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• *CASE REPORT* •

Acute sensorineural hearing loss associated with peginterferon and ribavirin combination therapy during hepatitis C treatment: Outcome after resumption of therapy

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Abstract

Peginterferon and ribavirin combination therapy for the treatment of hepatitis C virus (HCV) is well known to be associated with significant adverse effects. Sensorineural hearing loss, that in most cases is unilateral, has been reported as a consequence of therapy with both non-pegylated and pegylated interferon (pegIFN) but is not a well-known adverse effect. We report a 45-year-old Caucasian woman who developed acute sensorineural hearing loss 2 mo after starting therapy with pegIFN-α 2b and ribavirin for the treatment of chronic HCV, genotype 1a. She did not report the hearing loss to the hepatitis clinic until 1 mo, later whereupon therapy was promptly discontinued. Although her serum alanine aminotransferase (ALT) normalized and her HCV-RNA became undetectable after 12 wk of pegIFN and ribavirin therapy, after discontinuation, her HCV-RNA became detectable with significant elevations of serum ALT. Four months after initial discontinuation, the patient re-commenced pegIFN and ribavirin combination therapy. After 44 of 48 wk of therapy, the patient's liver biochemistry has normalized and the HCV-RNA is undetectable. She has not developed worsening of her hearing loss and hearing on the left-side is unaffected. Both patients and physicians should be aware that sensorineural hearing loss may occur with pegIFN therapy. Our experience suggests that re-institution of therapy is not always associated with further hearing impairment.

Key words: Peginterferon; Hepatitis C; Sensorineural hearing loss

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INTRODUCTION

Chronic hepatitis C affects an estimated 300 million people worldwide, and within Canada, the prevalence is estimated between 0.75% and 1.0% of the general population[1]. Treatment of hepatitis C virus (HCV) with interferon alpha (IFN-α) 2b and ribavirin therapy has been shown to be effective for many years now, with 41-47% of patients achieving a sustained virologic response[2-4]. With the current pegylated interferons (pegIFN) and ribavirin combination, overall sustained virologic response rates are reported to be 54-56%[5-7].

In spite of the current popularity of pegIFN and ribavirin therapy, many reported side-effects with standard IFN-α ARE also seen with pegIFN combination therapy. Flu-like symptoms such as fever, chills, muscle ache, nausea, vomiting, and fatigue are common side effects of treatment. Depression and related symptoms, such as anxiety, irritability, insomnia, and mental confusion, are not rare and may be significant in patients with a previous history. Common hematologic side effects that require monitoring include neutropenia and thrombocytopenia. Withdrawal rates in IFN-based combination studies due to side effects have ranged from 6% to 7%[4,8].

Although IFN-based therapy has been reported to affect any organ system, there have been occasional reports of sudden hearing loss while on IFN therapy[9-14]. We report a case of sudden unilateral hearing loss in a patient with HCV being treated with pegIFN and ribavirin combination therapy. The interesting aspect of our case is that pegIFN combination therapy was re-commenced at the patient's request, despite the reservations of the hepatitis clinic staff.

CASE REPORT

A 45-year-old Caucasian woman with chronic hepatitis C (genotype 1a) acquired 25 years previously after the administration of Rh immune globulin, developed sudden onset of right sided hearing loss 2 mo after beginning therapy with pegIFN-α 2b at a dose of 1.5 μg/kg per week subcutaneously (100 μg/wk) and ribavirin 1 000 mg/d (Pegetron, Schering-Canada, Point-Clare QC, Canada). Before treatment, she had no evidence of decompensated liver disease and her serum alanine aminotransferase (ALT) was 132 U/L (upper limit of normal <36 U/L). At the time of her acute unilateral hearing loss, she had completed a course of antibiotics for an otis media in the left ear. The right-sided hearing loss was described as a sudden onset of deafness followed by marginal improvement such that the

patient could hear a telephone dial tone and low-pitched sounds associated with tinnitus. She was seen in consultation by an otolaryngologist who reported that both middle ears were normal on visual inspection. Audiometric testing performed approximately 1 mo after the acute hearing loss was consistent with severe unilateral right-sided sensorineural loss. The patient's pegIFN and ribavirin combination was discontinued immediately after the patient's disclosure, to the hepatitis clinic, of the unilateral hearing impairment 1 mo after onset and 3 mo after commencement of antiviral therapy. Although her liver enzymes normalized and her HCV-RNA was undetectable (qualitative Cobas Amplicor HCV Test, Roche-Diagnostics Canada, Laval QC, Canada; lower detection limit = 10-15 IU/mL) after 12 wk of therapy, within 2 mo after discontinuation, the HCV-RNA was again detectable and her serum ALT flared to 267 U/L. Symptomatically, her unilateral hearing impairment did not improve further and she was advised not to continue with further anti-HCV therapy. Despite medical advice to the contrary, she re-commenced pegIFN and ribavirin therapy 4 mo after the initial discontinuation. After 44 wk of continued pegIFN and ribavirin therapy, her serum liver biochemistry has remained persistently normal (serum ALT = 16 U/L at mo 9 of therapy) and her HCV-RNA was undetectable at wk 24 of therapy. She has not had any left-sided hearing impairment although her right-sided hearing remains significantly impaired.

DISCUSSION

Side effects of IFN therapy for HCV have been well documented. However, acute sensorineural hearing loss is relatively rarely reported and not well known amongst those who provide treatment for HCV. Several cases were reported of sudden hearing loss in patients with HCV being treated with the previous standard of non-pegylated IFN-α2 therapy[10–13], presumably on the basis of focal small vessel vasculitis. One prospective study of 73 patients reported tinnitus and/or hearing loss in 32 patients (43.8%) during IFN therapy, and audiometry-documented sensorineural hearing loss in 27 cases (36.9%)[14]. These investigators reported that auditory disability frequently developed in the later stages of treatment, but most patients in this report recovered 7-14 d after the discontinuation of therapy.

More recently, Formann *et al*.[9], reported six cases of hearing loss that was associated with the current standard treatment of pegIFN and ribavirin combination therapy. In contrast to the study by Kanda *et al*., these authors reported that hearing loss did not fully resolve after discontinuation of the therapy with pegIFN but also did not worsen on continued treatment. Our patient developed unilateral sensorineural hearing loss that was associated with pegIFN and ribavirin therapy. Therapy was discontinued but subsequently re-instituted at the patient's request. Although the unilateral hearing loss was persistent, it did not worsen on re-treatment and bilateral hearing loss has not occurred.

We believe that sudden hearing loss as a side effect should be discussed, along with the other more commonly known side effects, with patients prior to being treated with standard or pegIFN therapy. We recommend that patients on interferon-based therapies should be monitored during treatment for changes in hearing perception. It remains possible that those who do develop sudden hearing loss can be continued on IFN therapy, if the risk-benefit ratio of treatment dictates.

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