, pessimistic outlook that aggravated anxiety, premature awakenings and insomnia with one hour and half of sleep per night. Additionally, she also complained of moments of confusion with cognitive function deterioration (especially concerning the short-term memory). The psychiatrist prescribed flurazepam 15 mg per night that was switched to zolpidem 10 mg per night after sleep improvement.

After 36 weeks of therapy, the patient referred increased irritability, anxiety, insomnia and frequent headaches. A neurological evaluation was then performed, from which no clinically relevant

findings emerged. Panic attacks also started to occur in closed spaces. Her hematological profile showed a marked anemia with hemoglobin level 9.7 g/dL. Levosulpiride was added to the therapy (40 mg twice daily). In the following period, F reported an episode of delirium, and she got so scared by those symptoms that she wanted to discontinue the antiviral treatment. Psychopharmacotherapy was further enhanced (Alprazolam up to 0.50 mg in need, Sertraline up to 125 mg daily, Levosulpiride up to 56 mg daily, Zolpidem up to 15 mg for night) and an intensive supportive approach was undertaken for 8 weeks, allowing to continue the antiviral treatment. At week 40, the psychiatric symptoms had gradually improved. The patient completed her 48 weeks of antiviral therapy, and finally achieved a sustained virological response through the 24 post-treatment weeks, being cured from CHC.

Discussion

Interferon, which is used for the treatment of several conditions, such as CHC, multiple sclerosis, melanoma, myeloma or lymphoproliferative disorders, can induce or exacerbate psychiatric symptoms and unmask subclinical psychopathological conditions. Therefore, the need for a psychiatric monitoring is mandatory whenever interferon is used.

This report presents the case of a patient with CHC who developed psychiatric symptoms during peg-IFNα based therapy. Interestingly, this patient did not present any baseline clinical feature that could somehow predict the occurrence of psychiatric symptoms under treatment, outlining once more the need that clinicians always pay attention to the mental health of patients undergoing interferon-based treatments. However, the presence of particular personality traits and subclinical psychiatric conditions, as it likely was the case with our patient, may escape the clinical evaluation by the hepatologist alone, and would make it appropriate that every patient candidate to receive interferon is subject to psychiatric screening before therapy. On this respect, we would like to outline that although the recent European expert consensus statement [8] emphasizes the importance of a multidisciplinary approach in the management of antiviral therapy, yet the need of screening for mental disorders by a psychiatrist prior to treatment with interferon is not clearly emphasized.

Our patient developed different psychiatric symptoms, thus confirming that not only mood changes can occur during interferon treatment, but also a variety of symptoms whose etiology is not always clear. Indeed, if some symptoms seem to be caused by its direct effects, others might have a purely psychological matrix. Namely, in some patients, peg-IFNα induces marked deterioration of several capabilities (such as: work ability, social skills and self-care) which are fundamental to maintain a healthy psychological state. Mrs. F firstly developed irritability, then anxiety, depressed mood, insomnia, loss of appetite, panic attacks and, finally, an episode of delirium. As a consequence, she needed a cognitive constructivist psychotherapy to empower her psychological general condition.

This clinical case represents a good example of a patient that, without an intensive psychiatric and psychological support, would have discontinued the therapy, losing the ability of being cured. In fact, the adherence to treatment was undermined several times with risk of a drop-out. Thus, once more the importance of a multidisciplinary patient-centred approach, including an expert psychiatrist and a psychotherapist, emerges quite clearly.

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