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Case Report

Interferon Side Effects: When Somatization Betrays You - A Case Report

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Abstract: Neuropsychiatric symptoms are widely reported in association with both hepatitis C and IFN α treatment [1] its sequelae, and its treatment. In particular, interferon, a primary component of treatment for chronic hepatitis C, has been strongly associated with depressive symptoms. This review summarizes current knowledge about the etiology, course, and treatment of neuropsychiatric problems associated with hepatitis C and interferon alpha (IFN-alpha and lead to discontinuation of interferon in up to 13% of cases [2]. When on interferon treatment, cognitive, affective and behavioral symptoms are not easily distinguished from each other or from depression [2,3] mechanism, course, and treatment of neuropsychiatric problems associated with interferon alfa (IFN-alpha. The challenge is even higher if in somatoform cases. We describe a case of somatoform disorder while on classic therapy for hepatitis C and discuss the management of the patient main complaints and evolution.

Keywords: Interferon; side Effects; Somatization; Hepatitis C Virus

Introduction

Neuropsychiatric symptoms are widely reported in association with both hepatitis C and IFN α treatment [1] its sequelae, and its treatment. In particular, interferon, a primary component of treatment for chronic hepatitis C, has been strongly associated with depressive symptoms. This review summarizes current knowledge about the etiology, course, and treatment of neuropsychiatric problems associated with hepatitis C and interferon alpha (IFN-alpha and lead to discontinuation of interferon in up to 13% of cases [2].

During both acute and chronic stages of hepatitis C, cognitive, affective and behavioral symptoms are frequently reported (60-20%). When on interferon treatment, these symptoms are not easily distinguished from each other or from depression [2,3] mechanism, course, and treatment of neuropsychiatric problems associated with interferon alfa (IFN-alpha. Beside these, almost all patients who are treated with IFN- α experience an acute flu-like syndrome hours af-

ter the initial injection. Only after a few weeks of treatment, fatigue, malaise, apathy, cognitive and behavioral changes commonly develop.

Neurological side effects appear in 1/3 of patients during IFN- α therapy [3] mechanism, course, and treatment of neuropsychiatric problems associated with interferon alfa (IFN-alpha. Peripheral neuropathy including demyelinating polyneuropathy related to IFN is extremely rare [2]. IFN- α 2a showed to have caused peripheral sensory neuropathy given for a period of twenty months [2] and we know that some patients develop antibodies to peripheral nerves antigens during treatment, but its pathogenicity has not been proved.

Neuropsychiatric symptoms like mania and hypomania are considered a rare occurrence. Yet, an European study found that 20% of patients receiving pegylated IFN α plus ribavirin for HCV developed manic and hypomaniac symptoms at some point during the 24 weeks of treatment [4]. To ease diagnostic skills some authors pointed out some possible

risk factors for psychiatric side effects of IFN- α : dose and application form (intravenous > intramuscular > subcutaneous), older age, organic brain injury or dysfunction, drug and alcohol abuse, HIV infection, depression, a premorbid personality or a personality disorder [3].

The majority of these disturbances disappear with cessation of IFN- α . However in some patients serious affective or psychotic symptoms persist for many months despite adequate therapy [3]. Clinicians should be aware of the challenge of diagnosing [5].

To our knowledge this is the first somatoform disorder described while on peginterferon based therapy for hepatitis C.

Case Report

A 47-year old woman followed at our clinic with a history of drug addiction, depression, and co-infection HCV (genotype 3a) / HIV1 stage B2 with virological suppression for many years, under tenofovir+emtricitabine and lopinavir/r. She had a moderate fibrosis (METAVIR score F2) and began treatment with peginterferon alpha2b (1.5 μ g/kg/wk) and ribavirin (800mg/daily).

In the first weeks of treatment she complained of sleep disturbances, anxiety and flu-like syndrome. Starting from this point she assumed alprazolam 1mg bid and fluoxetine 20mg id with apparent symptomatic control.

Rapid clinical and virological responses were achieved. At week 15 she emerges with tingling, numbness and weakness, complaining of a right lumbar paresthesia and paresis of the ipsilateral lower limb, with inbalance and falls. On the initial neurological examination she had a right crural hemiplegia (proximal and distal segment), flabby tonus but with brisk and symmetrical osteotendinous reflexes, cutaneoplantar reflex bilaterally in flexion, plain anesthesia to touch, pinprick test and temperature sensation, and no proprioceptive sensitivity. Surprisingly, she had a positive Hoover maneuver making more likely the suspicion of somatization. However, she couldn't walk by herself, using a wheelchair. Brain CT, lumbar and dorsal MRI, cerebrospinal fluid and electromyography were normal. She still complained about her lack of locomotion and, within one week, she developed inappropriate behavior, with verbiage and persecutory ideas.

Her laboratory tests included a normal blood count, chemistry profile and C-reactive protein. Antinuclear and antiganglioside antibodies, rheumatoid factor, serum crioglobulin level, Epstein-barr and cytomegalovirus serology were tested negative. Immunoelectrophoresis for monoclonal antibodies in cerebrospinal fluid, thyroid function and B12 vitamin were normal. Organic causes were excluded and the psychiatric evaluation and workout, concluded for a somatoform disorder and psy-

chosis. Peginterferon alpha2b and ribavirin were suspended at week20. She was submitted to physiotherapy and optimization of psychiatric therapy (aripiprazole 15 mg/day) that she kept for one year round and gradually recovering humor (currently controlled) and sensitive and motor pseudo deficits (now recovered). By now she has a sustained virological response.

