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Oral sarcomatoid squamous cell carcinoma: a retrospective study based on 14 cases

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Summary. The treatment outcomes for oral sarcomatoid squamous cell carcinoma (OSSCC) are far from satisfactory in our hospital. The aim of this study was to retrospectively summarize the OSSCC cases admitted to our department. From 2003 to 2017, 14 patients were hospitalized and diagnosed with OSSCC. We summarized and analysed the medical histories, diagnostic examinations, treatment strategies, and clinical outcomes of the involved cases. Of the 14 cases, 8 were located in the gingiva. The imageological diagnosis identified the existence of a mass with an infiltrative morphology pre-operatively. The cytopathologic features revealed a malignant neoplasm with a mixture of squamous cell carcinoma (SCC) components and spindle cell neoplastic components. To confirm the diagnosis of OSSCC, the use of the immunohistochemical markers AE1/AE3 and Vimentin were more indicative. Complete follow-up data were available for 12 patients, and at the last follow-up, all 12 of the patients had died. The median overall survival for these patients was 11.67 months (range: 3-24 months). OSSCC patients respond poorly to the strategies solely referring to experiences from oral squamous cell carcinoma (OSCC) treatment. The effective diagnosis and treatment of OSSCC at an early stage is necessary. The treatment for OSSCC still poses a great challenge for clinical oncologists.

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Introduction

Sarcomatoid carcinoma is an extremely rare but aggressive neoplasm found in various organs, most commonly located in the head and neck, lung, and female genital tract (Terada, 2011; Chang et al., 2013; Ung et al., 2016; Akhtar et al., 2017). Histologically, sarcomatoid carcinoma is composed of both malignant epithelial and malignant mesenchymal components (Shetty et al., 2015; Perrone et al., 2016). The presence of overlapping morphological features confers great challenges for its diagnosis and treatment (Bi et al., 2016; Perrone et al., 2016). Due to its rarity and the lack of large-scale clinical evidence, the clinical behaviors and biological pathogenesis of sarcomatoid carcinoma have not been well elucidated.

Although the head and neck area is one of the common sites for developing sarcomatoid carcinoma, its involvement in the oral cavity is unusual, accounting for less than 1% of all tumors in the oral cavity (Gupta et al., 2017). Sarcomatoid carcinoma of the oral cavity is a rare variant of oral squamous cell carcinoma (OSCC) with a variable component of sarcomatoid spindle cells (Kim et al., 2015). This variant is associated with a high frequency of recurrence and metastasis (Viswanathan et al., 2010; Chang et al., 2013; Shetty et al., 2015; Gamez et al., 2018). Currently, the histopathological diagnosis and treatment strategies for oral sarcomatoid squamous cell carcinoma (OSSCC) remain controversial. Because

of its rare prevalence, more clinical evidence is needed for the improvement of clinical practice and the development of laboratory investigations.

The treatment outcomes for OSSCC are far from satisfactory in our hospital. To obtain a clear and systematic knowledge of this disease, we summarized and analysed the clinical characteristics, diagnosis, treatment and prognosis of OSSCC based on 14 cases in this retrospective study. Regarding the tumor site, OSSCC was observed to most commonly occur in the gingiva. The clinical phenotypes and pre-operative imageological examinations indicated masses with infiltrative morphology. The final diagnosis for OSSCC required both microscopic examination and immunohistochemical staining. Retrospectively, treatments for OSSCC have not reached a standardized strategy based on our previous experiences. Generally, OSSCC patients exhibit a poor prognosis with a high risk for recurrence and metastasis.

Materials and methods

Patients

Retrospectively, we reviewed and enrolled patients who were pathologically diagnosed with sarcomatoid carcinoma of the oral cavity between 2003 and 2017 at the Department of Oral Maxillofacial-Head and Neck Oncology, Shanghai Ninth People's Hospital. To be included in this study, the following criteria were met for each case: (a) intact medical histories of diagnosis and treatments in our department; (b) intact histopathological data; (c) intact imagelogical records; (d) follow-up information in our department as complete as possible. The patients with only histopathological biopsy but not subsequent treatments were excluded. This study was approved by the Medical Ethics Committee of the Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine (retrospectively registered).

