Clinical Characteristics and Management of External Auditory Canal Squamous Cell Carcinoma in Post-irradiated Nasopharyngeal Carcinoma Patients

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Objective: To describe the clinical characteristics and management of patients with external auditory canal (EAC) squamous cell carcinoma (SCC) that arose after they received radiotherapy for nasopharyngeal carcinoma (NPC) and to compare them with primary EAC SCC patients.

Study Design: Retrospective clinical analysis.

Setting: Hospital.

Patients: Nine irradiated NPC patients who subsequently developed secondary EAC SCC and 41 primary EAC SCC patients at a single hospital.

Intervention: Clinical characteristics and management outcomes of patients were reviewed.

Main Outcome Measures: Clinical manifestations, regions of tumor involvement, the pathological staging, cumulative overall survival rates, Kaplan-Meier method, log rank test, and Mann-Whitney U test.

Results: The most common symptoms of both groups were otorrhea, otalgia, and hearing loss. The region most involved in both groups was the EAC. The proportions of early stage (T1, T2) tumors in the post-irradiated and primary EAC SCC group were 56 and 22%, respectively. The 6-month, 1-year, 2-year, and 3-year cumulative overall survival rates of the post-irradiated EAC SCC group were 100, 100, 89, and 89%, respectively. The incidence of radionecrosis was higher in the post-irradiation EAC SCC group than in the primary EAC SCC group.

Conclusions: Post-irradiation EAC SCC has similar symptoms and invades similar regions as primary EAC SCC. The proportion of early stage tumors in the post-irradiated EAC SCC group was higher than that in the primary EAC SCC group. High incidence of radionecrosis was observed after the second course of radiotherapy. Aggressive surgical treatment is strongly recommended, but adjuvant radiotherapy for early stage EAC SCC should be provided cautiously.

Keywords: External auditory canal—Nasopharyngeal carcinoma—Post-irradiated malignancy—Radiotherapy—Squamous cell carcinoma—Survival analysis.

Otol Neurotol 00:00–00, 2015.
In addition, the EAC, middle ear, and temporal bone are located within the skull base, so that tumors in these sites often extend to involve the parotid gland and jugular foramen, and even the internal carotid artery and the dura. The complexity of the anatomy of these regions makes surgical management very challenging (11). Because EAC carcinoma can demonstrate very aggressive behavior, it demands aggressive surgical treatment. A previous study showed that complete tumor resection in the first attempt is crucial to achieve good prognosis, aggressive surgical intervention can guarantee a tumor-free margin. The overall survival rates are much better for patients treated adequately at the first opportunity than for patients who undergo salvage surgery for recurrent disease (12).

EAC carcinoma in post-irradiated NPC patients occurs with an incidence of approximately 0.15% (13), which is much higher than the incidence of primary EAC carcinoma among the general population. Are the clinical characteristics, management, and prognosis of EAC carcinoma in post-irradiated NPC patients similar to those of primary EAC carcinoma in patients without a history of previous radiation? In this study, we retrospectively reviewed the clinical characteristics, management strategy, and outcomes of nine EAC squamous cell carcinoma (SCC) patients who had previously received radiotherapy for NPC and of 41 primary EAC SCC patients from the same period, who served as the control group.

## PATIENTS AND METHODS

From January 2006 to December 2013, a total of 50 patients who were diagnosed with EAC SCC were included in this study. Among them, nine (18%) were patients who had received radiotherapy for NPC before their diagnosis of EAC SCC and 41 (82%) were primary EAC SCC patients. All of these patients were operated on by the senior author (C.D.). Their clinical data, obtained from the hospital records, were retrospectively reviewed for analysis of the demographic characteristics, treatments, and outcomes.

The criteria used for the diagnosis of post-irradiated EAC carcinoma is a modification of the criteria originally described by Cahan et al. (14) and Arlen et al. (15). The criteria included the following: 1), a previous history of irradiation, 2), the development of a new malignancy in the radiation field, 3), a latent period of at least 2 years between radiation and the diagnosis of a newly developed malignancy, and 4), a tumor proven histologically to be different from the original malignancy.

