A series Cases study of Carcinomas derived from myoepithelial cells in head and neck regions

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Research

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Abstract

Background and Objectives: Carcinomas derived from myoepithelial cells in head and neck regions (CMCHN) are rare. The aim of this study was to demonstrate the clinical behaviors and treatment outcomes of these tumors.

Methods: A retrospective review of fifteen CMCHN cases between 2002 and 2019 in a single institution was performed. Results: All of the fifteen patients (100%) underwent primary surgical resection. Eleven patients (73.3%) received conventional postoperative radiotherapy and four (26.7%) received systemic chemotherapy. Consequently, six patients (40%) had frequently recurrence after surgical resection, and seven patients (46.7%) received second or even third operations. Up to the time of last follow-up, only one patient died and the mean survival time was 15.8 years.

Conclusions: Currently, complete surgical excision with or without systemic therapy is preferred, but it has limited efficacy on reducing the risk of recurrence. Thus, more effective systemic therapies are required and the researches on the mechanism of CMCHN recurrence should be encouraged.

Introduction

Myoepithelial cells are usually located in glandular epithelium as a thin layer of basement membrane, generally beneath the luminal cells. Myoepithelial differentiation refers to that the myoepithelial cells and epithelial cells, which are normally stable, and can proliferate rapidly to produce basal cells and luminal cells in case of wound healing [1]. Besides, these myoepithelial cells can inhibit tumor growth [2] by encapsulating tumor-derived luminal epithelial cells and providing a separative enclosures between luminal tumor cells and nearby vasculature [3]. Myoepithelial cells differentiation has been commonly observed in carcinomas of salivary glands [4]. In addition, tumors derived from the myoepithelial cells have been reported in nasal sinuses, larynx and hypopharynx area in head and neck [5].

Carcinomas derived from myoepithelial cells in head and neck regions (CMCHN) can be mainly divided into three types: 1) myoepithelial carcinoma (MEC), which is purely composed of myoepithelial cells and accounted for < 2% of all salivary gland carcinomas[6]; 2) the epithelial myoepithelial carcinoma (EMC, also called adenomyoepithelioma), represents approximately 1% of salivary gland tumors [7], and is histologically consist of a biphasic arrangement of inner luminal ductal cells and outer myoepithelial cells; 3) adenoid cystic carcinoma (AdCC), a biphasic tumor comprised of ductal and myoepithelial cells which tends to be arranged in a more cribriform pattern.[8]

The main therapy for CMCHN is surgical resection with clear margins, with or without pre-/post-operative radiation [9]. However, due to the rarity of this carcinoma, its clinical characteristics, proper treatment modalities, and their correlation with prognosis remain unclear [9–11].

This study aimed at describing the management strategies and corresponding prognosis for patients with CMCHN at a single center, in order to provide a reference for clinical practice and future studies.

Method

Data collection

This study was approved by West China Hospital of Sichuan University Biochemical Research Ethics Committee (2019 – 357). In total, fifteen consecutive patients diagnosed with CMCHN in our hospital from Jan 2002 to Jan 2019 were confirmed and included in this study. Clinical data (such as age, time of diagnosis, sex, tumor site, adjuvant treatment) and survival outcomes (such as tumor recurrence, etc) were retrieved from electronic medical records. (Table 1)

Histology and immunochemistry

A total of six MEC, six EMC and five AdCC were diagnosed by pathologists according to the WHO Classification of Head and Neck Tumors [12]. The histomorphology characteristics and immunohistochemical staining of tumor were combined to support the diagnosis. Twelve patients had immunohistochemical records, such as myoepithelial marker (p63, S100, SMA, Vimentin, Calponin), epithelial marker (PCK, CK, EMA, CK5/6), and proliferative marker (Ki-67).(Table 2)

Clinical management

The clinical staging was refered to The American Joint Committee on Cancer (AJCC) classification (seventh edition) [13]. Recurrence and metastasis were determined by the clinical examination or images. Survival status were determined by no evidence of disease, alive with disease, first recurrence, metastasis, dead of disease, or dead of other causes. (Table 1 and Table 2)

Result

Clinical Characteristics

The clinical and pathological findings of patients were summarized in Table 1 and Table 2. There were 6 men and 9 women diagnosed as CMCHN, and their median age at diagnosis was 45.4 years (range 22–76 years). These tumors originated from various locations including parotid gland (n = 11, 73.2%), laryngeal region (n = 2), nasal cavity (n = 1), and maxillary sinus (n = 1), among which six (40%) were MEC, six (40%) were EMC, and three (20%) were AdCC (Table 1).