The demographic data of the involved patients, including sex, age, primary tumor site, clinical presentation, and previous OSCC history, were summarized according to their first visit. The TNM staging for each involved case referred to the American Joint Committee on Cancer (AJCC) Cancer Staging manual for head and neck cancer (8th Edition, 2017) (Lydiatt et al., 2017). Retrospectively, some patients had diagnostic computed tomography (CT) and/or magnetic resonance imaging (MRI) of the maxillo-facial & head and neck pre-operation, and chest CT imaging was performed selectively. The treatment strategies, including surgery plans and adjuvant therapies, were extracted from their medical records. The clinical outcomes were collected and summarized retrospectively from the follow-up information.

Histopathological evaluations

The original pathology impressions were indicated with frozen-section examinations during the operation. The final pathological reports were presented based on postoperative pathologic examinations by using haematoxylin-eosin (HE) and immunohistochemical (IHC) staining. The proportion of sarcomatoid and squamous cell carcinoma (SCC) components for each case was measured from 3 randomly selected HE sections according to the cellular morphologies by two oral pathologists using Image J Version 1.51t software, downloaded from the National Institutes of Health (NIH) website (https://imagej.nih.gov/ij/). The presence of vascular invasion and perineural invasion was observed and analyzed.

IHC staining was performed to confirm the diagnosis of OSSCC. For IHC staining, a routine panel

Table 1. Clinical and pathological characteristics of patients.

Case	Sex	Age	Location	Presentation	DOI (mm)	T	ENE	N	Previous SCC
1	M	79	R mouth floor	Mass	>10	T4a	0	N1	No
2	M	51	L Lower lip	Swelling and ache	>10	T4a	0	N1	No
3	M	80	R root of Tongue	Mass	>10	T3	0	N0	Yes
4	M	49	R mandible gingiva	Tooth movement and mass	6.0	T4a	0	N1	No
5	F	76	L maxillary gingiva	Ulcer mass	8.0	T2	0	N0	No
6	F	39	R maxillary gingiva	Mass	7.5	T2	0	N0	No
7	F	68	L maxillary gingiva	Mass	6.0	T2	0	N0	No
8	M	47	L mandible gingiva	Ulcer mass and restriction of mouth opening	6.5	T4a	0	N2b	No
9	M	59	Anterior Mouth floor	Mass	>10	T3	0	N0	Yes
10	M	57	L maxilla gingiva	Mass	6.0	T2	0	N0	No
11	F	41	R palate	Mass	7.5	T2	0	N0	No
12	M	35	A maxillary gingiva	Mass	8.0	T2	0	N0	No
13	F	55	R mandible gingiva	Mass	6.0	T2	0	N0	Yes
14	F	23	R mouth floor	Tongue numbness	>10	T4a	0	N0	No

M, male; F, female; R, right; L, left; A, anterior; DOI, depth of invasion (According to the imagelogical data, for the cases with microscopical DOI>10mm, the actural DOI could not be acquired exactly, and their DOI were recorded as ">10 mm"); T, tumor size; ENE, extranodal extension; N, lymphoid metastasis; SCC, squamous cell carcinoma.

for the diagnosis of malignant tumors was used. IHC was performed with primary antibodies against AE1/AE3 (pancytokeratin marker), Cytokeratin-high molecular weight (CKH, cytokeratin marker), Epithelial membrane antigen (EMA, epithelial marker), transcription factor p63 (epithelial marker), Vimentin (EMT marker), and Soluble protein-100 (S-100, EMT marker) (Autostainer/Autostainer Plus, DAKO, Denmark). In addition, the expression levels of tumor suppressor p53 and p40 (marker for squamous cell carcinoma) were detected with rabbit anti-human primary antibodies purchased from Abcam (USA). As previously reported, the immune-reactivity scores for the IHC staining were compared and recorded by two independent observers based on the staining intensity and the percentage of positive cancer cells (Xiao et al., 2017).

