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Original Article

Clinical characteristics and treatment outcome of adenoid cystic carcinoma in the external auditory canal

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ABSTRACT

Background: This study reviewed the clinical manifestations, pathological findings, and treatment outcomes of adenoid cystic carcinoma (ACC) in the external auditory canal (EAC).

Methods: This was a retrospective review of 12 patients with a diagnosis of ACC in the EAC seen in a single institution over a 30-year period. Data on the demographics, clinical presentation, treatment strategy, and outcome, as well as the pathological features of ACC, were reviewed and analyzed.

Results: The male-to-female ratio was 1:3 and the mean patient age was 55.9 years. The most common clinical presentation was otalgia (75%). Ten patients underwent surgical interventions, including radical mastoidectomy in five patients, wide excision in three, and lateral temporal bone resection in two. Adjuvant radiotherapy or concurrent chemo-radiotherapy (CCRT) was performed in case of incomplete resection. Two patients underwent non-surgical treatments: radiotherapy in one and CCRT in the other. Microscopic perineural invasion was not associated with otalgia or histological subtype. The mean follow-up period was 84.6 months. Local recurrence occurred in 33% of patients. One-quarter of patients had distant metastasis, and all had lung metastasis. The 5-year overall survival rate for these patients was 82.5%.

Conclusion: EAC ACC should be included in the differential diagnosis when a patient presents with otalgia and a mass in EAC for more than 6 months, particularly if the patient is a middle-aged female. Otalgia might not be associated with perineural invasion or

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histological subtype. The lung is the most common site of distant metastasis in patients with EAC ACC. Further studies should determine the optimal treatment protocol for this rare malignancy.

At a glance of commentary

Scientific background on the subject

Adenoid cystic carcinoma (ACC) involving the external auditory canal (EAC) and temporal bone are exceedingly rare. Only a few case reports or series have been published in the English literature. This study presents the clinical manifestations, pathological findings, and surgical and oncological outcomes of this rare malignancy of the EAC.

What this study adds to the field

In the ACC of EAC, the local recurrence occurred in 33% patients and the 5-year overall survival rate of these patients was 82.5%. One-quarter of patients had distant metastasis, and all had metastasis to the lungs.

Malignant tumors involving the external auditory canal (EAC) and temporal bone are exceedingly rare, and the most common type is squamous cell carcinoma. Adenoid cystic carcinoma (ACC) of the head and neck is usually found in the salivary glands, oral cavity, palate, nasal cavity, and nasopharynx [1]. The annual incidence of the primary cancers in the EAC is approximately 1–6 cases per million people [2], while ACC arising in the EAC is even rarer, around 0.04 per million [3]. Furthermore, the diagnosis of EAC ACC can be challenging due to its rarity and nonspecific features. The condition may be misdiagnosed as the otitis externa or otitis media [2]. One case was misdiagnosed as basal cell carcinoma (BCC) at initial biopsy due to the basaloid morphologic features shared by BCC and ACC [4]. Multiple biopsies might be needed to establish the diagnosis, since the specimens could be non-representative due to a small size and associated granulation tissue.

The optimal treatment for EAC ACC has not been established. Only a few case reports or series have been published in the English literature [1]. This study presents the clinical manifestations, pathological findings, and surgical and oncological outcomes of this rare malignancy of the EAC in patients seen in a single institution over a 30-year period. We also evaluated the correlation between the pathology and clinical presentation.

Materials and methods

This was a retrospective review of 12 patients diagnosed with EAC ACC in the Department of Otolaryngology of Chang Gung Memorial Hospital, Linkou, Taiwan, from January 1985 to January 2018. All medical records were retrieved for the analysis. The study was approved by Institutional Review Board (IRB) of Chang Gung Medical Foundation (IRB No. 201800214B0). Data on patient age, sex, clinical presentation, tumor stage, surgical treatment, histopathology, adjuvant radiotherapy or chemoradiotherapy, treatment outcome, and follow-up duration were analyzed. Concerning the histopathology, the subtypes of ACC (*i.e.*, tubular, cribriform, and solid) and the presence of perineural invasion were examined and reviewed. The duration of follow-up was defined as the time from the date of surgery to the date of the last visit or death. Any local recurrence, distant metastasis, and survival status of the patients were recorded. Overall survival was calculated from the time of biopsy. The EAC ACC was staged using the modified Pittsburgh staging system [5,6]. The associations among otalgia, perineural invasion, and histological subtypes were analyzed statistically using SPSS 19.0 version (IBM, New York, USA). Fisher's exact test was used to compare the variables. A p-value < 0.05 was regarded as statistically significant.

