

# Bilateral Hearing Loss as a Presentation of Leptomeningeal Carcinomatosis

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## Abstract

Unilateral idiopathic sudden sensorineural hearing loss is often encountered, but bilateral progressive hearing loss is rare. Here we present a case of a 46-year-old man who was diagnosed as the leptomeningeal carcinomatosis (LC) from lung adenocarcinoma. An enhanced magnetic resonance imaging (MRI) showed a strong enhancement effect of bilateral vestibulocochlear nerves. High-resolution T2-weighted imaging additionally revealed the accompanying metastasis in bilateral internal auditory canals (IACs). Hearing loss due to LC started from in higher frequencies and rapidly progressed from unilateral to bilateral. Otoacoustic emission showed the positive response inconsistent with the poor hearing results in pure tone audiometry, but this response disappeared soon with the rapid deterioration of hearing. IAC metastasis with LC caused an irreversible cochlear damage and the hearing of this patient could not recover even after the IAC mass disappeared on MRI. Audiometric evaluation, including PTA and OAE, would provide diagnostic clues and we should proceed with the investigation of brain MRI and CSF cytology urgently to reach the earlier diagnosis of LC.

**Keywords:** Leptomeningeal carcinomatosis; Internal auditory canal metastasis; Otoacoustic emission; Hearing loss

## Introduction

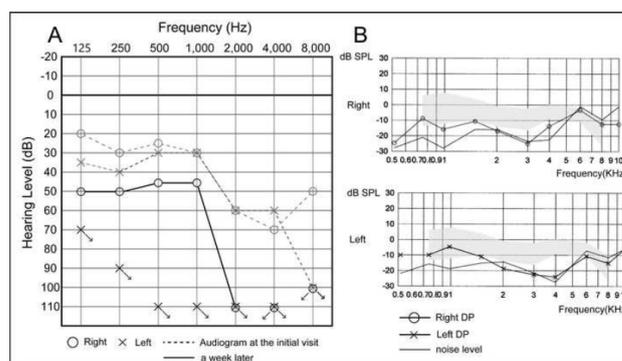
Leptomeningeal carcinomatosis (LC) is characterized by multifocal spread of neoplastic cells in the leptomeninges. A diagnosis of LC is usually suggested by the presence of a variety of multiple neurological symptoms in a patient with a known history of malignancy. The primary tumors responsible for LC are commonly breast or lung adenocarcinoma, melanoma, and lymphomas [1]. The report describes a case of a patient with bilateral progressive hearing loss as the first manifestation of LC from lung adenocarcinoma.

## Case Report

A 46-year-old man was referred to our otolaryngology department with a history of progressive bilateral hearing loss, tinnitus, and imbalance. His past medical and family histories were unremarkable. He developed left aural fullness and a neck lump at 1 month before presenting to our institution. Two weeks later, the aural fullness and hearing loss were noted to be bilateral and grew worse over a period of several days. He visited the ear, nose, and throat clinic and was diagnosed with bilateral high-pitch sensorineural hearing loss. Head computed tomography (CT), including imaging of the temporal bone and internal auditory canals (IACs), showed no abnormalities. He was treated with a 1-week course of intravenous steroid under the tentative diagnosis of idiopathic sudden sensorineural hearing loss. His hearing loss became more severe despite steroid treatment, and then he was referred to our department (Figure 1A).

On examination, he had two swollen mobile lymph nodes on his left neck. No abnormal findings were seen in the ear, nose, or throat. No obvious nystagmus, facial paralysis, and other neurological deficits (except for those of the auditory nerve), or cerebellar signs were observed. Pure tone audiometry (PTA) demonstrated left deafness and

