



## Case Report

# Treatment for Progressive Hearing Loss Due to Paget's Disease of Bone – A Case Report and Literature Review

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Paget's disease is a common bone remodeling disorder that typically begins with excessive bone resorption in the elderly. Bilateral progressive hearing loss is the most frequently encountered complication of Paget's disease. The types of hearing loss identified by audiometry are conductive, sensorineural, or both. However, the precise mechanism of hearing loss remains unclear, and the treatment has been controversial. We present a 73-year-old man who suffered from bilateral progressive hearing loss due to Paget's disease. Potent bisphosphonates, oral risedronate in daily adjusted dosages for 6 months, did not decrease or suppress the worsening of the hearing loss. The Nucleus CI24 Contour electrode array was successfully inserted on the left side without surgical and postoperative complications. The Japanese open set monosyllable word recognition test in a sound field at 65 dB had a result of 74%. This cochlear implantation can be an indication for cases of profound hearing loss due to Paget's disease.

**KEYWORDS:** Paget's disease, hearing loss, bisphosphonates, cochlear implant

## INTRODUCTION

James Paget<sup>[1]</sup> first described Paget's disease as a chronic inflammation of the bone in 1877. Paget's disease is commonly encountered in North America and Western Europe; however, it is rare in Asia<sup>[2]</sup>. Approximately 70–90% of patients with Paget's disease are asymptomatic<sup>[3]</sup>. However, bilateral progressive hearing loss is the most frequently encountered complication in Paget's disease. Pure tone audiometry often presents an air-bone gap, which has been assumed to represent conductive hearing. However, surgery has been found to be less efficient in cases of Paget's disease<sup>[4]</sup>. We present a case of Paget's disease with profound hearing loss treated by cochlear implant surgery. The relevant literature on hearing loss due to Paget's disease was reviewed regarding the present case.

## CASE PRESENTATION

A 73-year old man seeking treatment for bilateral severe hearing loss visited our department. When he was 47 years old, he was found to have high levels of serum alkaline phosphatase (ALP) with normal serum calcium levels. However, a needle bone biopsy and a bone scan did not yield an accurate diagnosis. Since then, his hearing became progressively worse and required hearing aids. At his first visit to our department, audiological assessment revealed a bilateral severe hearing loss and an air-bone gap with 45 dB in the low frequency range (250–1000 Hz) with profound sensorineural hearing loss in the high frequency range (Figure 1). Neither the auditory brainstem response nor the stapedial response was found bilaterally. The Japanese monosyllabic open-set word recognition test in a sound field at 65 dB had a result of 20% with the hearing aid. Also, the conductive hearing loss was not ameliorated by a bone conduction hearing aid (Figure 2, gray triangles).

The image findings showed a geographic lucency in the skull bone in the X-ray and an increased uptake in the skull in the bone scan, which is useful in determining the extent and activity of the condition. Computed tomography (CT) findings revealed homogeneously diffused hyperostosis of the skull and a slight loss of bone mineral density in the cochlear capsule (Figure 3). The T2-weighted magnetic resonance imaging (MRI) analysis demonstrated that the eight nerves and the perilymph in the cochlea were visible bilaterally (Figure 4). The image findings suggested the diagnosis of Paget's disease, and the serum ALP level rose to 5309 U/L (normal serum range is from 20 to 141 U/L), with normal serum calcium levels.

The creatinine clearance level was less than 40 mL/h, and the concentration of circulating 1,25-dihydroxyvitamin (373 pg/mL), intact parathyroid hormone (iPTH, 61 pg/mL), and % tubular reabsorption of phosphate (69%) were within the normal ranges. A potent bisphosphonate, oral risedronate (Actonel, Eisai Co., Ltd; Tokyo, Japan), was prescribed in daily adjusted dosages for

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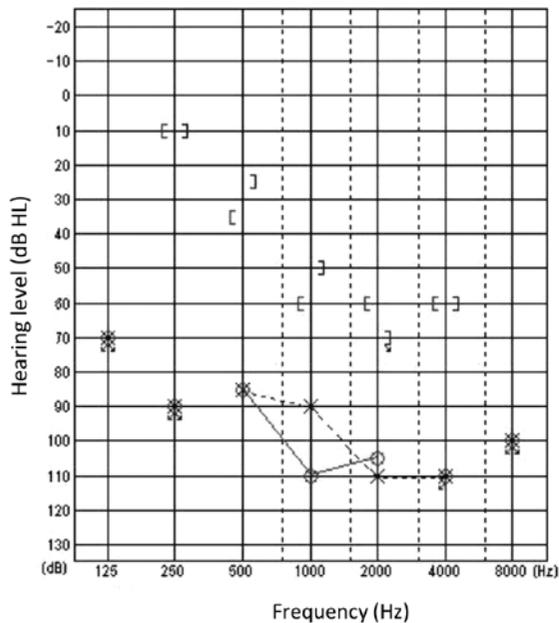