Results

Clinical characteristics of the involved patients

As shown in Table 1, of the 14 OSSCC patients, 8 patients were male (average age 57.1 years, range 35-80 years), and 6 patients were female (average age 50.3 years, range 23-76 years). Regarding the tumor sites, 8 cases were located in the gingiva, 3 in the mouth floor, 1 in the lip, 1 in the tongue and 1 in the hard palate. The most common symptom was the presentation of a mass with or without dysfunction of the oral maxilla-facial system. At the time of primary diagnosis, 7 patients developed tumors at the T2 stage, 2 patients developed tumors at the T3 stage, and 5 patients developed tumors at the T4 stage. Lymph node metastasis was pre-operatively evaluated in 4 patients. In addition, no distal metastasis was detected in any of the cases at their primary diagnosis. Based on the medical history of the involved patients, 3 patients had records of OSCC history, and no radiation therapy had been involved in their previous treatment.

Imaging characteristics of OSSCC

Imageological diagnosis based on CT and/or MRI was still necessary pre-operation. These images confirmed the existence and invasion range of the lesions involved in the complicated oral maxillofacial-head and neck areas, which was essential for the subsequent treatments. The imaging features based on CT indicated a heterogeneous mass without a clear tumor boundary (Fig. 1). Examinations with MRI identified the existence of a mass with an infiltrative morphology and heterogeneous T2 signal intensity and enhancement (Fig. 1). Though the CT/MRI findings could not differentiate OSSCC from OSCC or other malignant masses well, larger tumor sizes and definitely malignant impressions were indicated.

Histological and immunohistochemical characteristics of OSSCC

The relative rarity and histopathological pattern of OSSCC posed great diagnostic challenges. For intraoperative frozen-section examination, the original pathological impression was indicated as poorly differentiated carcinoma with abnormal spindle cells. A definitive diagnosis was difficult to achieve intraoperatively, and postoperative pathological