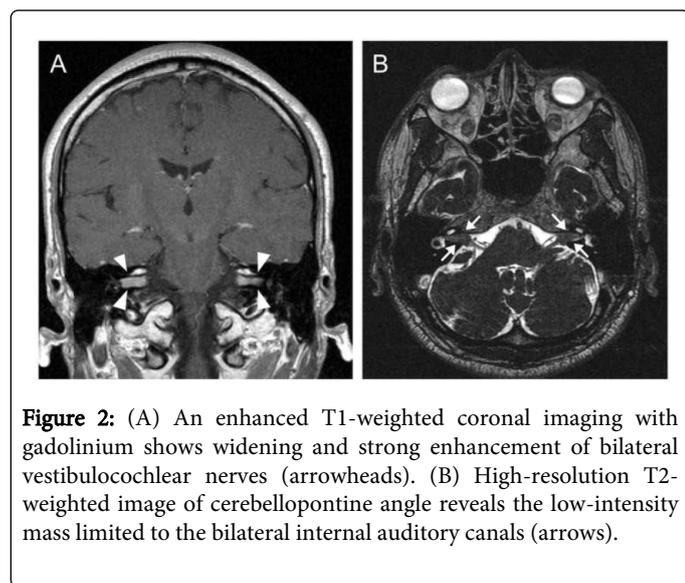
severe right sensorineural hearing loss. Distortion product of otoacoustic emission (OAE) response was bilaterally positive mainly in the lower frequencies below 2 kHz, which indicated the partial survival of outer hair cell function (Figure 1B). Serological tests showed a slight increase in white blood cell count ( $107 \times 10^2 \mu\text{L}$ ) and C-reactive protein ( $1.7 \times 10^4 \mu\text{g/L}$ ), and screening for syphilis was negative.



**Figure 1:** Pure tone audiogram recorded at the initial visit (dotted line) and a 1 week later (line). Hearing deteriorates bilaterally in a week in spite of the steroid treatment. Each symbol indicates as follows: circle; right ear air-conduction, cross; left ear air-conduction, downward arrow; no response at the maximum output of the audiometer. B) Distortion products (DP) of otoacoustic emission a week later the initial presentation. The DP response curve above the noise level in lower frequencies below 2 kHz is regarded as positive bilaterally. (DP type; 2f<sub>1</sub>-f<sub>2</sub> evoked by two tones of frequencies f<sub>1</sub><f<sub>2</sub>. Stimulus intensity levels of primary tones; L1=65dB SPL, L2=55dB SPL)

Enhanced magnetic resonance imaging (MRI) with gadolinium showed a strong contrast enhancement effect in the bilateral vestibulocochlear (VIII) nerves. High-resolution T2-weighted imaging revealed a low-intensity mass limited to the bilateral IACs, similar to neurofibromatosis type 2 (Figure 2). Examination of biopsy specimens from neck lymph nodes revealed malignant cell proliferation with round swollen nuclei and clear eosinophilic cell bodies. Positive immunostaining with thyroid transcription factor 1 (TTF-1) suggested that the primary lesion was lung. The cytology of cerebrospinal fluid (CSF) was compatible with a diagnosis of metastatic adenocarcinoma (Figure 3), and chest CT identified the primary lung carcinoma. During these intervals for diagnosis, his hearing deteriorated and developed bilateral total deafness. DPOAE response was completely lost with the deterioration of hearing.

The patient was treated with systemic chemotherapy using cisplatin and pemetrexed. No radiation therapy was added. Right facial palsy appeared at 1 month after starting chemotherapy. After five cycles of chemotherapy, the enhancement of VIII nerves resolved. No obvious mass lesions in IACs were observed, and the T2 signal of the cerebellopontine angle (CPA) cistern had normalized (Figure 4). In spite of the improved findings on MRI, the patient's hearing did not improve, and no response remained to be observed both in PTA and DPOAE. He died of respiratory failure at 7 months after the onset of hearing loss. An autopsy was not performed.