All of the data based on patients’ medical records and follow-up interviews, including age, gender, case history, presenting symptoms, results of the clinical examinations and assessments, stage, surgical management, postoperative outcomes, and follow-up findings, were collected until September 2014. Two of the primary EAC SCC patients were lost to follow-up, so their data were not included in the Kaplan-Meier survival analysis and log rank test.

All patients had undergone a hearing test and a facial-nerve functional evaluation. High-resolution computed tomography (HRCT) and magnetic resonance imaging (MRI) of the temporal bone had been performed. In the hearing examination, the pure-tone audiometry (PTA) value was calculated as the mean of the thresholds at 500, 1000, 2000, and 3000 Hz. The Pittsburgh staging system as modified by Moody et al. (16) was used to grade the EAC carcinomas.

All of the patients in this study underwent surgical treatment. The surgical procedures included local-canal resection (LCR), lateral temporal-bone resection (LTBR), and subtotal temporal-bone resection (STBR). The region and extent of the tumors determined whether a parotidectomy was necessary, which included a superficial parotidectomy (SP) and a total parotidectomy (TP). Neck dissection was indicated when the patient had advanced-stage SCC.

The rates of cumulative overall survival were calculated using the Kaplan-Meier method. Correlations between the survival rates and associated factors were assessed using the log rank test. The statistical significance was tested using the Mann-Whitney U test, and a p value of less than 0.05 was considered to be significant. All of the statistical analyses were performed using SPSS version 19.0 software (SPSS Inc., Chicago, IL, USA).

## RESULTS

The clinical data for the nine patients who developed post-irradiated EAC SCC are shown in Table 1, and the summary and comparative data vis a vis the primary EAC SCC patients are shown in Table 2.

### Demographic Characteristics

In the group of nine patients with post-irradiated EAC SCC, there were six males and three females, with a median age of 61 years. The interval between the completion of previous radiotherapy for NPC and the diagnosis of EAC carcinoma ranged from 14 to 28 years, with a median of 19 (SD, 4.86) years.

In the group of 41 patients with primary EAC SCC, there were 25 males and 16 females, with a median age of 60 years.

There were no significant differences between the two groups regarding age or gender (Table 2).

### Clinical Manifestations

The common symptoms in the post-irradiated EAC SCC group are shown in Table 1; the most frequent symptoms were otorrhea/bloody otorrhea (n = 9, 100%), otalgia (n = 7, 78%), and hearing loss (n = 9, 100%).

The most frequent symptoms in the primary EAC SCC group were otorrhea/bloody otorrhea (n = 35, 85%), otalgia (n = 27, 66%), and hearing loss (n = 29, 71%).

### Clinical Examinations

In the PTA examination, all of post-irradiated EAC SCC patients were found to have hearing loss and the affected ear exhibited a higher PTA threshold than the
contralateral ear. Seven patients had bilateral hearing loss and two patients had unilateral hearing loss.

The region and extent of the tumors, shown in Table 1, were evaluated based on the imaging manifestations and were confirmed by the intraoperative findings and the pathology results. In the post-irradiated EAC SCC group, the most frequently invaded region was the EAC (n = 9, 100%), followed by the mastoid (n = 3, 33%), tympanum (n = 2, 22%), parotid gland (n = 1, 11%), digastric muscle (n = 1, 11%), Eustachian tube (n = 1, 11%), sigmoid sinus (n = 1, 11%), facial nerve (n = 1, 11%), parapharyngeal space (n = 1, 11%), and dura (n = 1, 11%).

In the primary EAC SCC group, the most frequently invaded region was the EAC (n = 36, 88%), followed by the tympanum (n = 18, 44%), parotid gland (n = 12, 29%), mastoid (n = 7, 17%), temporomandibular joint (n = 7, 17%), facial nerve (n = 6, 15%), dura (n = 6, 15%), and jugular foramen (n = 5, 12%). The occasionally invaded regions such as the parapharyngeal space (n = 4, 10%), digastric muscle (n = 3, 7%), temporal muscle (n = 2, 5%), and sigmoid sinus (n = 2, 5%) were encroached sparingly.

### Staging of Disease

Based on the Pittsburgh staging system for EAC carcinomas, there were five tumors in the early stage (T1, T2) and four tumors in the advanced stage (T3, T4) in the post-irradiated EAC SCC group. None of the patients had metastasis to the cervical lymph nodes or distant metastases.