Result

During the 30-year period, 12 patients were diagnosed with EAC ACC: three men (25%) and nine women (75%), for a male-to-female ratio of 1:3. The mean (±standard deviation) age at diagnosis was 55.9 years ± 18.46 (range: 25 to 87). The most common clinical presentation was otalgia (75%), followed by an EAC mass (25%), otorrhea (25%), hearing impairment (16%), facial nerve palsy (8%), and vertigo (8%) [Table 1]. The mean duration of symptoms before confirming the diagnosis was 27 months (median: 9 months). Table 2 summarizes the patient demographics, treatment course, and follow-up duration. Based on the modified Pittsburgh staging system, five patients were T1, two were T2, four were T3, and one was T4.

Regarding treatment, 10 patients underwent surgery, while two refused surgery. For those who underwent surgery, five

Table 1 Symptoms and signs of 12 patients with ACC of the EAC.

Symptoms and signs	Patients (n)	Percentage (%)
Otalgia	9	75
Mass in the EAC	3	25
Otorrhea	3	25
Hearing loss	2	16
Facial palsy	1	8
Vertigo	1	8

Abbreviations: ACC: adenoid cystic carcinoma; EAC: external auditory canal.

Table 2 Patient demographics.

Patients	Sex	Age	Side	Durations of symptoms (months)	TNM status	Stage	Initial treatment	Adjuvant RT/CCRT	Local recurrence (months)	Distant metastasis (months)	Follow-up (months)	Outcome
01	F	59	R	1.00	T4N0M0	IV	RM + Crat	CCRT	–	–	7	DWD
02	F	55	L	36.00	T1N0M0	I	RM	–	61	56	84	DWM
03	F	56	R	120.00	T3N0M0	III	RM	RT	–	–	133	DUC
04	M	79	R	0.50	T1N0M0	I	WE	–	21	75	75	DWM
05	F	62	R	12.00	T3N0M0	III	RM + TP	RT	–	–	48	DUC
06	F	56	L	0.25	T3N0M0	III	RM + TP	RT	69	–	141	NED
07	F	25	L	6.00	T2N0M0	II	LTBR + SP	CCRT	–	–	52	NED
08	M	60	R	60.00	T1N0M0	I	RT	–	–	–	91	NED
09	F	35	L	0.25	T1N0M0	I	WE	–	30	–	119	NED
10	F	67	R	12.00	T2N0M0	II	LTBR + SP	CCRT	–	–	35	NED
11	M	30	L	1.50	T3N0M0	III	CCRT	–	–	52	140	DWM
12	F	87	L	72.00	T1N0M0	I	WE	–	–	–	90	NED

Abbreviations: WE: wide excision; RM: radical mastoidectomy; Crat: craniotomy; LTBR: lateral temporal bone resection; SP: superficial parotidectomy; TP: total parotidectomy; RT: radiotherapy; CCRT: concurrent chemoradiotherapy; DWD: die with disease; DWM: die with metastasis; DUC: die with medical cause; NED: alive with no evidence of disease.
Follow-up time is from the date of the first diagnostic pathology report until the date of last visit to the out-patient department of otolaryngology or the date of death.
Patient #2 and #4 had distant metastasis to the lungs. Patient #11 had distant metastasis to the lung, liver, spleen and kidney.

had radical mastoidectomies, three had wide excisions, and two had lateral temporal bone resection [Fig. 1]. Of the five patients who had radical mastoidectomies, two had additional total parotidectomies and adjuvant radiation therapy (RT) and the remaining three had, respectively, an additional craniotomy and adjuvant concurrent chemoradiotherapy (CCRT); adjuvant RT; and a radical mastoidectomy alone. Both patients who had lateral temporal bone resections, had superficial parotidectomies and adjuvant CCRT. Of the two patients who refused surgery, one underwent RT and the other took CCRT as the primary treatment. Table 3 summarizes the treatments for each patient.

The main histological subtypes were the tubular pattern in six patients (50%), cribriform pattern in four patients (33%), and no dominant histological subtype in the remaining two patients (17%). Perineural invasion occurred in eight patients (66.7%). The associations between otalgia and perineural invasion; otalgia and the main histological subtype; advanced stages and the main histological subtype; and perineural invasion and the main histological subtype were analyzed using Fisher's exact test. No statistically significant associations were found.

