

# Malignant external otitis following radiotherapy for oral cancer

## A case report

Takanori Eguchi, DDS, PhD<sup>a,\*</sup>, Akihiko Basugi, DDS, PhD<sup>a</sup>, Ikuyo Kanai, DDS, PhD<sup>a</sup>, Yukinaga Miyata, DDS, PhD<sup>a</sup>, Tomomitsu Nasuno, MD, PhD<sup>b</sup>, Yoshiki Hamada, DDS, PhD<sup>c</sup>

### Abstract

**Rationale:** Although an ototoxicity is well-known as adverse event of the radiotherapy, it is not widely known that immunosuppressed patients who underwent radiotherapy in head and neck region have risk of malignant external otitis.

**Patient concerns:** A 68-year-old man with diabetes, who had been diagnosed as intraosseous squamous cell carcinoma of the right mandible, underwent surgical resection. He received a total of 60 Gy/30Fr postoperative radiation. Four months after the course of radiation, he suffered from right aural fullness, otalgia and otorrhea.

**Diagnoses:** Clinical examination revealed granulation and existence of *Pseudomonas aeruginosa* in the external auditory canal. Computed tomography showed expansive inflammation and erosion in the temporal bone. The patient is elderly and diabetes. These findings led to the diagnosis of malignant external otitis.

**Interventions:** The ear irrigation and administration of quinolones were started. Afterwards, fistula was formed in the oral cavity, and connected to the right external auditory canal. Therefore, irrigations were performed not only from ear but also from the oral fistula.

**Outcomes:** Eight weeks after starting treatment, the malignant external otitis was completely healed.

**Lessons:** Physicians should raise awareness of malignant external otitis in immunosuppressed patients with oral cancer after radiotherapy.

**Abbreviations:** AIDS = acquired immune deficiency syndrome, CT = computed tomography, PMMC = pectoralis major myocutaneous.

**Keywords:** head and neck cancer, malignant external otitis, necrotizing otitis externa, radiotherapy, skull base osteomyelitis

## 1. Introduction

Malignant external otitis is invasive infection of external auditory canal, and can readily spread into adjacent structures, such as the temporal bone and occipital bone.<sup>[1]</sup> Although malignant external otitis is not malignant disease, it was termed ‘malignant’ by Chandler in 1968 because of the progressively aggressive behavior of the disease process.<sup>[2]</sup> Malignant external otitis can

occur in immunosuppressed patients, such as the elderly and those with diabetes mellitus or acquired immune deficiency syndrome (AIDS).<sup>[3]</sup> *Pseudomonas aeruginosa* is the most common pathogen, having been isolated in 90% of patients with malignant external otitis.<sup>[4]</sup> Antibiotics are generally used in treatment, and the mortality rate was reported as over 50% when appropriate antibiotics were not used.<sup>[2]</sup>

Radiotherapy, alone or associated with surgery or chemotherapy, is widely used for many malignancies of the head and neck region. High doses of irradiation in head and neck region may result in several adverse events such as, oral mucositis, osteoradionecrosis, and xerostomia.<sup>[5]</sup> An ototoxicity is also well-known as adverse event of the radiotherapy.<sup>[6]</sup> However, it is not widely known that malignant external otitis can develop after radiotherapy.

This report describes malignant external otitis developed in an elderly patient with diabetes after radiotherapy for oral cancer.

## 2. Case report

In July 2016, a 68-year-old Japanese man with diabetes mellitus (HbA1c:6.6%) presented to our clinic with intraosseous squamous cell carcinoma of the right mandible. A hemimandibulectomy, functional neck dissection on the affected side and immediate reconstruction using a pectoralis major myocutaneous (PMMC)-flap without hard tissue reconstruction were performed (Fig. 1). Histopathology of the surgical specimen confirmed a moderately

Editor: N/A.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

The authors declare no conflicts of interest.

<sup>a</sup> Department of Oral and Maxillofacial Surgery, <sup>b</sup> Department of Otorhinolaryngology, Toshiba Rinkan Hospital, Sagami-hara, <sup>c</sup> Department of Oral and Maxillofacial Surgery, School of Dental Medicine, Tsurumi University, Yokohama, Japan.