The primary EAC SCC patients were classified as follows: nine patients were in the early stage (T1, T2) and 32 patients were in the advanced stage (T3, T4) of disease. One patient had metastasis to a parotid lymph node and one patient had metastasis to a cervical lymph node.

There were significant differences between the two groups regarding the tumor stage (Table 2). Within the groups, early-stage disease was more commonly found in the post-irradiation group.

### Surgical Managements

In the post-irradiated EAC SCC group, one patient underwent LCR, five underwent LTBR + SP, one underwent STBR + TP, one underwent STBR + SP, and one underwent STBR + TP + neck dissection. Five patients received adjuvant radiation therapy and three of these patients developed radionecrosis.

In the primary EAC SCC group, the surgical procedures conducted were LCR in three patients, LTBR + SP in 16 patients, LTBR + SP + neck dissection in four patients, LTBR + TP in three patients, LTBR + TP + neck dissection in one patient, STBR in four patients, and STBR + TP + neck dissection in one patient, STBR in four patients.

### Table 1.

<table>
<thead>
<tr>
<th>No.</th>
<th>Age/Sex</th>
<th>Interval, yr</th>
<th>Region</th>
<th>Symptoms</th>
<th>Procedure</th>
<th>Adjuvant Therapy</th>
<th>Stage</th>
<th>Differentiation Degree</th>
<th>Outcome</th>
<th>Follow-up, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67/F</td>
<td>25</td>
<td>LE, LST</td>
<td>Otalgia, tinnitus, BO, HL</td>
<td>LTBR, SP</td>
<td>—</td>
<td>T2</td>
<td>PD</td>
<td>DOC</td>
<td>52</td>
</tr>
<tr>
<td>2</td>
<td>59/F</td>
<td>18</td>
<td>EST, ME, MA, DU, MEMW</td>
<td>Otalgia, BO, HL</td>
<td>STBR, SP</td>
<td>—</td>
<td>T3</td>
<td>PD</td>
<td>DOD</td>
<td>42</td>
</tr>
<tr>
<td>3</td>
<td>63/M</td>
<td>19</td>
<td>EST, MA, PA, LST</td>
<td>Otalgia, tinnitus, HL</td>
<td>STBR, TP, ND</td>
<td>RT</td>
<td>T3</td>
<td>MD</td>
<td>NED</td>
<td>37</td>
</tr>
<tr>
<td>4</td>
<td>58/F</td>
<td>17</td>
<td>LE, LST</td>
<td>Otalgia, BO, HL, FP</td>
<td>LTBR, SP</td>
<td>—</td>
<td>T2</td>
<td>WD</td>
<td>NED</td>
<td>33</td>
</tr>
<tr>
<td>5</td>
<td>64/M</td>
<td>14</td>
<td>EST, ME</td>
<td>Otalgia, tinnitus, HL</td>
<td>LTBR, SP</td>
<td>—</td>
<td>T2</td>
<td>WD</td>
<td>NED</td>
<td>16</td>
</tr>
<tr>
<td>6</td>
<td>66/M</td>
<td>28</td>
<td>EST, ME</td>
<td>Otalgia, tinnitus, HL</td>
<td>LTBR, SP</td>
<td>—</td>
<td>T2</td>
<td>WD</td>
<td>NED</td>
<td>17</td>
</tr>
<tr>
<td>7</td>
<td>49/M</td>
<td>15</td>
<td>LE</td>
<td>Otalgia, tinnitus, HL</td>
<td>LTBR, SP</td>
<td>—</td>
<td>T2</td>
<td>WD</td>
<td>NED</td>
<td>17</td>
</tr>
<tr>
<td>8</td>
<td>58/M</td>
<td>14</td>
<td>LE</td>
<td>Otalgia, tinnitus, HL</td>
<td>LTBR, SP</td>
<td>—</td>
<td>T2</td>
<td>WD</td>
<td>NED</td>
<td>24</td>
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<tr>
<td>9</td>
<td>65/M</td>
<td>20</td>
<td>LE</td>
<td>Otalgia, tinnitus, HL</td>
<td>LTBR, SP</td>
<td>—</td>
<td>T2</td>
<td>WD</td>
<td>NED</td>
<td>26</td>
</tr>
</tbody>
</table>