Discussion

In 2015 we have access to multiple highly effective, tolerable and safe antivirals for the treatment of hepatitis C virus (HCV) infection. We are able to forego the use of interferon- α (IFN α) and, for many patients, ribavirin is no longer needed. Neuropsychiatric symptoms management implies dose reduction and discontinuation of interferon that can be effective for mania, depression and other interferon-related neuropsychiatric syndromes, but when the psychopathology is severe or persistent, pharmacotherapy with psychotropic agent is necessary [3]mechanism, course, and treatment of neuropsychiatric problems associated with interferon alfa (IFN-alpha. Mania, especially when severe, is a clinical emergency. Under close monitoring and adequate treatment mania doesn't necessarily require discontinuation of IFN therapy. If mania is severe or difficult to control, IFN should be discontinued, but resuming antiviral treatment should be considered after remission of mania symptoms [3]mechanism, course, and treatment of neuropsychiatric problems associated with interferon alfa (IFN-alpha. Generally, neuropsychiatric symptoms seem to improve 3 to 4 days after the dose of conventional IFN therapy is reduced, although compromising optimal dosing and efficacy. Therefore, current evidence supports managing the patient without changing the IFN dose in order to optimize treatment outcome [5]which can significantly compromise epidemiological virus control. This review summarizes current knowledge about the etiology, course, and management of neuropsychiatric symptoms in patients with CHC.\n\nMETHOD: Studies were identified using computerized searches, with further references obtained from the bibliographies of the reviewed articles.\n\nRESULTS: Psychopathological syndromes that occur during interferon-alpha treatment frequently have atypical features that may complicate their recognition using standard diagnostic criteria. In addition, prospective studies in this area often exclude patients with psychiatric disorders and have methodological disparities that make it difficult to develop guidelines for management of psychiatric side effects induced by interferon-alpha. Despite the high prevalence of chronic hepatitis C virus (HCV. Our patient had typical complains related to IFN side effects during treatment. The last five weeks were ultimately decisive to the suspension of the therapy, not only because we were thinking about a peripheral neuropathy, that surprisingly was somatization not widely described, but also for the process of mania that was a psychiatric emergency. However, she completed 20 wk of therapy without relapse of the disease and recovered the deficits.

Coinfected persons appear to have a greater number of somatic concerns than do persons with HIV or HCV infection alone. However, coinfecting persons do not report more neuropsychiatric symptoms or higher prevalence of other psychiatric disorders than do mono-infected persons.

Nowadays, there is a growing consensus about the importance of diagnosing and treating depressive and anxious symptoms in all patients being considered for IFN treatment, even when the symptoms are subclinical, as well as the need to regularly assess for such symptoms during treatment [5] which can significantly compromise epidemiological virus control. This review summarizes current knowledge about the etiology, course, and management of neuropsychiatric symptoms in patients with CHC.

METHOD: Studies were identified using computerized searches, with further references obtained from the bibliographies of the reviewed articles.

RESULTS: Psychopathological syndromes that occur during interferon-alpha treatment frequently have atypical features that may complicate their recognition using standard diagnostic criteria. In addition, prospective studies in this area often exclude patients with psychiatric disorders and have methodological disparities that make it difficult to develop guidelines for management of psychiatric side effects induced by interferon-alpha. Despite the high prevalence of chronic hepatitis C virus (HCV), patients should be screened regularly for depression during the first six months of IFN therapy. Monitoring every 2-4 weeks during the first 3 months of hepatitis treatment appears sufficient for identifying patients who may require psychiatric intervention [3].

mechanism, course, and treatment of neuropsychiatric problems associated with interferon alpha (IFN-alpha).

Learning points

- Neuropsychiatric symptoms are widely reported in association with both hepatitis C and interferon- α (IFN α) treatment and lead to discontinuation of interferon.
- Patients proposed for IFN therapy should be screened regularly for depression during the first six months of IFN therapy. Monitoring every 2-4 weeks during the first 3 months may be sufficient for identifying patients who may require psychiatric intervention.
- Somatoform disorders are not easy to diagnose under IFN therapy. Although, the majority of neuropsychiatric disturbances disappear with cessation of IFN- α , however in some subjects serious affective or psychotic symptoms may continue for many months despite adequate therapy.

References

1. E. Dieperink, M. Willenbring, S. B. Ho. "Neuropsychiatric symptoms associated with hepatitis C and interferon alpha: A review." *Am. J. Psychiatry.* 2000, 157(6):867-876.
2. J. Y. J. Wu, B. Shadbolt, N. Teoh, A. Blunn, C. To et al. "Influence of psychiatric diagnosis on treatment uptake and interferon side effects in patients with hepatitis C," *J. Gastroenterol. Hepatol.* 2014, 29(6): 1258-1264.
3. Y. R. Al-Huthail, "Neuropsychiatric side-effects of interferon alfa therapy for hepatitis C and their management: a review." *Saudi J. Gastroenterol.* 2006, 12(2): 59-67.
4. C. L. Raison, M. Demetrashvili, L. Capuron, A. H. Miller, "Neuropsychiatric adverse effects of interferon-alpha: recognition and management." *CNS Drugs.* 2005, 19(2): 105-123.
5. R. Quelhas, A. Lopes. "Psychiatric problems in patients infected with hepatitis C before and during antiviral treatment with interferon-alpha: a review," *J. Psychiatr. Pract.* 2009, 15(4): 262-281.