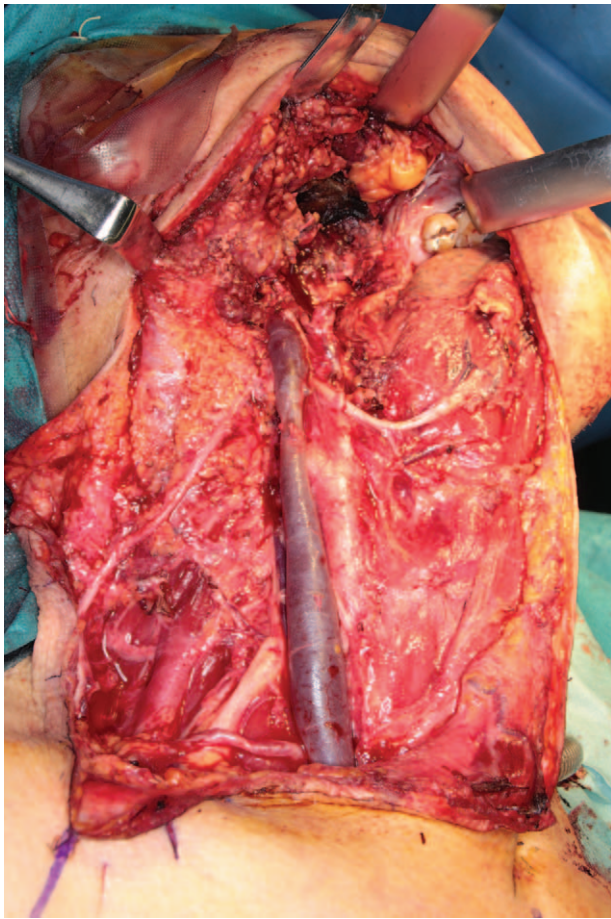
\* Correspondence: Takanori Eguchi, Department of Oral and Maxillofacial Surgery, Toshiba Rinkan Hospital, 7-9-1 Kamitsuruma Minami-ku, Sagami-hara 252-0385, Japan (e-mail: fhb19830419@yahoo.co.jp).

Copyright © 2018 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution-NoDerivatives License 4.0, which allows for redistribution, commercial and non-commercial, as long as it is passed along unchanged and in whole, with credit to the author.

Medicine (2018) 97:21(e10898)

Received: 9 March 2018 / Accepted: 8 May 2018

<http://dx.doi.org/10.1097/MD.00000000000010898>

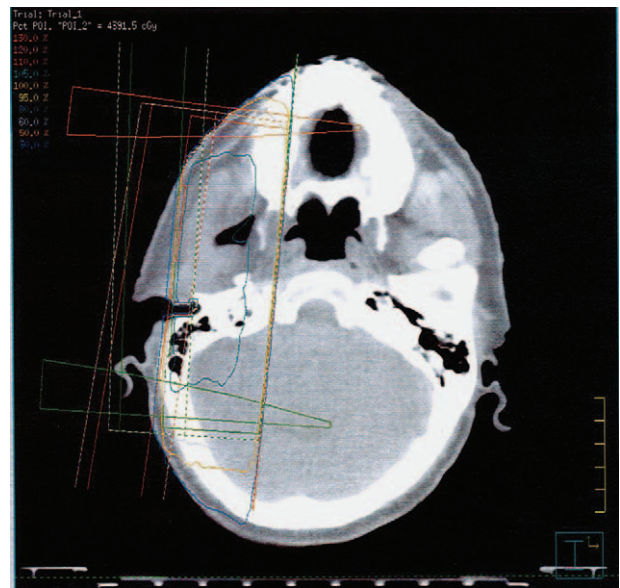


**Figure 1.** The image is captured from the hemimandibulectomy and functional neck dissection on the right side.

differentiated squamous cell carcinoma with lymphatic, perineural, vascular invasions, and cervical lymph-node metastasis in the level 2 (pT4aN1M0). A total of 60Gy/30Fr irradiation to the head and neck region was performed as adjuvant therapy from September to October 2016. The 2-field irradiation with total of 36Gy/18Fr was used for primary site and lymph-node metastasis, and the box-field irradiation with total of 24Gy/12Fr was only used for primary site (Fig. 2).

In January 2017, the patient complained of right aural fullness, otalgia and otorrhea. He did not have fever, and the facial nerve paralysis, which had developed after surgery, was unchanged. Ear endoscopy revealed granulation of the right ear canal (Fig. 3). The expansion of inflammatory reaction to the mastoid cell of temporal bone and temporal-bone erosion were identified on the computed tomography (CT) images (Fig. 4). *P. aeruginosa* was cultured from the right external auditory canal; the organism was sensitive to quinolones. Based on the clinical and imaging examinations, the diagnosis of malignant external otitis of the right ear was established.

