

# Intratympanic steroids treat autoimmune inner ear disease caused by pembrolizumab

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## ABSTRACT

Immune checkpoint inhibitors such as pembrolizumab are a class of medications which have recently been used for the treatment of advanced melanoma with great success. Treatment with immune checkpoint inhibitors was previously associated with the development of autoimmune disorders.

We describe the first documented case of autoimmune inner ear disease in a patient with advanced sinonasal melanoma treated with pembrolizumab, and successful recovery of the associated hearing loss after intratympanic steroid injections.

## INTRODUCTION

Pembrolizumab is a programmed cell death 1 (PD-1) checkpoint inhibitor that combats melanoma by enhancing immune responses and can cause immune-related adverse events (irAEs) in various organ systems. PD-1 checkpoint inhibitors have been used for the treatment of advanced melanoma since 2014 with great results.

We present the first known case of autoimmune inner ear disease (AIED) presumably caused by pembrolizumab. The associated sensorineural hearing loss was successfully treated with intratympanic (IT) dexamethasone injections.

## CASE PRESENTATION

81 year old man presented with complaints of nasal fullness, bulging eyes, and vision changes. CT and MRI imaging revealed a large mass centered in the ethmoid sinuses with bilateral orbital invasion and extension into the anterior skull base.(Figure 1)

Biopsy confirmed primary mucosal melanoma of the ethmoid sinuses. PET scan revealed widespread metastatic disease.

Patient was started on systemic therapy initially with a cytotoxic T-lymphocyte associated protein 4 (CTLA 4) inhibitor with continued progression of disease after 4 doses. At this point, he was immediately switched to the PD-1 checkpoint inhibitor pembrolizumab with scheduled doses every 3 weeks. Two weeks after his second dose (5 weeks after the first dose), the patient reported sudden onset of bilateral hearing loss.

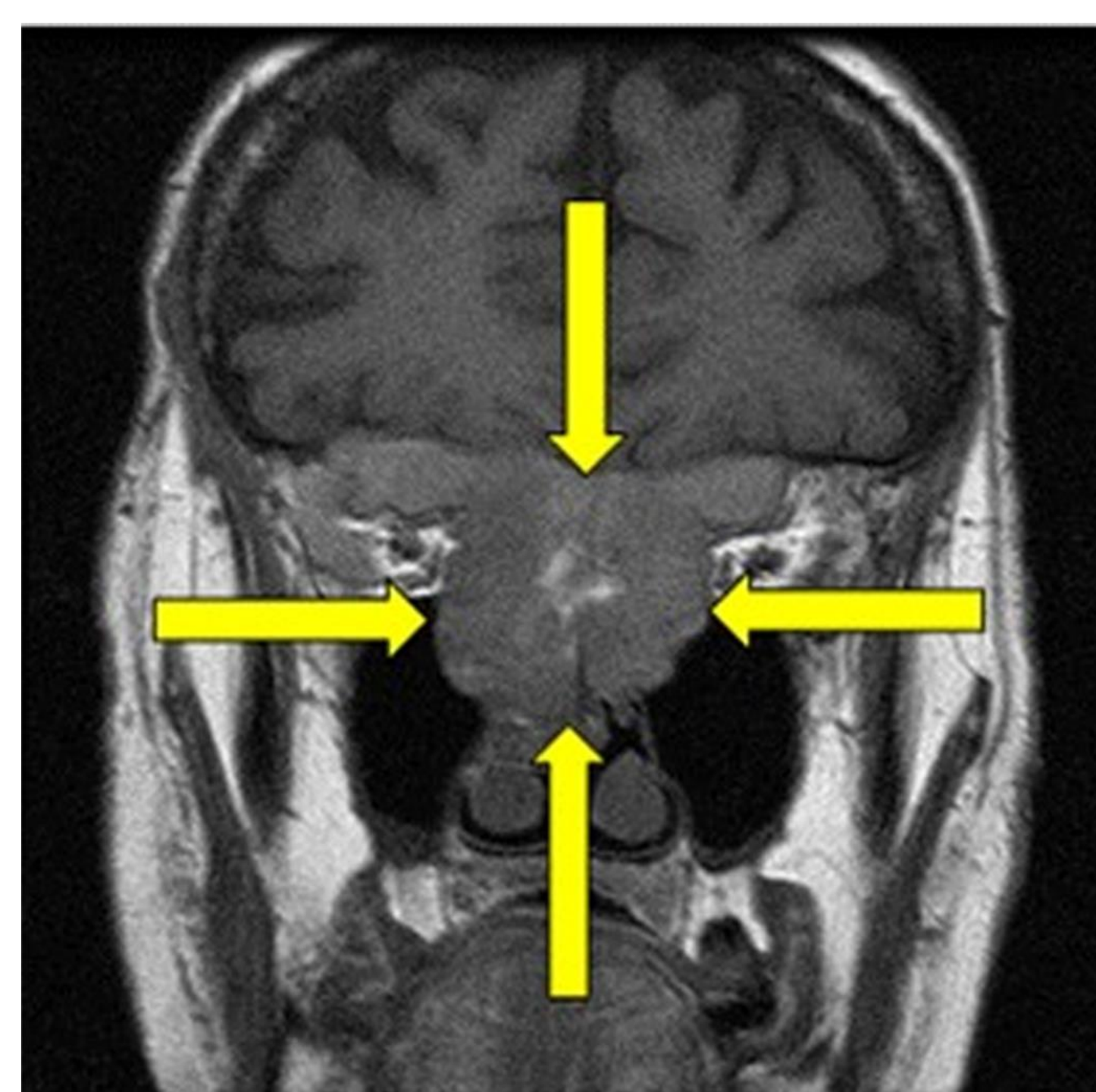


Figure 1. Coronal MRI image showing extensive tumor with skull base invasion.