LE, limited canal erosion; LST, limited soft tissue involvement; EST, extensive (>5 mm) soft tissue involvement; ME, middle ear involvement; MA, mastoid involvement; DU, dural invasion; PA, parotid involvement; MEMW, invasion of medial wall of middle ear; FP, facial palsy; BO, bloody otalgia; HL, hearing loss; LTBR, lateral temporal bone resection; STBR, subtotal temporal bone resection; SP, superficial parotidectomy; TP, total parotidectomy; ND, neck dissection; LCR, local canal resection; RT, radiotherapy; PD, poorly differentiated; MD, moderately differentiated; WD, well differentiated; NED, no evidence of disease; DOC, died of other causes; DOD, died of disease.

### Table 2.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Post-irradiated Patients</th>
<th>Primary Patients</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis</td>
<td>61 ± 5.66 yr</td>
<td>60 ± 8.42 yr</td>
<td>0.762</td>
</tr>
<tr>
<td>Range</td>
<td>49–67 yr</td>
<td>40–75 yr</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>6 (67%)</td>
<td>25 (61%)</td>
<td>0.753</td>
</tr>
<tr>
<td>Female</td>
<td>3 (33%)</td>
<td>16 (39%)</td>
<td></td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early</td>
<td>5 (56%)</td>
<td>9 (22%)</td>
<td>0.044</td>
</tr>
<tr>
<td>Advanced</td>
<td>4 (44%)</td>
<td>32 (78%)</td>
<td></td>
</tr>
<tr>
<td>Differentiation degree</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well</td>
<td>3 (33%)</td>
<td>12 (29%)</td>
<td>0.377</td>
</tr>
<tr>
<td>Moderately</td>
<td>5 (56%)</td>
<td>21 (51%)</td>
<td></td>
</tr>
<tr>
<td>Poorly</td>
<td>1 (11%)</td>
<td>8 (20%)</td>
<td></td>
</tr>
</tbody>
</table>

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STBR + neck dissection in one patient, STBR + SP in two patients, STBR + SP + neck dissection in two patients, and STBR + TP + neck dissection in five patients. Twenty-eight patients received adjuvant radiation therapy; one patient received adjuvant chemotherapy. Only two patients developed radionecrosis after radiotherapy in the primary EAC SCC group.

Pathological Outcomes

The degree of differentiation of the tumors is shown in Table 1 and Table 2.

In the post-irradiated EAC SCC group, there were three cases of well-differentiated tumors, five cases of moderately differentiated tumors, and one case of a poorly differentiated tumor.

In the primary EAC SCC group, there were 12 cases of well-differentiated tumors, 21 cases of moderately differentiated tumors, and eight cases of poorly differentiated tumors.

There was no significant difference in the degree of differentiation of the tumors in the two groups (Table 2).

Follow-up Findings

The follow-up findings of the nine patients with post-irradiated EAC SCC are given in Table 1. The mean follow-up time was 28 (SD, 12.07) months. When the post-treatment follow-up concluded, two patients had died and seven patients survived. The 6-month, 1-year, 2-year, and 3-year cumulative overall survival rates were 100, 100, 89, and 89%, respectively (Fig. 1). The 1-year, 2-year, and 3-year cumulative overall survival rates of patients with early-stage and advanced-stage disease were 100 and 100%, 100 and 75%, and 100 and 75%, respectively (Fig. 2).

One post-irradiated EAC carcinoma patient with early-stage disease underwent LCR and received a second course of adjuvant radiotherapy postoperatively at a dose of 66 Gy. One year later, he developed osteoradionecrosis in the temporal bone and parapharyngeal space. A radical mastoidectomy was conducted to improve drainage. In the follow-up of the other four post-irradiated EAC carcinoma patients with early-stage disease who did not accept adjuvant radiotherapy, all were found to have survived without complications.

Of the four post-irradiated EAC SCC patients with advanced-stage disease who received a second course of adjuvant radiation therapy, one died 14 months later, two developed severe radionecrosis in the radiation field at 18 (Fig. 3) and 28 months, respectively, and only one had no complications.