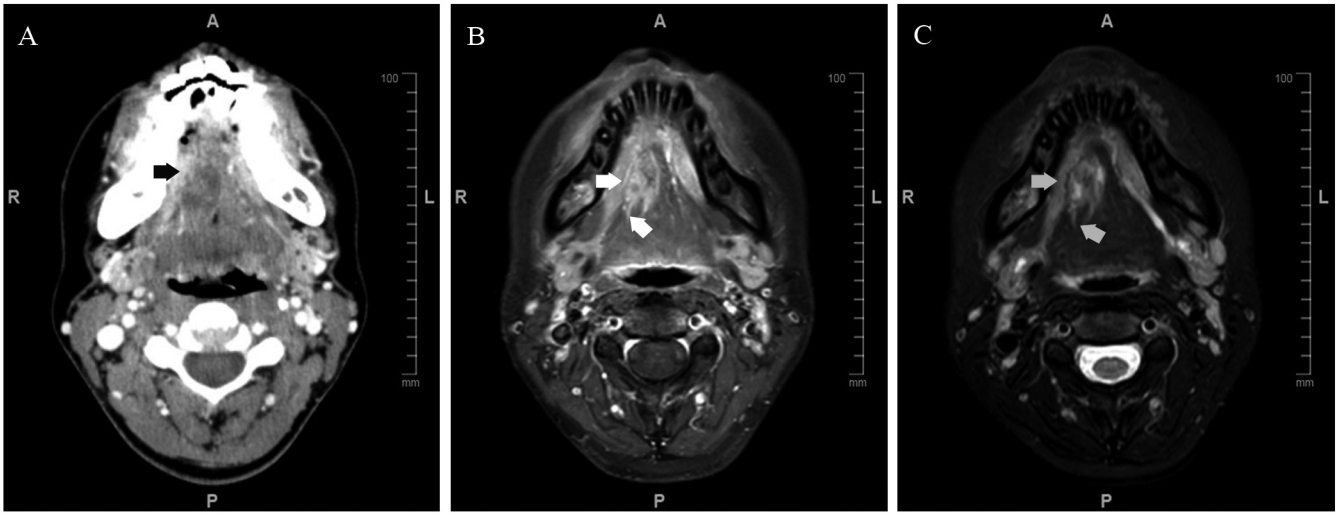

Fig. 1. Representative imageological manifestations for OSSCC. **A.** Computed tomography (CT) of head and neck indicated a heterogeneous mass existing at the right mouth floor (Black arrow). **B-C.** Magnetic resonance imaging (MRI) of head and neck identified the existence of a mass with an infiltrative morphology under T1 signal (White arrow), and with heterogeneous T2 signal intensity and enhancement (grey arrow).

examinations were conducted for the final diagnosis of OSSCC. The microscopic examination of HE-stained sections revealed a malignant neoplasm with a mixture of SCC components and spindle cell neoplastic components in different proportions (Fig. 2). Statistically, the proportion of SCC components ranged from 15% to 75%, and the proportion of sarcomatoid components ranged from 10%-80% in the 14 cases (Table 2). In 8 of the 14 cases, more sarcomatoid components were observed. Histologically, the presence of malignant invasion for blood vessels and perineural invasion could be observed (Fig. 2). In summary, vascular invasion was observed in cases 1, 2, 6, 8 and 14, and perineural invasion was observed in cases 1, 2, 3, 4, 8, 9, 11, 12, 13, and 14 (Table 2).

Accordingly, a comprehensive IHC analysis was necessary for the confirmation diagnosis of sarcomatoid carcinoma (Guan et al., 2014). Herein, a panel of IHC

Table 2. Histological characteristics of the OSSCC patients.

Case	SCC components	Sarcomatoid components	Vascular invasion	Perineural invasion
1	40%	55%	Y	Y
2	30%	60%	Y	Y
3	50%	30%	N	Y
4	60%	25%	N	Y
5	20%	70%	N	N
6	60%	35%	Y	N
7	75%	10%	N	N
8	15%	80%	Y	Y
9	30%	65%	N	Y
10	70%	15%	N	N
11	60%	35%	N	Y
12	35%	55%	N	Y
13	20%	70%	N	Y
14	40%	50%	Y	Y

SCC, squamous cell carcinoma; Y, Yes; N, No.