Figure 1. Pure tone audiogram of the right side (circle) and the left side (anex)

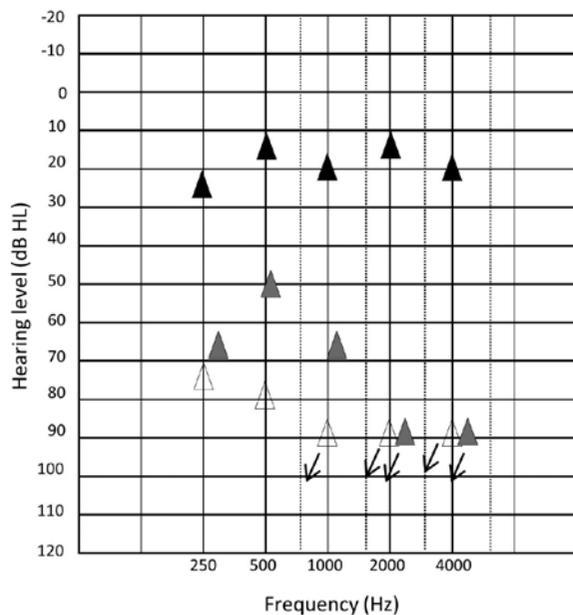


Figure 2. Audiometry with bone conductive hearing aids and with the cochlear implant on a sound field. White triangles: without aids, gray triangles: with bone conductive hearing aids, black triangles: with the cochlear implant

6 months. Because of renal dysfunction, the patient's serum level of ALP was slightly reduced (1928 U/L). However, the hearing level did not change after the treatment. We explained the possibility of the reasonable outcome of a cochlear implantation to our patient and performed the implantation on the left side after obtaining his informed consent.

The intraoperative finding showed that the skull bone was very rough; however, the incus and stapes were intact. Drainage of the perilymph was observed after the cochleostomy, and the Nucleus CI24RE Contour Advance electrode (Cochlear Corporation; Sydney,

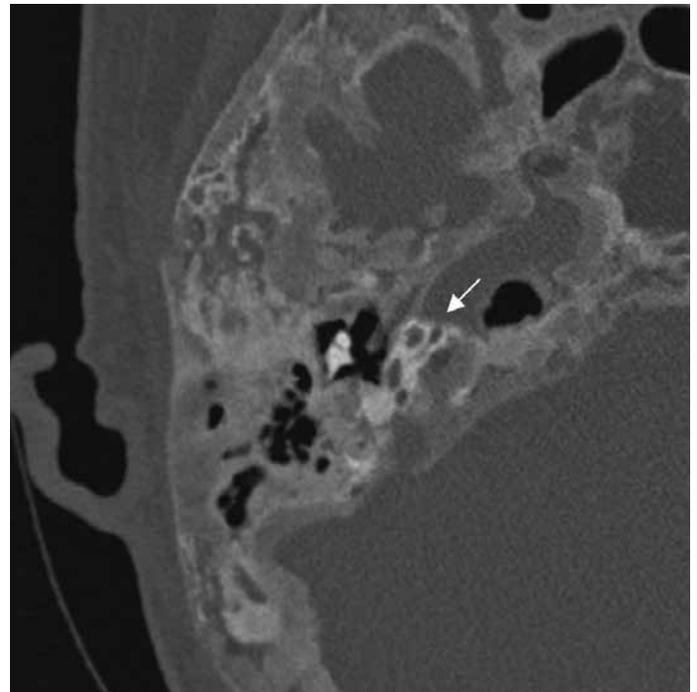


Figure 3. Axial high-resolution CT images of the temporal bone, showing diffused hyperostosis of the skull and a slight loss of bone mineral density in the cochlear capsule (white arrow)

