Reversible bilateral ototoxicity in a patient with chronic hepatitis B during peginterferon alpha-2a treatment

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ABSTRACT

Peginterferon alpha-2a (PEG IFN α-2a) is frequently used in chronic hepatitis B (CHB) treatment. Numerous adverse events can be noted during this therapy such as flu-like disease, rash, weight loss and depression. However, PEG IFN α-2a related ototoxicity seems to be an uncommon entity. Ototoxicity can be detected objectively by audiometry. In this paper, we present a case of CHB who developed reversible bilateral ototoxicity during PEG IFN α-2a treatment. Due to ototoxicity detected objectively by audiogram, treatment was ceased at sixth month and ototoxicity completely recovered one month after stopping the drug.

KEY WORDS: Adverse event, chronic hepatitis B, ototoxicity, Peginterferon alpha-2a

Introduction

Peginterferon alpha-2a (PEG IFN α-2a) is a common treatment for chronic hepatitis B (CHB) infection. PEG IFNs are immunomodulatory drugs which can cause many adverse events such as flu-like disease, rash, weight loss and depression.1,2 However, audiologic adverse events are uncommon (1%).3-5 Interruption or cessation of PEG IFN treatment may sometimes be required due to serious adverse events.

During our literature review, we could identify a limited number of reports dealing with vestibular and audiologic adverse effects of PEG IFNs. In this paper, we present a CHB case who developed bilateral ototoxicity during PEG IFN α-2a treatment which was completely reversible on drug withdrawal.

Case Report

A 41-year-old woman presented to outpatient clinic with complaints of severe fatigue and malaise. Her physical examination, past medical history and family history were normal. Laboratory values were as follows: Complete blood count within normal limits, glucose: 115 mg/dl, BUN, creatinine, lipid panel, electrolytes, alkaline phosphatase, gama glutamil transferase and bilirubin levels were all within normal ranges.

AST: 16 U/L, ALT: 10 U/L, HBsAg: Positive, HBeAg: Negative, AntiHBe: positive and HBV DNA: 46.010 IU/ml. Abdominal ultrasound showed a single 15 × 10 mm sized hemangioma in the right lobe of liver and splenomegaly (135 mm). In liver biopsy with modified Ishac scoring system, hepatitis activity index was 5 and fibrosis score was 3. She was diagnosed with CHB and PEG IFN α-2a 180 μg treatment once weekly was iniated.

At two month of PEG IFN α-2a therapy, our patient complained of bilateral tinnitus and hearing loss. At this stage, otorhinolaryngologist was consulted and audiological examination was found to be normal. Then, PEG IFN α-2a treatment was continued. Audiological examination was repeated every week. HBV DNA levels were undetectable at first, third and sixth month of treatment but at 6 month, symptoms of tinnitus and hearing loss got worsened and bilateral sensorineural ototoxicity was detected in audiological examination. Thus, PEG IFN α-2a was stopped. One month later, bilateral ototoxicity completely reversed and audiological exam returned to normal.

Lamivudine 100 mg once daily was planned whenever HBV DNA level exceeds 2000 IU/ml. However, HBV DNA remained negative during six month follow-up. She is now symptom free and continues to be followed.

Discussion

Audiometry-documented sensorineural hearing loss have been reported during IFN treatment for both chronic hepatitis B and C. Ototoxicity tends to become more frequent at doses of more than 100 MU, often develop in the late stage of treatment and reversible when IFN is discontinued early.2,9

While Hagr et al.,10 concluded that PEG-IFN therapy did
not induce ototoxicity. Sharifian et al.,[5] and Formann et al.,[6] concluded that PEG-IFN is associated with ototoxicity and encourage planning hearing monitoring in patients receiving this drug. Patterns of hearing loss on interferon may vary and there may not be good correlation between subjective complaints and objective assessment of auditory function. So, objective evaluation of auditory function reveals problem in many patients. In addition, low frequency hearing loss can not be detected with conventional audiometry. If subjective hearing loss gradually exacerbates, repeat audiometry must be performed with short periods to identify ototoxicity as soon as possible.[4-6]

Unilateral and reversible hearing loss in a CHB patient due to PEG IFN α-2a was described in a previous case report,[7] whereas our case developed bilateral and reversible tinnitus and hearing loss during PEG IFN α-2a treatment. Her subjective audiologic symptoms started at second month of therapy and gradually worsened. Ototoxicity was documented objectively on audiogram at sixth month. Ototoxicity completely recovered after one month of stopping PEG IFN α-2a.

Our patient received this treatment at therapeutic doses. She did not take any other medications that could cause ototoxicity. According to Naranjo’s scale, a score of 7 suggested that PEG IFN α-2a was the probable cause of ototoxicity.

Many adverse events of PEG IFN α-2a occurs due to changes or abnormalities in cytokine synthesis. Ototoxicity may occur due to direct toxic effect of PEG IFNs on the ear as well as through ototoxic or hematologic mechanisms.[8]

To summarize, PEG IFN α-2a treatment infrequently causes ototoxicity (1%).[3,5,6] Patients receiving this treatment may present with audiologic symptoms. Therefore, clinicians must be cautious against the possibility of ototoxicity in CHB patients seeking this treatment.

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