

## Sudden hearing loss associated with peginterferon and ribavirin combination therapy during hepatitis C treatment

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### Abstract

Adverse effects associated with peginterferon and ribavirin during hepatitis C treatment are well known. Sudden hearing loss has rarely been reported. Possible mechanisms involved include direct ototoxicity of interferon, autoimmunity, and hematological changes. Hearing loss is frequently fully resolved after discontinuation of antiviral therapy. We report a 47-year-old man with chronic hepatitis C, genotype 2 ac who developed sudden hearing loss 22 wk after starting therapy with peginterferon alpha 2a at a dose of 180 µg per week and ribavirin 800 mg per day. Since symptoms did not worsen, antiviral therapy was continued for 2 wk, according to the patient's wish. Hearing loss resolved within 2 wk after the end of treatment. Serum liver alanine aminotransferase remained normal during and after the end of antiviral therapy. HCV RNA was undetectable at the end of therapy and remained negative 24 wk later. Thus, patients should be aware that hearing loss may occur with peginterferon therapy, but the decision whether to continue or to stop the treatment is based on the clinical judgment of the physician and the wishes of the patient.

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**Key words:** Adverse effects; Hearing loss; Hepatitis C; Interferon; Ribavirin

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### INTRODUCTION

Chronic hepatitis C affects 250-300 million people worldwide, and in Tunisia, the prevalence is estimated to be 0.4%-1.6% of the general population<sup>[1-3]</sup>. The higher prevalence is in the north which corresponds to the south side of the Mediterranean basin. The most frequent genotype in Tunisia is 1b<sup>[4]</sup>.

Treatment of hepatitis C virus infection with the combination of peginterferon alpha (2a or 2b) and ribavirin therapy is now recommended<sup>[5,6]</sup>. Both peginterferon and ribavirin are well known to be associated with significant adverse effects<sup>[7]</sup>. Hearing loss has been reported as a consequence of therapy with pegylated and non-pegylated interferon<sup>[8-10]</sup>. However, we still pay little attention to auditory acuity. Moreover, contrary to standard interferon, hearing loss seems to not be fully resolved after discontinuation of peginterferon treatment<sup>[8,10]</sup>.

We report a case of sudden hearing loss in a patient with HCV infection treated with a combination of peginterferon and ribavirin. The interesting aspect of our case is that peginterferon therapy was continued during the last month and hearing loss was fully resolved after the end of treatment.

### CASE REPORT

A 47-year-old Tunisian man with chronic hepatitis C, with 10<sup>6</sup> UI/L HCV RNA and genotype 2a/2c, attended the Gastroenterology Department for follow-up. He did not have any pathological history and he had not taken any drugs prior to his visit. His initial physical and neurological examinations were normal. Serum levels of glucose, urea, creatinine, lipids, electrolytes, alkaline phosphatase, bilirubin, gamma-glutamyl transferase, blood cell count, ferritin and cryoglobulin were within normal limits. Alanine aminotransferase (ALT) was 62 UI/L (upper limit of normal < 45), aspartate aminotransferase (AST) was 39 UI/L (upper limit of normal < 45 UI/L). Antinuclear, smooth muscle, anti-liver-kidney microsome 1 and anti-mitochondrial antibodies were negative. He was treated with peginterferon alpha 2a (180 µg/wk) and ribavirin (800 mg/d) for a predetermined period of 24 wk. Twenty-two weeks after beginning therapy, he developed otalgia and sudden onset of left-sided hearing loss. He was seen in consultation by an otolaryngologist who reported that ear examination was normal. Since

symptoms did not worsen, and in accord with the patient's wishes, antiviral therapy was continued for 2 wk. Hearing loss resolved within 2 wk after the end of treatment. Serum liver ALT remained normal during and after the end of antiviral therapy, and no sign of thrombocytopenia was detected during blood cell count monitoring. HCV RNA was undetectable at the end of therapy and remained negative 24 wk later.

## DISCUSSION

This is another report on sudden hearing loss after treatment with peginterferon alpha, which adds to the observations made in patients treated with peginterferon and standard interferon for chronic hepatitis C<sup>[8-11]</sup>. Such hearing loss is mostly unilateral and sensorineural<sup>[12]</sup>. In one prospective study of 73 patients receiving interferon, hearing impairment (tinnitus and/or hearing loss) occurred in 32 patients (43.8%), among whom audiometry documented hearing loss in 27 cases (36.9%)<sup>[13]</sup>.

Several factors may cause sensorineural hearing loss in patients treated with interferon. First, the drug itself may be directly toxic to the auditory nerve hairy cells<sup>[9]</sup>. Also, an indirect effect of interferon due to its immunoregulatory and antiviral activity can explain this sensorineural pathology. Cadoni has detected anti-endothelial-cell antibodies in an HCV patient with sudden hearing loss during interferon therapy<sup>[11]</sup>. The finding of these antibodies suggests microvascular damage during therapy for vasculitis. In addition, interferon-induced thrombocytopenia may cause a microvascular accident in the inner ear.

Some authors have reported that hearing loss fully resolves 5 d to 1 mo after discontinuation of antiviral therapy with interferon<sup>[9,14]</sup>; whereas others have demonstrated that hearing impairment does not completely recover after cessation of peginterferon, and worsens with continued treatment<sup>[8,10]</sup>.

In the case reported here, hearing loss fully resolved after the end of treatment with peginterferon. Auditory disability frequently develops in the later stages of treatment<sup>[15]</sup>; in our case, it developed 2 wk before the end of the treatment (i.e., after 22 wk).

The average cumulative dose until development of auditory disability is about 176.9 mV<sup>[13]</sup>. In a recent study, hearing loss was detected in nine of 27 patients after 7 d, and the degree of hearing loss increased until 21 d of treatment<sup>[14]</sup>. Therefore, it is recommended that patients on interferon therapy should be monitored during treatment for changes in hearing perception. It remains possible that those who develop hearing loss can continue with inter-

feron therapy. The decision whether to continue or to stop the treatment when signs of ototoxicity appear is based on the clinical judgement of the treating physician and the wishes of the patient.

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