The mean follow-up period in the primary EAC SCC group was 31 (SD, 28.87) months. The 6-month, 1-year, 2-year, and 3-year cumulative overall survival rates were 87, 69, 55, and 51%, respectively (Fig. 1). The 1-year, 2-year, and 3-year cumulative overall survival rates of patients with early-stage and advanced-stage disease were 100 and 60%, 88 and 46%, and 88 and 41%, respectively (Fig. 4).

FIG. 1. Kaplan-Meier survival curves of post-irradiated external auditory canal (EAC) squamous cell carcinoma (SCC) patients and primary EAC SCC patients (p = 0.212 > 0.05). Patients with post-irradiated EAC SCC exhibited similar survival outcomes (green line) to patients with primary EAC SCC (blue line).
Correlation Analysis

Based on statistical analysis using the log rank test, there was no significant difference in the 6-month, 1-year, 2-year, and 3-year cumulative overall survival rates of the two groups (Fig. 1).

The stage and the cumulative overall survival rate were significantly correlated in the primary EAC SCC group (Fig. 4). However, there was no significant correlation between the stage and the cumulative overall survival rate in the post-irradiated EAC SCC group (Fig. 2), which may be that the sample size of post-irradiated EAC SCC patients was too small.

There was no significant correlation between gender or receiving adjuvant radiation therapy and the cumulative overall survival rate in the primary EAC SCC group or the post-irradiated EAC SCC group (see Figures, Supplemental Digital Content 1 [http://links.lww.com/MAO/A290] and Supplemental Digital Content 3 [http://links.lww.com/MAO/A292]).
There was no significant correlation between facial paralysis or tumor differentiation and the cumulative overall survival rate in the post-irradiated EAC SCC group. However, these two factors were significantly correlated with the cumulative overall survival rate in the primary EAC SCC group (see Figures, Supplemental Digital Content 2 [http://links.lww.com/MAO/A291] and Supplemental Digital Content 4 [http://links.lww.com/MAO/A293]).

**DISCUSSION**

Reviewing the previous literatures showed that post-irradiated EAC carcinoma has been infrequently reported (17–23). Lo et al. (13) reported that the incidence of EAC carcinoma in the post-irradiated NPC population was 1000 times greater than the reported incidence of primary EAC carcinoma in the general population. That study included 7500 patients with NPC, and one-third to half of the NPC patients survived for more than 10 years after radiotherapy, so the data were very persuasive. Patients with primary radiation treatment and a long remission period may develop post-irradiation carcinomas or sarcomas (24).

In this study, there were no significant differences between the two groups regarding age and gender. The interval between the previous radiotherapy for NPC and the diagnosis of EAC SCC was 19 years, which is consistent with the results of Lo’s study (13). Radiation-induced carcinogenesis takes time. The latency period for post-irradiated EAC SCC was more than 14 years. The long interval was sufficient for the development of lesions.

The post-irradiated EAC SCC patients had no special symptoms compared with those of the primary EAC SCC patients. There was no significant correlation between the existence of facial paralysis and the overall survival rate in the post-irradiated EAC carcinoma group. However, the existence of facial paralysis was significantly correlated with prognosis in the primary EAC SCC group.

The most invaded region was the EAC in both the post-irradiated and primary EAC SCC patients. Tumors can readily encroach upon the tympanic cavity through the tympanic membrane and the parotid gland through the Santorini notch; thus, the tympanum, mastoid, and parotid gland are also frequently encroached upon. The invaded regions were heterogeneous in the primary EAC SCC patients. To ensure tumor-free margins, such irregular tumors should be evaluated based on the preoperative imaging manifestations with confirmation obtained through the intraoperative findings and pathology examinations.

The tumors stages were classified in this study according to the Pittsburgh staging system for EAC carcinomas. The proportion of early stage cases in the post-irradiated EAC SCC group was higher than that in the primary EAC SCC group. There were significant differences regarding the tumor stage in the two groups. This result may be due to there being no specific symptoms in the early stage of EAC.
SCC, so that early diagnosis of primary EAC SCC is very difficult. However, post-irradiated patients are more aware of lesions in the irradiation field because they once had NPC, and they may seek evaluation by physicians as soon as possible. This action may have resulted in the early diagnosis of EAC SCC in the irradiated patients. According to our data, the NPC patients had more symptoms at initial presentation than did the primary EAC SCC patients. Perhaps this is another reason the NPC patients presented earlier than the primary EAC SCC patients.