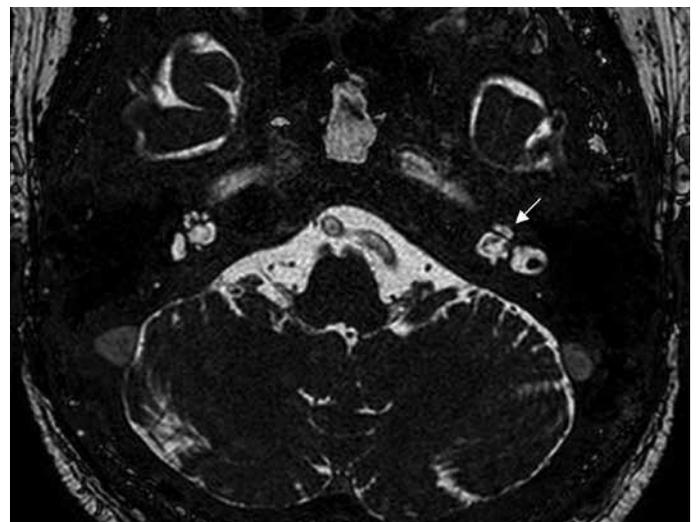
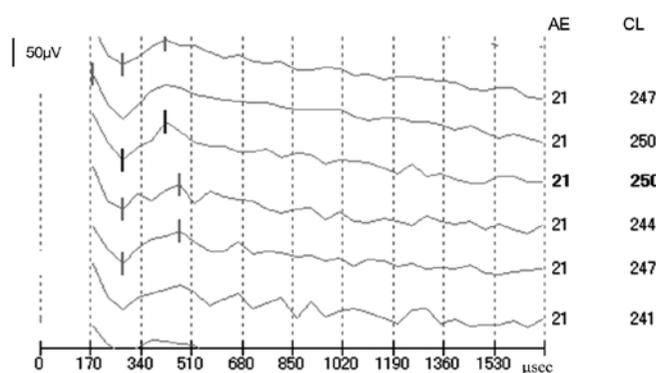


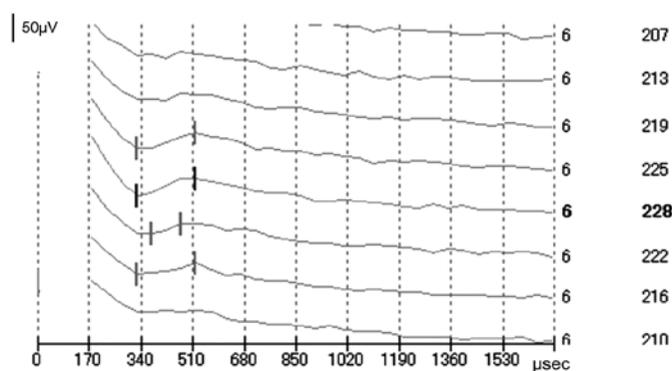
Figure 4. The T2-weighted MRI demonstrated that the eight nerves and the perilymph in the cochlea (white arrow) were visible bilaterally

Australia) was completely inserted. We measured the intraoperative response by neural response telemetry (NRT, Auto-NRT™, Cochlear Corporation; Sydney, Australia), which is a noninvasive, direct physiological measurement of the evoked compound action potentials of the cochlear nerve via the implant [5]. The NRT responses were observed in all measured channels (Figure 5, 6).

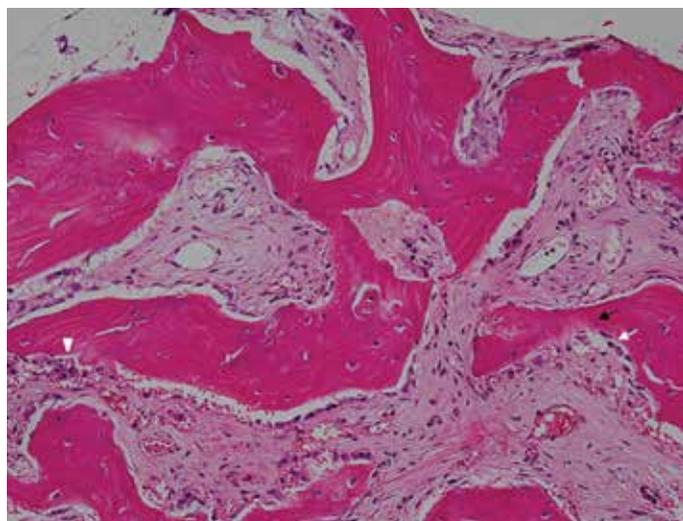
The histopathological examination of the bone specimen after the biopsy during the operation showed a structure composed of early bone and fibrous stroma. The osteoblastic and osteoclastic cells were scattered in the bone, and the fibrous arrangement was interrupted; this is called woven bone, a characteristic pattern of Paget's disease (Figure 7) [6].



