Case Report

Bell's Palsy Associated with Chronic HCV Infection Before and During Peginterferon Alfa and Ribavirin Therapy

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Abstract

Neuropsychiatric side effects of peginterferon-α (PEG-IFN-α) therapy consist of a large spectrum of symptoms. Organic personality syndrome, organic affective syndrome, psychotic manifestations and seizures are more common side effects of PEG-IFN-α whereas cranial neuropathy and movement disorders are less common. Bell's palsy is often idiopathic, but has been linked to some viral infections, particularly with herpes viruses. Other infections, such as human immunodeficiency virus infection and Lyme disease, may also lead to idiopathic facial paralysis. Neither acute nor chronic Hepatitis C infection has been implicated previously in Bell's palsy, but PEG-IFN-α may play a role. Two patients with CHC who developed Bell's palsy before and during treatment with PEG-IFN-α and Ribavirin are presented here.

Keywords: facial nerve palsy, HCV, interferon

Introduction

There is ample evidence that the central nervous and the neuroendocrine systems can influence the immune system, which can in turn influence the brain activity. Also, experiments have revealed that endogenous cytokines play a critical role in the pathophysiology of many diseases including the diseases of the nervous system. Neuropsychiatric side effects of Interferon-alpha therapy, as an exogenous cytokine, consist of a large spectrum of symptoms. Interferon-alpha have been used in thousands of patients, so that the information accumulated with this group of closely related products is essential to delineate the potential and severity for non-immunological, but largely immune-mediated adverse effects to develop in patients treated with immuno-activating agents. Organic personality syndrome, organic affective syndrome, psychotic manifestations and seizures are more common side effects of PEG-IFNα whereas cranial neuropathy and movement disorders are less common.[1]

Facial paralysis has numerous etiologies ranging from the most common, Bell's palsy and trauma, to rare tumors and congenital anomalies. Some authors divide the etiologies of facial paralysis into five major classifications: idiopathic, traumatic, infectious, neoplastic and neurologic. Bell's palsy is often idiopathic, but has been linked to some viral infections, particularly with herpes viruses.[2] Other infections, such as human immunodeficiency virus infection and Lyme disease, may also lead to idiopathic facial paralysis. Neither acute nor chronic Hepatitis C (CHC) infection has been implicated previously in Bell's palsy, but PEG-IFNα may play a role.[3]

First-line therapy for Hepatitis C Virus (HCV) infection comprises interferon-alpha (IFN-α), pegylated or non- pegylated forms, and ribavirin for 6 or 12 months. Mild complications of therapy are common, but more serious complications are rare. There are few case reports of idiopathic facial paralysis (Bell's palsy) during therapy, with spontaneous resolution after withdrawal of treatment. Large-scale cohort studies reveal that IFNs are associated rarely with neurologic complications, and only one previous report has linked IFN-alpha therapy and Bell's palsy.[3]

Here, we present two patients with CHC who had evidence of Bell's palsy before and during treatment with PEG-IFNα and Ribavirin, respectively.

Case reports

Case presentation 1

The first patient was a 29-year-old male, an Ex- Injection Drug User (Ex- IDU), with history of alcohol consumption and smoking of about 20 pack years of cigarettes.

Physical examination revealed that the patient had a blood pressure of 125/80 mmHg, pulse rate of 78 beats/ minute, respiratory rate of 14/min, and a weight of 82 kg with a BMI of 25.9.

Laboratory results were as follows:

- Quantitative HCV RNA: 119000 IU/mL; genotype 3a
- Hepatitis B surface antigen (HBs Ag): negative
- HIV antibody (HIV Ab): negative
- Aspartate transaminase (AST) 105 IU/mL Alanine transaminase (ALT) 208 IU/mL, Alkaline phosphatase (ALP) 249 IU/mL
- Thyroid stimulating hormone (TSH): negative
- White blood Cell Count (WBC) 7100 cells/mm^3; Hemoglobin (Hb): 18 g/dL; platelet count: 216000 cells/mm^3
- Liver biopsy: grade 8/18 and stage 2/6 in Ishak nodular score.

The remainder of the patient's history, physical examination and lab data were within normal limits.

Therapy was initiated with PEG-IFN-α2b (Pegaferon[4]; 120 microgram/week) and Ribavirin (800 mg/day). Two weeks after starting the combination therapy, the patient began to manifest symptoms of loss of muscle tone in the right side of his face to the extent that he was not able to completely close his right eyelid. Following a neurologist consultation and after initial workups, the patient was prescribed vitamin B1 (100 mg/day) for 30 days and recommended to continue anti- HCV therapy.