The mean follow-up period was 84.58 (range: 7–141) months. Four patients (33%) developed local recurrence after a mean of 45.25 (range: 21–69) months. Three patients (25%) developed distant metastasis after a mean of 61 (ranged: 52–75) months. Of the three patients with distant metastasis, two also had local recurrence. All three patients with distant metastasis had lung metastasis (100%) and one had multiple metastases to the kidney, spleen, and liver. Six patients died during follow-up: three patients (25%; two T1, one T3) from distant metastasis at 75, 84, and 140 months respectively, and two patients (17%, both T3) from medical diseases at 48 and 133 months, respectively; and one patient (8%, T4) from intracranial invasion with this disease at 7 months. Six patients (50%) were alive at their last follow-up and two were alive with local recurrence after a mean follow-up period of 88 (median: 90.5) months. Fig. 2 shows the Kaplan–Meier survival curve.

Discussion

Being rare, only a few case series on EAC ACC have been reported in the English literature [3,7–9]. As a result, there is no universal consensus on its treatment. The current study reviewed 12 patients with EAC ACC in a single institute during a 30-year period and analyzed the demographics, clinical presentations, pathological characteristics, and treatment outcomes. Demographically, the ratio of men to women in previous reports [3,7–9] of total 160 patients was 1:1.35. The male-to-female ratio of 1:3 in this study is consistent with the female predominance although one study reported male predominance [9].

The clinical presentation of EAC ACC is non-specific, making the diagnostic process challenging. The most common clinical presentation was otalgia (75%), which was consistent with the literature [7–10]. Other presenting symptoms or signs included an EAC mass (25%), otorrhea (25%), hearing loss (16%), facial palsy (8%), and vertigo (8%). Six of the nine patients with

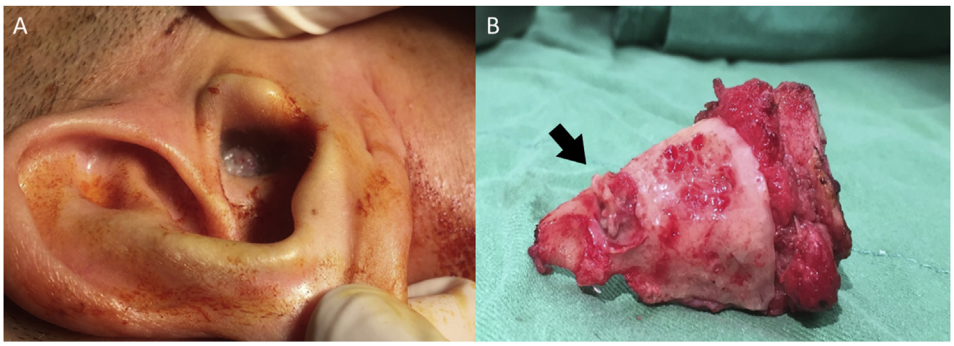

Fig. 1 Intraoperative findings of patient #10, who underwent lateral temporal bone resection. (A) Smooth-surfaced mass bulging from the superior and posterior aspects of the external auditory canal. (B) *En bloc* surgical removal of the lateral temporal bone along with the tympanic membrane and the ossicles (arrowhead).

Table 3 Clinical stages associated with the treatment.

Stage	WE	RM	LTBR + SP + CCRT	RM + RT	RM + TP + RT	RM + Crat + CCRT	RT	CCRT
T1 (n = 5)	3	1	–	–	–	–	1	–
T2 (n = 2)	–	–	2	–	–	–	–	–
T3 (n = 4)	–	–	–	1	2	–	–	1
T4 (n = 1)	–	–	–	–	–	1	–	–

Abbreviations: WE: wide excision; RM: radical mastoidectomy; LTBR: lateral temporal bone resection; SP: superficial parotidectomy; TP: total parotidectomy; Crat: craniotomy; RT: radiotherapy; CCRT: concurrent chemoradiotherapy.

otalgia (67%) had the symptom for over 6 months. Most patients were initially misdiagnosed with chronic otitis externa or benign lesions [Fig. 3] because of the low level of awareness of EAC carcinoma [2]. It has been reported that a bloody discharge is a major indicator of EAC carcinoma, and in such case, a biopsy is strongly recommended [2]. Nevertheless, no patients in our series complained of bloody discharge from the EAC.