**Figure 5.** The evoked potential of the intraoperative neural response telemetry (NRT) on electrode 21. AE: active electrode, CL: current level



**Figure 6.** The evoked potential of the intraoperative neural response telemetry (NRT) on electrode 6. AE: active electrode, CL: current level



**Figure 7.** The histopathological examination of the bone specimen by biopsy during the operation. It represents the intermediate phase, which includes the osteoclast (white arrow head), osteoblast (white arrow), and woven bone (black arrow)

The behavioral T (threshold) and C (comfortable) levels on a 900 Hz advanced combination encoder (ACE) map were acquired within normal dynamic range with relatively high impedance. An average hearing level of approximately 20 dB was reacquired by the cochlear implant (Figure 3, black triangles). The Japanese monosyllabic open set word recognition test presented in a sound field at 65 dB was

74%. Finally, we obtained written informed consent from the patient for the publication of this paper and the accompanying audiological results and images.

## DISCUSSION

Monsell et al.<sup>[4]</sup> demonstrated that a loss of bone mineral density in the cochlear optic capsule in the CT is associated with both high-tone hearing loss and a low-tone air-bone gap in Paget's disease. The otic capsule is composed of three layers: the endosteal layer, the endochondral layer, and the periosteal layer. The osteolytic change occurs only in the periosteal layer of the otic capsule in the temporal bone in Paget's disease, and the ossicles and stapedial footplate are often intact. Continuous remodeling of the pagetic otic capsule results predominantly in progressive sensorineural hearing loss. Degeneration of the spiral ligament is often found in patients with otosclerosis, but not in Paget's disease<sup>[4]</sup>. Abnormalities of the metabolic homeostasis of the cochlea as a result of the liberation of cytokines may also cause inner ear dysfunction in otosclerosis and Paget's disease<sup>[7]</sup>.

The air-bone gap in audiometry is often observed in cases of Paget's disease. Histopathologic temporal bone studies failed to detect abnormal changes within the middle ear associated with Paget's disease<sup>[4, 8]</sup>. Further examination of temporal bones with Paget's disease revealed multiple microfractures within the otic capsule<sup>[9]</sup>. Although bone conductive hearing aids slightly improved the hearing thresholds of 250, 500, and 1000 Hz in the current case, the speech performance skill and the hearing thresholds in the high frequency range (greater than 2000 Hz) did not change with bone conductive hearing aids or air conductive hearing aids. The air-bone gap may be associated with the acoustical mechanics of hearing by the enhanced conduction of low-frequency sound energy by pagetic bone. The diffuse lesions or microfractures act as a third window which may permit the dissipation of acoustic energy into the cranial cavity as an amplifier for bone-conducted sounds<sup>[4, 10]</sup>.

One case illustrates the invasion of the internal auditory meatus by Paget's disease, with infiltration of the acoustic division of the nerve and profound deafness. The narrow cranial foramen causes neurological complications, including hearing loss from cochlear nerve damage<sup>[4]</sup>. However, the internal auditory canal and the cochlear nerve were intact in the CT and MRI scans of our case. Abnormal changes in the internal auditory canal are not always found in imaging results of patients with profound hearing loss due to Paget's disease.

Neural response telemetry is a method that enables the direct measurement of auditory nerve compound action potentials in cochlear implant patients<sup>[5]</sup>. NRT provides valuable information regarding the response of the auditory nerve to electrical stimulation. Action potentials with NRT in the intraoperative examination could be elicited in all measured electrodes in the current case. One case study reported that a case with profound hearing loss due to Paget's disease showed no response on the postoperative NRT, despite an excellent postoperative outcome of the cochlear implant<sup>[11]</sup>. Auditory nerve function may be preserved even in cases of Paget's disease with profound hearing loss.