Under hospitalization, the ear irrigation and administration of intravenous ciprofloxacin (800 mg/day) were daily performed for 3 weeks. In February 2017, at 3 weeks after starting treatment, the patient was discharged on the 24th hospital day, and treatments were changed to daily oral garenoxacin (400 mg/day) and the ear irrigation with 3 times per week, because ear symptoms was improved. On the other hands, a fistula was formed to the suturing border between PMMC-flap and oral

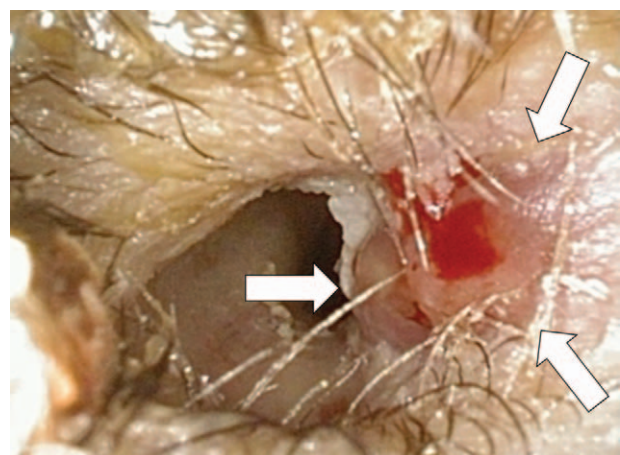


**Figure 2.** Radiation dose distribution in 2-field irradiation with total of 36Gy is shown. Total of 28.8Gy (80%) irradiation to right ear canal and 28.8~34.2Gy (80%~95%) to temporal bone were exposed.

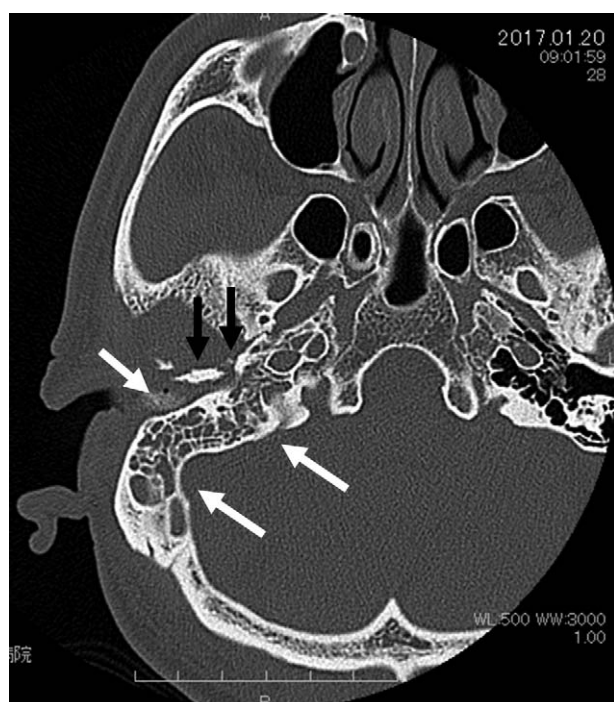
mucosa, and pus discharge was observed. We could confirm that the fistula connected to the external auditory canal, because the normal saline using ear irrigation was drained to the oral cavity via the fistula. Therefore, the irrigation was performed both from the ear and fistula. In March 2017, at 8 weeks after treatment of 3-week intravenous ciprofloxacin and 5-week oral garenoxacin, a few white debris were drained from oral fistula. Histopathological examination revealed that debris was fibrous necrotic tissue. Afterward, granulation of the right ear canal and pus discharge from the oral and ear disappeared completely, and the oral fistula was naturally closed in April 2017. No clinical evidence of recurrence has observed for 9-month follow-up.

### 3. Discussion

Malignant external otitis and ototoxicity associated with radiotherapy have common clinical features, such as aural



**Figure 3.** Granulation exists in the external auditory canal (arrows).



**Figure 4.** Axial CT scan indicate that pneumatization of the mastoid cell is not identified (white arrows), and temporal bone erosion is identified (black arrows).

fullness, otalgia, otorrhea, and existence of necrotic bone.<sup>[1,7]</sup> Therefore, ear symptoms after radiotherapy are generally diagnosed as ototoxicity, and it is difficult to suspect malignant external otitis.<sup>[8]</sup> The diagnosis of malignant external otitis is made on the basis of clinical and radiographic features, such as immunosuppressed individuals, ear canal granulation, bone erosion, cranial nerve palsies and isolation of *P. aeruginosa*.<sup>[1]</sup> Especially, diabetic patients and isolation of *P. aeruginosa* are important factor for its definitive diagnosis. Because over 90% of malignant external otitis are caused by *P. aeruginosa*, and most cases have been reported in diabetic patients.<sup>[11]</sup> Also in our case, an elderly patient with diabetes mellitus, isolation of *P. aeruginosa* and ear canal granulation led to the diagnosis as malignant external otitis. The possibility of malignant external otitis should be considered when an immunosuppressed patient has ear symptoms after radiotherapy for head and neck cancer.