CT and MRI can both be useful for demonstrating the extent of invasion in EAC ACC [Fig. 4]. However, the use of MRI in cases of ACC of the EAC has not been fully delineated [11]. ACC occurring elsewhere in the head and neck may show low-signal intensity on T1-weighted (T1W) MRI images and high or low intensity on T2-weighted (T2W) images, depending on its cellularity. Tumors with high signal intensity on T2W images

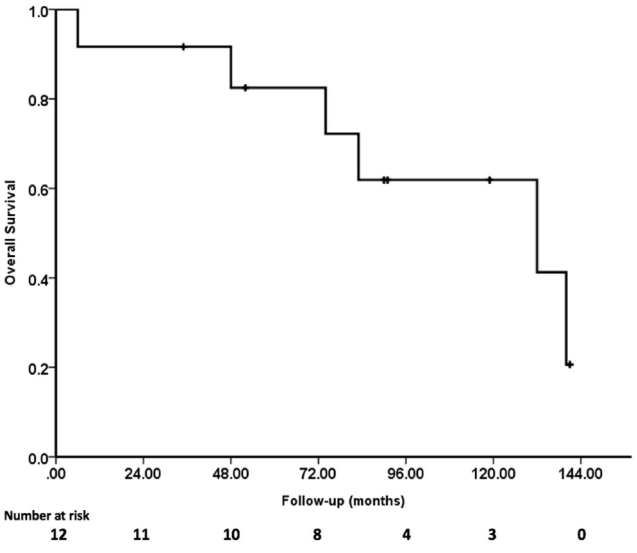

Fig. 2 The overall survival rate of the 12 patients determined from the Kaplan–Meier survival curve with the number at risk. The 5-year survival rate was 82.5%. The number at risk is the number of patients still alive and being followed to that point on the survival curve.

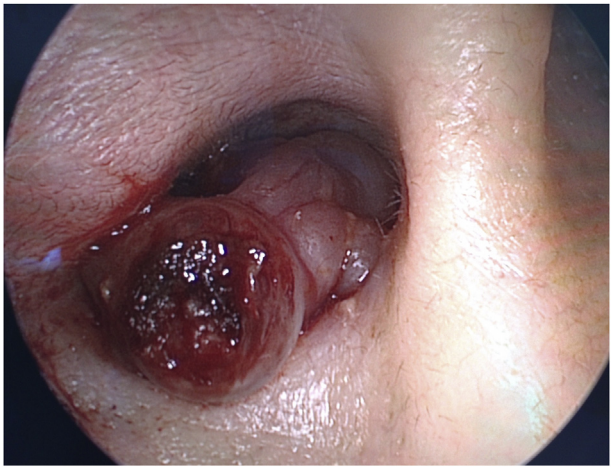

Fig. 3 A mass protruding into the external ear canal of patient #12, which was initially misdiagnosed as a ceruminous gland adenoma. An adenoid cystic carcinoma was diagnosed after three biopsies were performed.

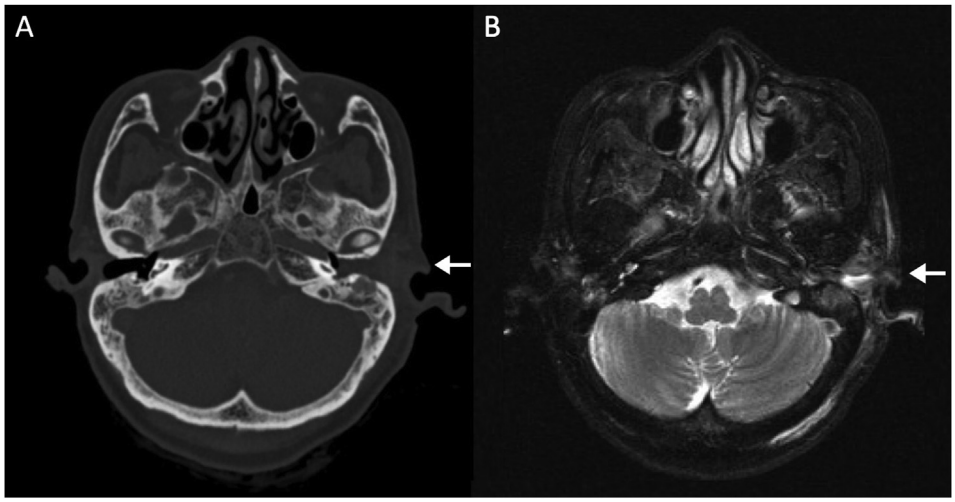

Fig. 4 Image finding of patient #6, who was staged as cT3N0M0. **(A)** In the CT finding, the abnormal soft tissue lesion (arrow) was located in the left EAC with obvious erosion of the mastoid bone in inferior-lateral aspect. **(B)** In the MRI T2 image, this irregular enhancing mass (arrow) invaded to the left superior parotid gland and to the lateral margin of the left temporomandibular joint.