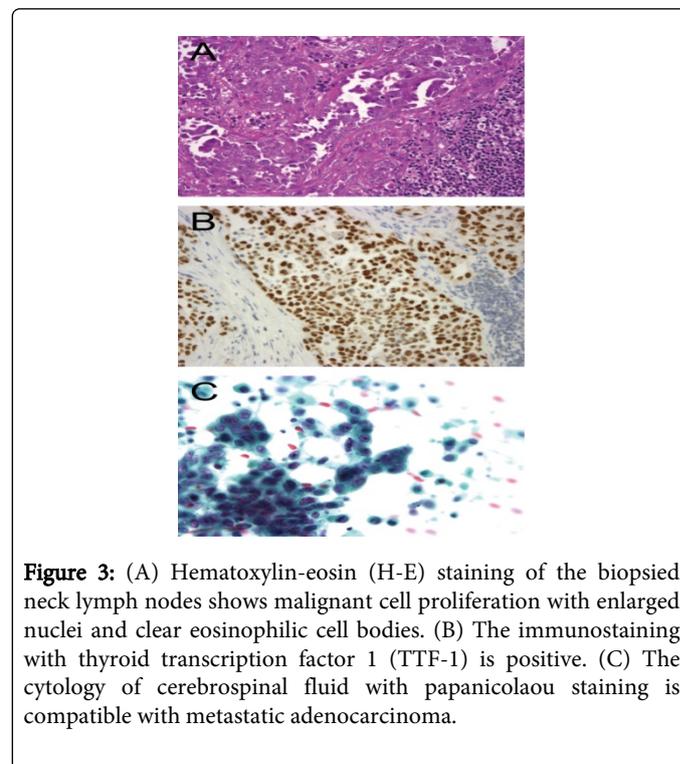


**Figure 2:** (A) An enhanced T1-weighted coronal imaging with gadolinium shows widening and strong enhancement of bilateral vestibulocochlear nerves (arrowheads). (B) High-resolution T2-weighted image of cerebellopontine angle reveals the low-intensity mass limited to the bilateral internal auditory canals (arrows).

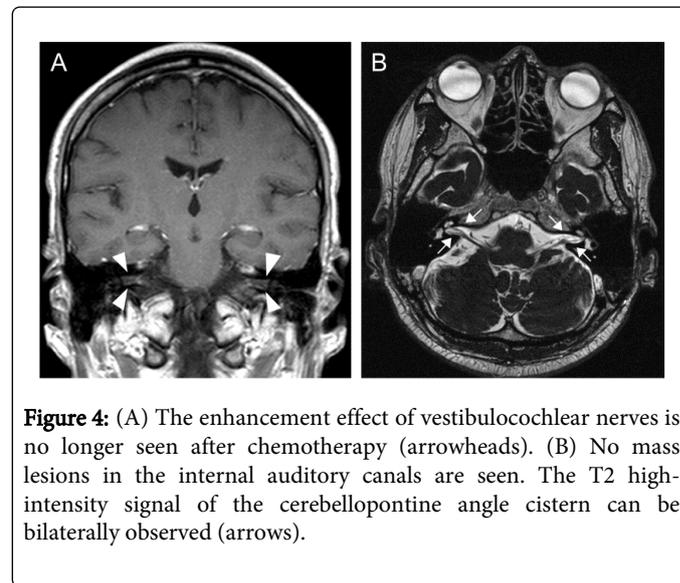
### Discussion

LC occurs in approximately 5-8% of patients with cancer [1] and 10% of them have VIII nerve involvement [2]. Neoplastic cells gained access to CSF spread to subarachnoid space containing the proximal portions of cranial nerves. Involvement of multiple cranial nerves is common, with cranial nerves III, IV, VI and VII nerves most often affected. Slow CSF flow and gravity are supposed to promote the deposition of circulating cells. One of the most frequent affected region is posterior fossa [3], which includes the CPA and IAC cistern containing cranial nerves VII, VIII, and anterior inferior cerebellar artery. While several previous literatures reported isolated hearing loss due to LC [4-8], audiometric characteristics including OAE were rarely evaluated [9]. In addition, this is the first report that we can

evaluate the hearing after the chemotherapy induced the disappearance of IAC mass on MRI.



**Figure 3:** (A) Hematoxylin-eosin (H-E) staining of the biopsied neck lymph nodes shows malignant cell proliferation with enlarged nuclei and clear eosinophilic cell bodies. (B) The immunostaining with thyroid transcription factor 1 (TTF-1) is positive. (C) The cytology of cerebrospinal fluid with papanicolaou staining is compatible with metastatic adenocarcinoma.