The patient finished the 24 weeks of HCV-therapy without incident and achieved ETR and SVR at the end of week 24 and six months after treatment cessation, respectively. His facial paralysis resolved after one month and no further problems were noted at the one year post treatment follow up.

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Case presentation 2

Our second patient was a 53-year-old male whose positive HCV serology was noted while he was evaluated for skin lesions which eventually were diagnosed as lichen plan. The patient was a former alcohol drinker, Ex- IDU and cigarette smoker, but he did not have symptoms of diabetes or other co-existing diseases. His physical exam was notable for weight of 68 kg and a body mass index of 21.

The patient's laboratory results were as follows:

- Quantitative HCV RNA1745000 IU/mL; HCV genotype 1a
- HBs Ag: negative
- HIV Ab: negative
- AST 28 IU/mL, ALT: 35 IU/mL, ALP: 171 IU/mL
- TSH: 0.9 (0.2 – 5)
- WBC 6200 cells/mm^3; Hb 16.1 g/dL; platelet count 154000 cells/mm^3
- Liver biopsy: grade 6/18 and stage 2/6 in Ishak nodular score

The remainder of the patient's history, physical examination, and lab data were unremarkable.

Just prior to HCV treatment he showed decreased muscle tone in the left side of his face; the extent of which he was not able to close his eyes and lips completely. A diagnosis of Bell's palsy was made on consultation with neurologists. Work up for other causes of facial palsy was negative for other underlying illnesses, except HCV infection. HCV therapy was stopped and a seven-day course of acyclovir with a tapering dose of prednisone 50 mg/d was initiated within three days of the onset of symptoms. His symptoms improved in about ten days and then therapy with PEG-IFN-α2b (Pegaferon;180 micrograms/week) and Ribavirin (1000 mg/day) were initiated. The patient did not exhibit similar symptoms during treatment. Therapy lasted for 48 weeks. He achieved partial Early Viral Response (pEVR), End- of- Treatment Response (ETR), and finally Sustained Viral Response (SVR).

Conclusion

Bell's palsy is an idiopathic deficit of the seventh cranial nerve, usually peripheral, with an incidence of approximately 23 in 100,000 annually.[5] The crude annual incidence of Bell's palsy was 15.2 and 13.1 per 100,000 population in The Greater Toronto Area (GTA) and Nova Scotia studies, respectively.[6] The average annual incidence of Bell's palsy per 100,000 in Rochester, Minnesota for 1968 through 1982 was 25.0 for both sexes combined; crude rates for males and females were 22.8 and 26.9, respectively based on 85 males and 121 females.[7] The incidence of facial palsy is about 50 per 100000 annually in Switzerland.[8]

There seems to be an association between hepatitis B and idiopathic facial paralysis. In addition, cytomegalovirus might contribute to the development of Bell's palsy in some cases. Further studies are required to confirm this data.[9]

It is possible that Bell's palsy occurs secondary to two mechanisms in HCV patients under treatment with interferon therapy: first, due to a viral infection that occurs as a result of immunosuppression caused by interferon therapy; and, second, as a direct effect of the interferon therapy. However, the paucity of reports of this neuropathy occurring with interferon treatment argues against interferon-α therapy causing a direct toxic effect. These cases serve to underscore the need for further research into the interaction between interferon and immune system activating agents.[10]

Here, we report the clinical course of two patients with chronic HCV infection who developed Bell's palsy before and during anti-HCV therapy with PEG- IFN-α2b and Ribavirin.

PEG- IFN, together with Ribavirin, is the current treatment regimen for chronic HCV. Large studies have shown that flu-like symptoms and reversible hematological cytopenia are common side effects of this treatment regimen, more serious side effects are rare. However, neuropsychiatric symptoms such as depression or anxiety have been commonly seen during IFN treatment. There are also reports of IFN therapy leading to ischemic optic neuropathy, retinopathy, peripheral neuropathy, oculomotor neuropathy and trigeminal sensory neuropathy.[1] The underlying mechanisms involved include autoimmunity or neurotoxic effects of IFN on the neuroendocrine system and neurotransmitters.

Although the exact mechanisms and causality are not well understood for reported associations between HCV and anti-HCV medications, especially those with interferon and Bell's palsy further investigation is needed to confirm these associations. Physicians however, should be aware of these rare neurotoxic effects.

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