have low cellularity, are predominantly tubular or cribriform in type and have a good prognosis; whereas tumors with low signal intensity have high cellularity and are predominantly solid lesions with a worse prognosis [12]. As MRI was not routinely performed on each case in this study, the correlation between histological features and MRI appearances of EAC ACC could not be assessed.

Table 3 summarizes the variety of treatments. Currently, there are roles for surgery, such as lateral temporal bone resection with parotidectomy, and RT or CCRT [13]. A Multidisciplinary team comprising surgeons, oncologists, radiologists, and pathologists is essential for tailoring the best treatment plan for individual patients.

Most of our patients (9 patients, 75%) complained of otalgia at presentation. The cause of the otalgia and the associations of the otalgia with other parameters were investigated. In our series, we found no statistically significant correlation between otalgia and perineural invasion. Our finding was in accordance with Liu et al., who postulated that otalgia may be related to local inflammation rather than perineural invasion [8]. Although one paper proposed that perineural invasion may lead to the otalgia [1], our sample size was insufficient to draw a representative conclusion. A larger investigation is warranted.

In our series, the main histological subtypes were the tubular (50%) and cribriform (33%). The remaining two patients (17%) had no dominant histological subtype. There was no solid subtype in the series. One study stated that the cribriform pattern had the highest prevalence (65.9%), followed by the tubular type (26.8%) and solid (7.3%) subtypes [1]. In Liu et al., the solid and cribriform subtypes were equally common (41%) and the rest were tubular (18%) [8]. Our results differed; however, the reason for this notable difference among these reports was unclear. Furthermore, we found no significant correlation between perineural invasion and the histological subtypes, whereas Liu et al. reported that the cribriform pattern was associated with a higher incidence of perineural invasion [1]. This difference may be biased, as there were more patients with the cribriform subtype ACC in Liu et al.

A prolonged duration of symptoms and a delay in establishing the diagnosis is common in this rare disease. Previous studies have noted that ACC has an indolent clinical course and grows for years before symptoms arise, delaying the diagnosis [1,7]. In our series, half of patients presented with otalgia for more than 6 months and the mean duration from initial symptom to diagnosis was 26.8 months. The disease progression in our patients was similar to that statement. The mean duration of follow-up is 84.58 (median: 87) months. Patient #6 and #9, who had local recurrence alone, are still alive and have been followed for 141 and 119 months, respectively. Although patient #11 died of distant metastasis, he was followed for 88 months after multiple diagnosis distant metastases were diagnosed.

The follow-up duration was relatively long and the 5-year survival rate high when compared with other cancers. The overall 5-year survival rate was 82.5%. However, Liu et al. observed that patients with the solid subtype or perineural invasion had a poorer prognosis [8]. The potential prognostic indicators for survival should be evaluated in a larger study.

Limitation of the article

There are a several limitations to our study. The retrospective study design resulted in problems with inadequate data collection and a potential information bias. In addition, this was a small case series, which precluded a statistical analysis of the histopathology type contributing to otalgia or perineural invasion. Furthermore, as knowledge and technology advance, surgical techniques and adjuvant treatment strategies evolving. Hence, it would be difficult to compare the treatment outcomes with other reports and to decide on the best treatment protocol.

Conclusion

In our experience, whenever a patient, especially a middle-aged woman, complains of otalgia and an EAC mass for more than 6 months, EAC ACC should be included in the differential diagnosis. A biopsy and further imaging studies are necessary. Otalgia was not associated with perineural invasion or any histological subtype in our patients. Since the most common site of distant metastasis is the lungs in patients with EAC ACC, regular imaging studies of the chest are mandatory. So far, there is no consensus on the standard treatment modality for this rare malignant tumor. Therefore, further studies are warranted to determine the optimal treatment protocol.

Conflicts of interest

Authors have declared that no competing interests.

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