Differential diagnosis of malignant external otitis includes cancer of the temporal bone, which has similar clinical findings, such as cranial nerve palsies and aggressive bone destruction.<sup>[3]</sup> In fact, there are case reports that a cancer of the temporal bone was misdiagnosed as malignant external otitis.<sup>[9]</sup> Imaging modalities cannot distinguish cancer from malignant external otitis. Thus, a biopsy is the only definitive method to diagnose malignant external otitis or cancer. In our case, the patient had suffered from intraosseous squamous cell carcinoma of the mandible expanding to the mandibular ramus, which had a potential to invade to the temporal bone. Although biopsy should be firstly performed to rule out a cancer of the temporal bone, we diagnosed malignant external otitis without biopsy, because symptoms improved by antibiotics.

Ototoxicity associated with radiotherapy occurs in the external ear, middle ear, and inner ear.<sup>[7]</sup> In external ear, the ototoxicity consist of early reaction and late reaction.<sup>[6]</sup> The early reaction is

only skin reaction during radiotherapy, and it naturally heal after radiotherapy. On the other hands, the late reaction appears as acute otitis externa, chronic otitis externa, skin ulcer, and osteo/cartilaginous necrosis after several months of radiotherapy.<sup>[7]</sup> In our case, external-ear symptoms developed 4 months after radiotherapy, and necrotic tissue was observed. These findings suggest that our patient suffered late reaction. We consider that late reaction of the external ear changed to the malignant external otitis by immunosuppressed conditions due to old age and diabetes.

Systemic antipseudomonal antibiotics are the primary therapy for malignant external otitis.<sup>[1]</sup> Quinolones, especially ciprofloxacin, have been used to treat malignant external otitis, because they are active against *P. aeruginosa* and have a low toxicity profile and excellent penetration into bone.<sup>[3]</sup> Therefore, we used quinolones for our patient, and they were effective. On the other hands, there are many reports that over 30% of *P. aeruginosa* organisms in malignant external otitis are resistant to ciprofloxacin, because it is widely used for respiratory infections and topical preparations for otitis media and externa.<sup>[10]</sup> To apply effective antibiotics to the malignant external otitis, microbial culture and sensitivity tests are necessary.

#### 4. Conclusion

Radiotherapy for immunosuppressed individuals with head and neck cancer are at risk for developing malignant external otitis. Physicians need to be aware of the possibility of malignant external otitis after radiotherapy for head and neck region.

#### Author contributions

**Data curation:** Takanori Eguchi, Akihiko Basugi, Yukinaga Miyata.

**Investigation:** Takanori Eguchi, Tomomitsu Nasuno.

**Visualization:** Takanori Eguchi.

**Writing – original draft:** Takanori Eguchi.

**Writing – review & editing:** Ikuyo Kanai, Yoshiki Hamada.

#### References

- [1] Rubin Grandis J, Branstetter BF, Yu VL, et al. The changing face of malignant (necrotising) external otitis: clinical, radiological, and anatomic correlations. *Lancet Infect Dis* 2004;4:34–9.
- [2] Chandler JR. Malignant external otitis. *Laryngoscope* 1968;78:1257–94.
- [3] Carfrae MJ, Kesser BW. Malignant otitis externa. *Otolaryngol Clin North Am* 2008;41:537–49.
- [4] Stern Shavit S, Soudry E, Hamzany Y, et al. Malignant external otitis: factors predicting patient outcomes. *Am J Otolaryngol* 2016;37:425–30.
- [5] Tolentino Ede S, Centurion BS, Ferreira LHC, et al. Oral adverse effects of head and neck radiotherapy: literature review and suggestion of a clinical oral care guideline for irradiated patients. *J Appl Oral Sci* 2011;19:448–54.
- [6] Jereczek-Fossa BA, Zarowski A, Milani F, et al. Radiotherapy-induced ear toxicity. *Cancer Treat Rev* 2003;29:417–30.
- [7] Bhandare N, Antonelli PJ, Morris CG, et al. Ototoxicity after radiotherapy for head and neck tumors. *Int J Radiat Oncol* 2007;67:469–79.
- [8] Rosenfeld RM, Brown L, Cannon CR, et al. Clinical practice guideline: acute otitis externa. *Otolaryngol Head Neck Surg* 2006;134(4 Suppl):S4–23.
- [9] Foden N, Burgess C, Damato S, et al. Concurrent necrotising otitis externa and adenocarcinoma of the temporal bone: a diagnostic challenge. *BMJ Case Rep* 2013;1–4.
- [10] Berenholz L, Katzenell U, Harell M. Evolving resistant pseudomonas to ciprofloxacin in malignant otitis externa. *Laryngoscope* 2002;112:1619–22.