Treatment and Follow-up

The main treatment was surgical resection supplemented by postoperative chemoradiotherapy. All of the patients (100%) underwent primary surgical resection (Table 1), among which three (20%) received primary surgery only, five (33.3%) received postoperative radiation or chemoradiation therapy, and seven (46.7%) received second surgery following primary excision. For the patients who received second operation, three received extended resection of the lesion or lymph node dissection within a year, and four received a second surgery when suffered from local recurrence.

One EMC patient involving larynx and one MEC patient involving maxillary sinus only underwent local surgical resection, and one EMC patient involving nasal cavity received both of surgery and postoperative radiotherapy. After local surgical resection of the parapharyngeal space, one EMC patient underwent secondary surgery and postoperative radiotherapy for 33 times due to recurrence one year later, in addition to four-cycle of TP chemotherapy (paclitaxel 210 mg d1 and cisplatin 40 mg d1-3). Five parotid MEC cases were treated with parotidectomy, among which two cases were combined with lymph node dissection, two with postoperative radiotherapy and one with postoperative chemoradiotherapy. Three EMC cases were located in parotid gland, one of which received surgery only and two cases received second operation due to recurrence. Among the two patients underwent secondary surgery, one case relapsed after 6 years, the other case underwent first relapse within 3 years and second relapse within 5 years. Three patients developed AdCC in the parotid gland, two underwent surgery and chemoradiotherapy, and one underwent surgery and radiotherapy.

Clinical follow-up was available for nine (60%) cases, and only one of them (6.7%) died within 4 years after surgery. Mean survival time was 15.8 years. Four patients (26.7%) were in progression-free survival and six patients (40%) relapsed after primary treatments. Among these recurrences, 26.7% were local-regional recurrences, and 20% were distant metastases. The status of three patients (20%) lost follow-up after they were discharged, and three patients(20%) were recorded only at the last hospital visits.

Immunohistochemistry and Histochemistry:

The immunohistochemical results were summarized in Table 2. Of the myoepithelial markers, p63 showed diffused strong staining in 11/12 (91.6%) cases. S100 protein, smooth muscle actin, calponin and vimentin protein, fairly sensitive markers for myoepithelial cells, were stained positive in 6/11 (54.5%), 3/6 (50.0%),1/2(50.0%) and 1/1 (100.0%) cases, respectively. The epithelial markers of PCK (4/4), CK (4/4), EMA (2/4) and CK5/6 (4/4) displayed significant positive. Ki-67, the marker of biologic potential, had the average proliferative index of 20% (n = 10, range 0 to 60%).

Discussion

There were only 198 Chinese and English literatures on carcinomas derived from myoepithelial cells in head and neck regions (CMCHN) from 1963 to 2020, most of which were case reports. These myoepithelial cell differentiated malignancy were indistinguishable, and immunohistochemical results were often required in the pathological diagnosis of these diseases. S-100 protein, vimentin and cytokeratin (CK) were the most sensitive markers of MEC[14].Double-layer tubular structure of EMC could be identified by CK staining for glandular epithelial cells in the inner layer, and by S-100 and smooth muscle actin (SMA) antibody staining for clear outer layer of myoepithelial cells[15].AdCC also presented a tubular structure composed of two layers of cells. Unlike EMC, S-100 protein staining was only positive in the inner layer of AdCC[16].

CMCHNs have been observed in the gingiva, palate and tongue, larynx, parapharynx, nasopharynx, nasal cavity, nasal sinus, lacrimal gland, inferior temporal fossa, etc[17, 18]. And literatures reported that approximately 75% of EMC[19, 20] originated from the parotid gland, 10% from the submandibular gland, 10–15% from the salivary glands, and the remaining occurred in the palate, maxillary sinus, nasal cavity, trachea, and the root of the tongue. The AdCC accouted for 28% in malignant submandibular gland tumors, making it the most common malignant salivary gland tumor in this region. Patients might survive for years with metastases because this tumors were generally well-differentiated and slow-growing[21].

Our results showed that the incidence of these diseases was low, and only one patient (6.7%) died from the disease over the last decade. Despite this, our study demonstrated high recurrence rate, since 40% of the patients with CMCHN had recurrences after primary treatments, among which, 26.7% were local-regional recurrences, and 20% were distant metastases. These results were consistent with previous reports showing high incidences of local-regional recurrence and distant metastasis in patients with CMCHN[9–11]. In this study, the treatment was mainly complete surgical resection. Extended resection, lymph node dissection and chemoradiotherapy were important treatments for patients suffering from recurrence[22].

Due to the low incidence and varied biologic behaviors, limited evidences can be refered by physicians to predict outcome and determine management strategies. The correlation between the high recurrence potential and myoepithelial differentiation of this disease needs further laboratory verification. Meanwhile, the targeted therapy to reduce the recurrence rate is also worth of attention.

Declarations

Ethics approval and consent to participate

This study was approved by West China Hospital of Sichuan University Biochemical Research Ethics Committee (No.2019-357).