He underwent 1-2 weekly intratympanic (IT) dexamethasone (10 mg/mL) injections for a total of 6 injections in the right ear and 4 injections in the left ear. After each injection, he was supine for 20 minutes, to allow diffusion of the steroid solution through the round window membrane. He experienced slow improvement in hearing over the course of the serial intratympanic treatment. Both he and his wife felt his hearing had returned to his baseline by the completion of the IT steroid therapy. (Figure 2)

After the IT dexamethasone treatment, the patient's hearing remained stable. He was able to continue treatment with pembrolizumab with excellent tumor response.

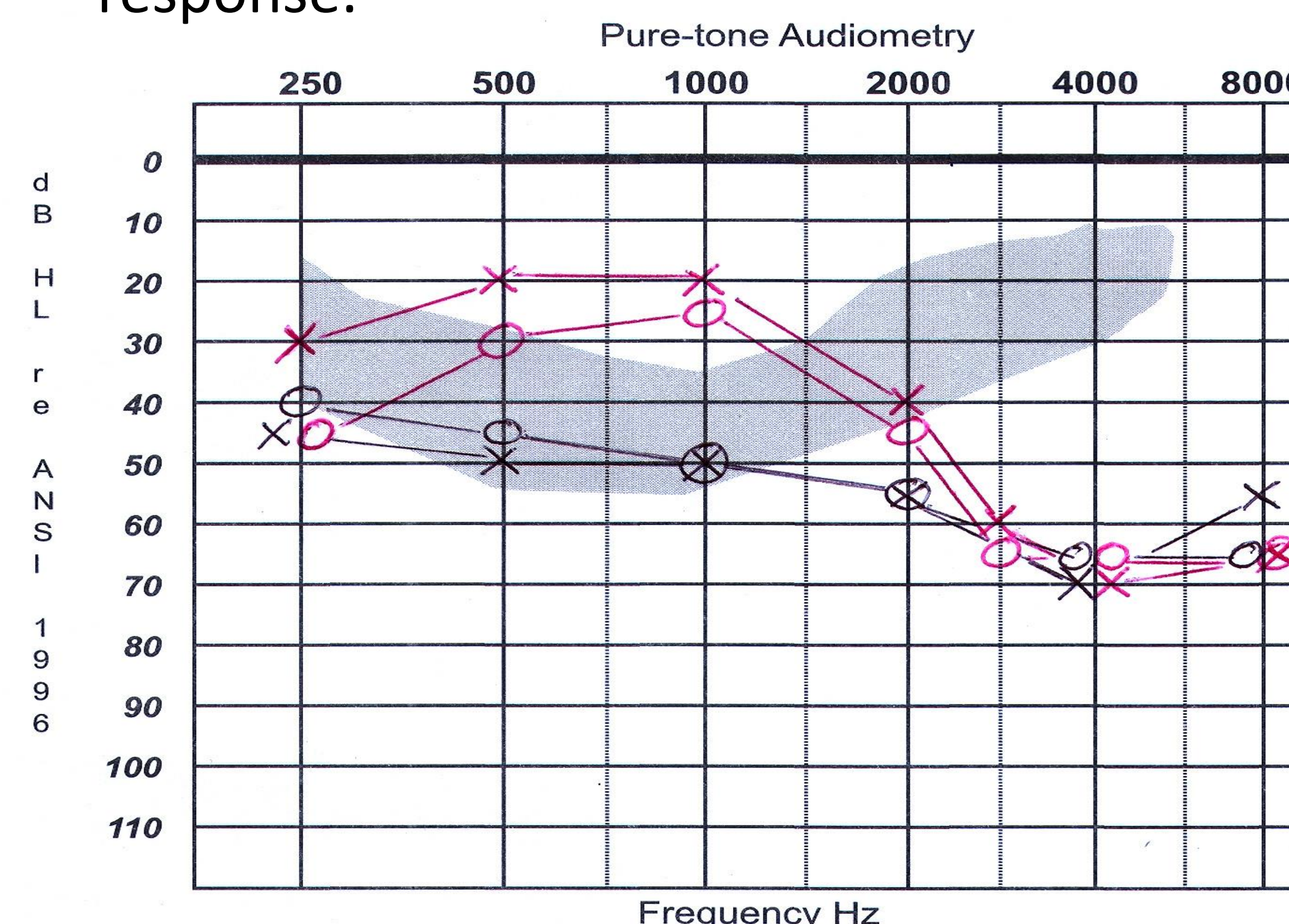


Figure 2. Audiogram showing hearing levels before and after intratympanic steroid treatment. Black line corresponds with pre-injection thresholds. Red line corresponds with post-injection thresholds.

## DISCUSSION

PD-1 checkpoint inhibitors such as pembrolizumab are associated with the development of autoimmune side effects (irAEs) of the skin, lungs, gastrointestinal tract, kidneys, liver, and endocrine system. These have been treated successfully with local or systemic steroids, with or without a PD-1 treatment holiday.

We report the first case of autoimmune inner ear disease (AIED) caused by the PD-1 checkpoint inhibitor pembrolizumab. As indications for checkpoint inhibitors increases, the incidence of AIED related to this type of treatment may increase as well.

With timely intratympanic steroid injections, our patient was able to regain his pre-treatment hearing levels and was able to continue treatment with pembrolizumab with a significant reduction in tumor burden.