EAC carcinoma can exhibit aggressive behaviors, so aggressive surgical treatments are necessary. The optimal surgical management of EAC carcinoma remains controversial. In this study, the management strategies for EAC SCC included LCR, LTBR, and STBR. In our study, the tumors never encroached upon the petrous apex; thus, total temporal-bone resection (TTBR) was not applied in our surgical treatments. A tumor can spread beyond the EAC and invade the parotid gland through the Santorini notch even if the patient was diagnosed in the early stage by radiographic evaluation. Therefore, specific attention was paid to whether a parotidectomy had been performed. Our current surgical strategy for T1 and T2 stage EAC SCC is LTBR with a superficial parotidectomy. For T3 stage tumors, the surgical strategy is LTBR or STBR, depending on the region and extent of the tumors revealed in the imaging studies and intraoperative evaluation. STBR is routinely adopted to treat T4 stage EAC SCC.

Some patients received adjuvant radiotherapy as a postoperative therapy; receiving this treatment was not significantly correlated with the overall survival rates but it is unnecessary for early stage EAC SCC, particularly those patient guaranteed intraoperative tumor-free margins. Moncrieff et al. (25) and Leong et al. (26) recommended postoperative RT for all patients, whereas adjuvant treatments were only administered to variously selected patients in most series. Some authors recommend radiotherapy systematically to T1 or T2 tumors in adjunct to surgery (27,28), but most authors recommend postoperative radiation for T3 or T4 tumors in combination with extended temporal bone resection (29,30). The post-irradiated EAC SCC patients had received radiotherapy for NPC previously, and adjuvant postoperative radiotherapy may induce serious complications even over the long term after the first radiotherapy. In this study, five post-irradiated EAC SCC patients received another course of adjuvant radiation therapy, three of whom developed severe radionecrosis. The high incidence of radiation-induced necrosis in the irradiated EAC SCC patients reminds us that postoperative radiation should be cautiously applied, particularly for patients with early-stage carcinoma. Accordingly, it is unnecessary to administer adjuvant radiotherapy to patients with early-stage EAC SCC with guaranteed tumor-free margins. Moreover, among the three patients with radionecrosis, one patient was diagnosed at an early stage. However, he underwent the LCR procedure and received radiotherapy. If LTBR with a superficial parotidectomy had been performed and resulted in clear surgical margins, then radiotherapy would have been waived. We suggest that irradiation-induced EAC SCC in an early stage should be managed with aggressive surgery that guarantees tumor-free margin.

Our data showed that the tumor differentiation did not correlate with the survival in T4 stage (31). However, Masterson’s study indicated that histopathologic grade was a significant predictor of survival (32). In this study, the degree of differentiation of the tumors was not significantly correlated with the overall survival rates of the post-irradiated EAC SCC patients, but there were significant differences in overall survival rates of primary EAC SCC patients according to tumor differentiation status. Anyway, because of the low incidence, the sample size in most studies is too small; this may have reduced statistical power to identify more subtle determinants of outcomes.

The Kaplan-Meier survival curves showed that there was no significant difference in the 6-month, 1-year, 2-year, and 3-year cumulative overall survival rates of the post-irradiated EAC SCC group and the primary EAC SCC group. The tumor stage significantly affected the overall survival rate of the primary EAC SCC patients, and adjuvant radiation therapy had no obvious effect on the overall survival rate of EAC SCC patients.

**CONCLUSION**

Post-irradiation-induced EAC SCC is extremely rare and the interval between the completion of previous radiotherapy for NPC and the diagnosis of EAC carcinoma in our data was all longer than 14 years. The symptoms and invaded regions are similar to those of primary EAC SCC. However, the proportion of early-stage tumors in the post-irradiated EAC SCC patients was higher than that of the primary EAC SCC patients. In addition, high incidence of radionecrosis was observed after a second course of radiotherapy. Aggressive surgical treatments are suggested, but it is unnecessary to administer adjuvant radiotherapy for early-stage EAC SCC with free margins postoperatively. There is no obvious difference between the overall survival rates of the post-irradiated and primary EAC SCC patients.

**REFERENCES**


*Otology & Neurotology, Vol. 00, No. 00, 2015*