Consent for publication

This is a retrospective case series study that has been granted exemption from signing informed consent by West China Hospital of Sichuan University Biochemical Research Ethics Committee.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

JJR and DNC designed the study; DNC and YFR analyzed and interpreted data in including studies; JQQ and KQ performed quality control of data and algorithms; YJD, DD and DNC performed the statistical analysis; JJR and YZ reviewed the manuscript. All authors read and approved the final manuscript, and have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work.

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Tables

Table1 Pathologic, treatments and survival outcomes in patients with malignant carcinomas derived from myoepithelial cells in head and neck regions

Clinical Characteristics											Treatment			Survival						
No	Sex	Age of Diagnosis	Smoke	Alcohol	Subsite	Pathology	T	N	M	Stage	First	Second	Third	Survival Status	Time of death	Recurrence	Local recurrence	Time of local recurrence	Distant recurrence	Time of distant recurrence
1	M	64	No	Social	Larynx	EMC	2	0	0	II	S			Unknown		Unknown				
2	M	41	Yes	Social	Maxillary Sinus	MEC	3	0	0	III	S			Unknown		Unknown				
3	F	67	No	No	Nasal Cavity	EMC	1	0	0	I	S+R			Alive		No				
4	F	28	No	No	Parapharynx	EMC	2	0	0	II	S1	S2	S3+R+C	Alive		Yes	Yes	2013		
5	F	46	No	No	Parotid Gland	MEC	2	0	0	II	S+R			Alive		No				
6	M	29	No	No	Parotid Gland	MEC	2	0	0	II	S1	S2+R		Alive		Yes	Yes	2015	Lung	2016
7	F	46	No	No	Parotid Gland	MEC	2	0	0	II	S+R+C	C		Alive		Yes			Lung	2012
8	F	76	No	No	Parotid Gland	MEC	3	0	0	III	S1	S2*+R		Dead	2015	No				
9	M	61	No	Social	Parotid Gland	MEC	2	2b	0	IVA	S1	S2*+R		Unknown		No				
10	M	22	No	No	Parotid Gland	EMC	3	0	0	III	S1	S2		Unknown		Yes	Yes	2016		
11	F	38	No	No	Parotid Gland	EMC	2	0	0	II	S1	S2	S3+R	Alive		Yes	Yes	2014		
12	F	40	No	No	Parotid Gland	EMC	2	0	0	II	S			Alive		No				
13	F	37	No	No	Parotid Gland	AdCC	2	0	0	II	S+R			Unknown		Unknown				
14	F	46	No	No	Parotid Gland	AdCC	2	1	0	IVA	S+R+C			Alive		No				
15	M	40	Yes	No	Parotid Gland	AdCC	2	0	1	IVC	S	S2+R+C		Unknown		Yes			Lung	2014

M, male; F, female; EMC, epithelial myoepithelial carcinoma; MEC, myoepithelial carcinoma; AdCC, adenoid cystic carcinoma; S, surgery; S1, surgery once; S2, surgery twice (extended resection); S2*, surgery twice (lymph node dissection); S3, surgery third times; R, radiotherapy; C, chemotherapy.

Table 2 Clinical characteristics and immunohistochemical features of malignant carcinomas derived from myoepithelial cells in head and neck regions

Characteristic		Patients n (%)	Characteristic		Patients n (%)
Sex	Male	6 (40.0)	Pathologic subtype	EMC	6 (40.0)
	Female	9 (60.0)		MEC	6 (40.0)
	Median age	45.4		AdCC	3 (20.0)
T classification	T1	1 (6.7)	N classification	N0	13 (86.6)
	T2	11 (73.3)		N1	1 (6.7)
	T3	3 (20.0)		N2	1 (6.7)
M classification	M0	14 (93.3)	Stage	I	1 (6.7)
	M1	1 (6.7)		II	8 (53.3)
Tumor location	Larynx	1 (6.7)		III	3 (20.0)
	Maxillary sinus	1 (6.7)		IVA	2 (13.3)
	Nasal cavity	1 (6.7)		IVB	0 (0)
	Parapharyngeal space	1 (6.7)		IVC	1 (6.7)
	Parotid gland	11 (73.2)	Last contact	Alive	8 (53.3)
Recurrence	Total Local-regional Distant	6 (40) 4 (26.7) 3 (20)		Dead	1 (6.7)
				Unknown	6 (40)
Myoepithelial markers	P63	11/12(91.6)	Epithelial markers	PCK	4/4(100)
	S100	6/11(54.5)		CK	4/4(100)
	SMA	3/6(50)		EMA	2/4(50)
	Vimentin	1/1(100)		CK5/6	4/4(100)
	Calponin	1/2(50)	Markers of biologic potential	Ki-67(mean %)	20% (range 0 to 60%)