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Successful continual intratympanic steroid injection therapy in a patient with refractory sensorineural hearing loss accompanied by relapsing polychondritis

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ABSTRACT

Objective: To report the treatment efficacy of continual intratympanic steroid injection (ITSI) therapy in a patient with refractory sensorineural hearing loss accompanied by relapsing polychondritis.
Patient: A 49-year-old female diagnosed with relapsing polychondritis at the age of 45 years and who had been treated with corticosteroids and immunosuppressants developed sensorineural hearing loss in the left ear.
Intervention: Her unilateral hearing loss did not recover despite receiving one cyclophosphamide pulse treatment, one methylprednisolone pulse treatment, and weekly leukapheresis. Thus, we decided to initiate weekly ITSI therapy.
Main outcome measure: Pure tone audiometry.
Results: A week after the first ITSI treatment, the patient's hearing improved. We continued ITSI therapy and attempted to extend the interval between treatments, but her hearing worsened when ITSI therapy was delivered at 2- to 3-week intervals. Thus, we returned ITSI therapy to once per week for 21 months (total of 71 treatments). She experienced no adverse events, like tympanic perforation, and 1 year after terminating the therapy, her hearing remained stable and did not worsen.
Conclusions: Continual, weekly ITSI therapy was effective in treating sensorineural hearing loss accompanied by relapsing polychondritis. ITSI therapy may be a promising treatment option for sensorineural hearing loss caused by autoimmune disease.

1. Introduction

Relapsing polychondritis (RP) is a rare systemic inflammatory disease that repeatedly affects cartilage, such as that in the auricle of the ears, nose, larynx, tracheobronchial tree, and peripheral joints. Other proteoglycan-rich tissues can also be affected, such as the inner ear, eyes, heart, blood vessels, and kidneys [1,2]. The etiology of the disease has not been clearly elucidated, although some possibilities have been suggested. For example, RP patients have increased levels of serum autoantibodies against collagen and a high prevalence of human leukocyte antigen (HLA) class II (DR4) [3–5].

The estimated annual incidence rate in the Caucasian population in Rochester, Minnesota, for example, is reported to be 3.5 cases per million [6]. A questionnaire survey estimated the prevalence of RP patients in Japan to be similar to that in the USA [7]. Inner ear disorders appear in 40–50% of patients with

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RP during the course of the disease [8–10], and most patients are treated with systemic corticosteroids. However, the response rate with this treatment is not high [11–13].

In this study, we report the good hearing outcome resulting from continual intratympanic steroid injection (ITSI) therapy in an RP patient who experienced no improvement in hearing loss, despite receiving systemic administration of corticosteroids, immunosuppressants, and leukapheresis.

2. Materials and methods

The patient was a 45-year-old female who developed bilateral auricular swelling with systemic inflammation and was diagnosed in 2009 with RP. Intravenous administration of corticosteroids (starting dose was 50 mg of prednisolone at 1 mg/kg/day) failed to reduce her inflammation. Therefore, an immunosuppressant was added to her treatment. First, she was treated with cyclophosphamide, then with mizoribine, and finally methotrexate. She was treated continually with oral administration of corticosteroids and methotrexate. With repeated exacerbation and remission of symptoms, the hoarseness in her voice and deformation of the auricle and nose worsened. Intravenous cyclophosphamide pulse therapy (750 mg) was used to treat her during the exacerbation phase.

When she was 49 years old, she developed hearing loss, which prompted her to come to our department in May 2013. Pure tone audiometry (PTA) indicated that the patient had sensorineural hearing loss in the left ear (Fig. 1A). Tympanic membrane was normal. Severe hoarseness due to laryngeal cartilage deformation, and auricular and nasal deformation were found, although the patient reported that these conditions were not new, being the same as before developing hearing loss. We diagnosed her condition as acute sensorineural hearing loss caused by inner ear involvement of RP.

Her left-ear hearing loss failed to recover despite receiving one session of cyclophosphamide pulse therapy (750 mg), one session of methylprednisolone pulse therapy (1000 mg/day for 3 days), and weekly leukapheresis (Fig. 1B). We started to treat her with ITSI therapy in September 2013 after written informed consent was obtained.

3. Results

After one ITSI therapy, her hearing improved (Fig. 1C). We consulted with her and decided to continue once-per-week ITSI therapy while continuing daily oral administration of corticosteroids and methotrexate and weekly leukapheresis. In an effort to lengthen the intervals between ITSI treatments, we discovered that her hearing worsened with intervals of 2 or 3 weeks (Fig. 1D). Thus, we decided to return to the once-per-week ITSI treatment schedule. We continued weekly ITSI therapy for 18 months, and then gradually extended the interval between treatments while watching her carefully. Twenty-one months after her initial ITSI therapy (71 total treatments), we terminated therapy (Fig. 1E). She did not experience any adverse events, like tympanic membrane perforation. One year after terminating ITSI therapy, we found that her hearing did not worsen. During that 1-year period, however, she was on a daily regimen of systemic corticosteroid and immunosuppressant therapy, in addition to undergoing weekly leukapheresis (Fig. 1F).

All procedures were approved by the Ethics Review Committees of Japanese Red Cross Shizuoka Hospital.

3.1. Treatment protocol

ITSI therapy consisted of 0.3–0.5 ml of dexamethasone sodium phosphate (3.3 mg/ml) injections, which were introduced through the left-side tympanic membrane into the tympanic cavity under local anesthesia. To avoid spillage of the drug from the tympanic cavity, the patient was instructed to maintain a supine position with her head tilted 45 degrees toward the opposite side and to swallow as little as possible for 30 min after the injection.

4. Discussion

Although a consensus on an appropriate and effective treatment for RP-associated hearing loss has yet to be established, most patients in the past have been treated with systemic administration of corticosteroids. This protocol has shown limited efficacy. For example, Bachor et al. reported that only 2 of 9 cases treated with intravenous corticosteroids recovered from hearing loss [11]. Kanaya et al. reported that two cases failed to respond to systemic corticosteroid administration, although one case showed a temporary response [12]. On the other hand, Kumakiri et al. reported that early administration of steroids could lead to hearing loss recovery, if the patient is diagnosed with RP and treated early in the course of the disease [13].

In the present study, we report a good hearing outcome after treatment with continual, weekly ITSI therapy in a RP patient who had developed hearing loss despite receiving daily systemic corticosteroid and immunosuppressant therapy, weekly leukapheresis, and intermittent cyclophosphamide pulse therapy. Systemic delivery of corticosteroids is considered to be an effective treatment for both idiopathic sudden hearing loss and RP-associated hearing loss. Combining ISTI with systemic corticosteroid therapy has been demonstrated to be beneficial for treating idiopathic sudden hearing loss [14,15]. Therefore, we reasoned that including ISTI to this patient's treatment regimen would have a positive effect.

Because the pathogenesis of the sensorineural hearing loss seen in RP has not yet been elucidated, it is impossible at this time to determine the working mechanism of corticosteroids. Considering that the serum half-life of dexamethasone is approximately 190 min [16], it is unlikely that the dexamethasone concentration in the inner ear was high enough to be effective for 1 week. We considered the possibility that the corticosteroid concentration filtering into the patient's inner ear by ITSI was higher than that achieved by systemic administration. Thus, this high corticosteroid concentration strongly inhibited an inflammatory response in the inner ear. We hypothesized that while the combined effect of weekly ITSI and daily systemic treatment—which was continued during ITSI—suppressed damage to her inner ear, the effect of

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