The target of the pharmacological treatment for Paget's disease is to relieve related pain and reduce the rate of bone remodeling. Bisphos-

phonates are used to treat Paget's disease along with serial monitoring of bone markers such as serum ALP. Restoration of typical bone turnover may reduce the bone vascularization and the progression of the disease. Calcitonin treatment may prevent hearing loss compared with a control for 5-8 years of follow-up. However, hearing loss seems irreversible for most cases of Paget's disease [12]. We also failed to reduce or suppress progressive hearing loss in our case. Also, the conductive hearing loss was not ameliorated by either a bone conduction hearing aid or an air conduction hearing aid. A cochlear implantation was finally performed in our case, although only four cases of Paget's disease treated with cochlear implants have been successfully reported in the English literature [11, 13-15]. Our case also acquired an excellent hearing threshold in audiometry, and the cochlear implant has partially helped the patient's speech performance. This suggests that a cochlear implantation can be an indication for cases of Paget's disease with profound hearing loss. However, the postoperative word recognition of our case has gradually worsened over 3 years after the implantation. Careful and prolonged follow-up is required to evaluate the performance of the cochlear implantation in cases of Paget's disease.

### CONCLUSION

Bilateral progressive hearing loss is the most frequently encountered complication in Paget's disease. For profound hearing loss due to Paget's disease, only four cases of Paget's disease treated with cochlear implants have been successfully reported in the English literature. Our case also acquired an excellent hearing threshold in audiometry, and the cochlear implant partially improved his speech performance. Therefore, a cochlear implantation can be an indication for cases of Paget's disease with profound hearing loss.

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### REFERENCES

1. Paget J. On a Form of Chronic Inflammation of Bones (Osteitis Deformans). *Med Chir Trans* 1877; 60: 37-64. [\[CrossRef\]](#)
2. Abelson A. A review of Paget's disease of bone with a focus on the efficacy and safety of zoledronic acid 5 mg. *Curr Med Res Opin* 2008; 24: 695-705. [\[CrossRef\]](#)
3. Selby PL, Davie MW, Ralston SH, Stone MD. Guidelines on the management of Paget's disease of bone. *Bone* 2002; 31: 366-73. [\[CrossRef\]](#)
4. Monsell EM. The mechanism of hearing loss in Paget's disease of bone. *Laryngoscope* 2004; 114: 598-606. [\[CrossRef\]](#)
5. Shallop JK, Facer GW, Peterson A. Neural response telemetry with the nucleus CI24M cochlear implant. *Laryngoscope* 1999; 109: 1755-9. [\[CrossRef\]](#)
6. Applebaum EL, Clemis JD. Temporal bone histopathology of Paget's disease with sensorineural hearing loss and narrowing of the internal auditory canal. *Laryngoscope* 1977; 87: 1753-9. [\[CrossRef\]](#)
7. Parahy C, Linthicum FH, Jr. Otosclerosis: relationship of spiral ligament hyalinization to sensorineural hearing loss. *Laryngoscope* 1983; 93: 717-20. [\[CrossRef\]](#)
8. Khetarpal U, Schuknecht HF. In search of pathologic correlates for hearing loss and vertigo in Paget's disease. A clinical and histopathologic study of 26 temporal bones. *Ann Otol Rhinol Laryngol Suppl* 1990; 145: 1-16.
9. Bahmad F, Jr., Merchant SN. Paget disease of the temporal bone. *Otol Neurotol* 2007; 28: 1157-8.
10. Merchant SN, Rosowski JJ. Conductive hearing loss caused by third-window lesions of the inner ear. *Otol Neurotol* 2008; 29: 282-9. [\[CrossRef\]](#)
11. Wolfowitz A, Shihada R, Shpak T, Braun J, Luntz M. Cochlear implantation in a patient with Paget's disease. *Laryngoscope* 2011; 121: 358-60. [\[CrossRef\]](#)
12. Langston AL, Ralston SH. Management of Paget's disease of bone. *Rheumatology (Oxford)* 2004; 43: 955-9. [\[CrossRef\]](#)
13. Bacciu A, Pasanisi E, Vincenti V, Ingegnoli F, Guida M, Panu F, et al. Paget's disease and cochlear implantation. *J Laryngol Otol* 2004; 118: 810-3. [\[CrossRef\]](#)
14. Lee IW, Goh EK, Kong SK, Park SH. A case of cochlear implantation in a patient with Paget disease. *Am J Otolaryngol* 2011; 32: 353-4. [\[CrossRef\]](#)
15. Takano K, Saikawa E, Ogasawara N, Himi T. Cochlear implantation in a patient with Paget's disease. *Am J Otolaryngol* 2014; 35: 408-10. [\[CrossRef\]](#)