**Figure 4:** (A) The enhancement effect of vestibulocochlear nerves is no longer seen after chemotherapy (arrowheads). (B) No mass lesions in the internal auditory canals are seen. The T2 high-intensity signal of the cerebellopontine angle cistern can be bilaterally observed (arrows).

A diagnosis of LC is often made in the context of clinical suspicion in a patient with typical symptoms and a history of malignancy. Though hearing loss alone is usually not sufficient to raise the suspicion of underlying LC, the bilateral rapidly progressive nature and unresponsiveness to steroid treatment seem to be the signs pointing to LC. Additionally, a discrepancy between the threshold of PTA and OAE positive response indicating the retro-cochlear pathology would provide the further evidence to investigate the brain MRI. As previously reported, the present patient showed hearing loss starting from higher to lower frequencies [7-9]. OAE response was observed in the early stage but was completely lost with the rapid

deterioration of hearing. In retrospect, we should have the suspicion of LC and investigate the brain earlier.

CSF examination including cytological evaluation and enhanced MRI are the standard diagnostic methods of LC. CSF cytology has a high specificity (>95%), but its sensitivity is reported to be generally less than 50%. However, the sensitivity depends on the types of tumors, positive cytology was reported in 75% of breast cancer, 60% of melanoma, and 80% of non-small cell lung cancer. The enhanced MRI in LC diagnosis also have a high false-negative rates as high as 65% and false-positive rates approaching 10% [10]. The enhancement of VIII nerves is not a specific finding for LC, as similar changes in enhancement are also seen in other diseases, such as Ramsay-Hunt syndrome presenting with VII or VIII nerve palsies [11]. While the labyrinthine enhancement pattern might correlate with sensorineural hearing loss in LC patients [12], we could not identify this enhancement pattern in the present patient. IAC metastasis with LC in the present patient was identified most clearly with a high-resolution T2 image. Considering the rapid course and poor prognosis of LC, repeated lumbar puncture and MRI seem to be less invasive than biopsy of IAC region [13].

The supposed mechanism of hearing loss by LC is direct nerve infiltration, nerve ischemia by vascular compression, and tumor invasion of the cochlea [14]. According to several autopsy reports of LC, neoplastic cells often invaded the lower basal turn of the cochlea through the cribrose area of cranial nerve VIII. However, the organ of Corti and hair cells were relatively untouched [14,15]. Thus, when the malignant cells infiltrated the cochlea, the hearing loss started from the higher frequencies and could not be recovered, even after the neoplastic cells disappeared from the IACs. The clinical course of the present patient seemed to support this theory of cochlear invasion. IAC metastasis with LC seems to have a higher risk of direct tumor invasion of the cochlea and poor outcomes in terms of hearing. Before bilateral irreversible cochlear damage occurs, there is the possibility of avoiding total deafness.

The clinical characteristic of hearing loss due to LC was summarized by Alberts and Terrance as follows: (1) hearing loss is initially unilateral and associated with tinnitus; (2) unilateral hearing loss rapidly progresses to severe bilateral involvement; (3) audiometric and caloric studies reveal severe cranial nerve VIII impairment; and (4) facial nerve palsy is commonly noted at the time of hearing loss [2]. In our patient, hearing loss progressed rapidly from unilateral to bilateral. A MRI showed the enhancement of VIII nerves, and high-resolution imaging revealed metastasis in the IACs. Facial nerve palsy was not initially observed and appeared later. Taking into account the vulnerability of sensory nerves, facial nerve palsy seems to develop later after hearing loss. Total acquired deafness in the end stages of cancer is devastating. Early diagnosis and therapy is crucial to preserve neurologic function.

In conclusion, progressive hearing loss is a rare presenting symptom of LC. The bilateral rapidly progressive hearing loss and

unresponsiveness to steroid treatment seem to be the signs pointing to LC. IAC metastasis with LC caused an irreversible cochlear damage and the hearing of the present patient could not recover even after the remission was obtained. Audiometric evaluation, including PTA and OAE, would provide diagnostic clues and we should proceed with the investigation of brain MRI and CSF cytology urgently to reach the earlier diagnosis of hearing loss due to LC.

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