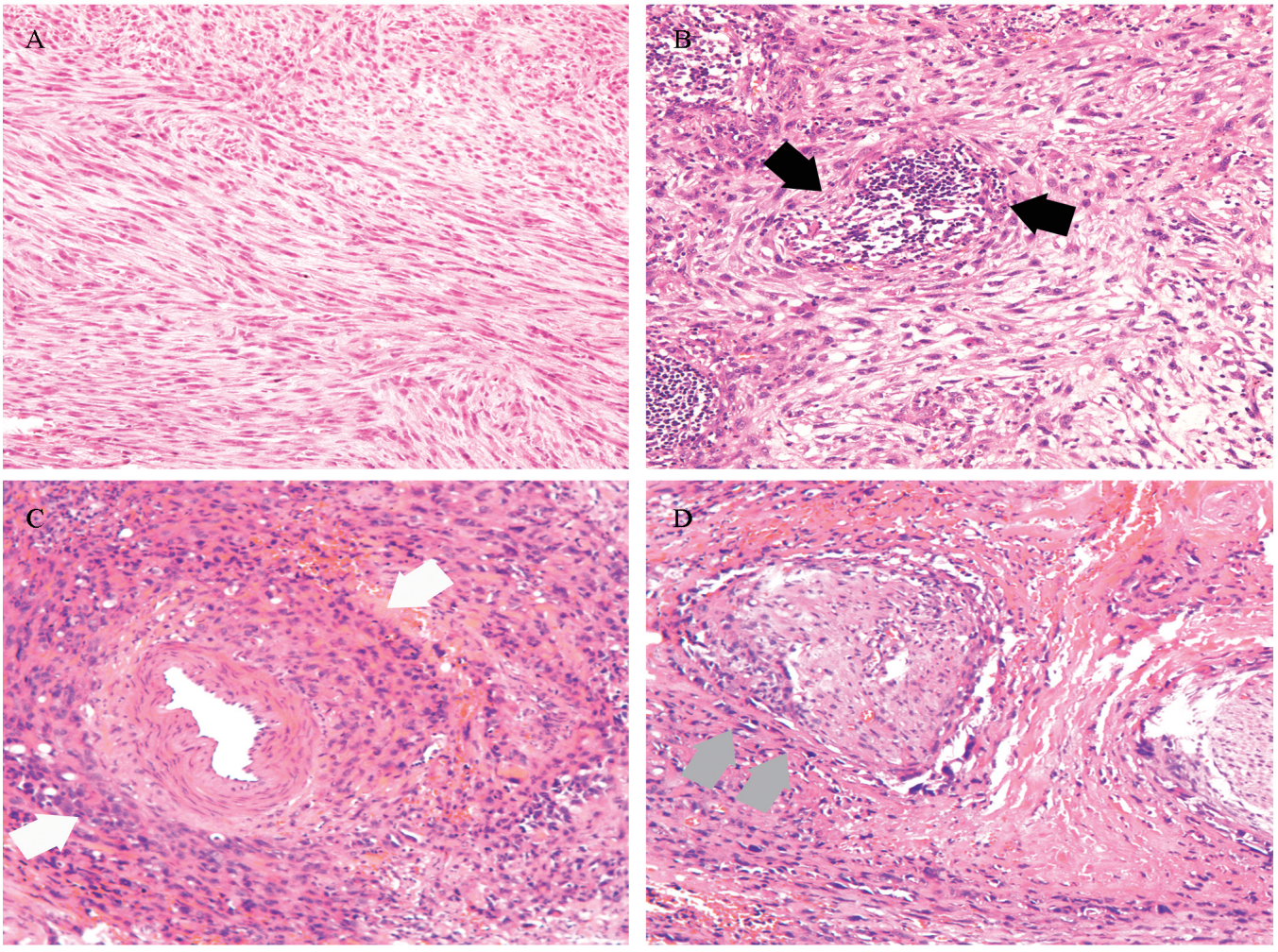

Fig. 2. Representative histologic figures for OSSCC. **A.** The histologic examination revealed a malignant neoplasm consisting of a mixture of squamous cell carcinoma and spindle cell neoplasm. **B-C.** Microscopic section shows representative malignant invasion for blood vessels (black arrow for intravenous invasion, white arrow for arterial invasion). **D.** Representative perineural invasion (grey arrow). HE. x 200.

markers was used to classify the final diagnosis of OSSCC. In the panel we used, the makers AE1/AE3, CKH, EMA, p63 and p40 were used to evaluate the epithelial characteristics, and the markers Vimentin and S-100 were used to evaluate the EMT characteristics (Table 3, Fig. 3). Besides, the expression levels of p53 were also evaluated (Table 3, Fig. 3). For the epithelial markers, AE1/AE3 (13/14) exhibited the highest expression ratio, and the expression levels for CKH (11/14), EMA (11/14), p63 (5/10), and p40 (9/14) were also observed and analyzed. For EMT markers, Vimentin (13/14) showed the highest expression ratio, and S-100 was observed to be positively expressed in 7/14 cases. Besides, in all of the detected 10 cases, p53 protein was positively expressed.

Treatment and prognosis of OSSCC

Retrospectively, the therapeutic strategies for OSSCC have not reached a consensus. The therapeutic

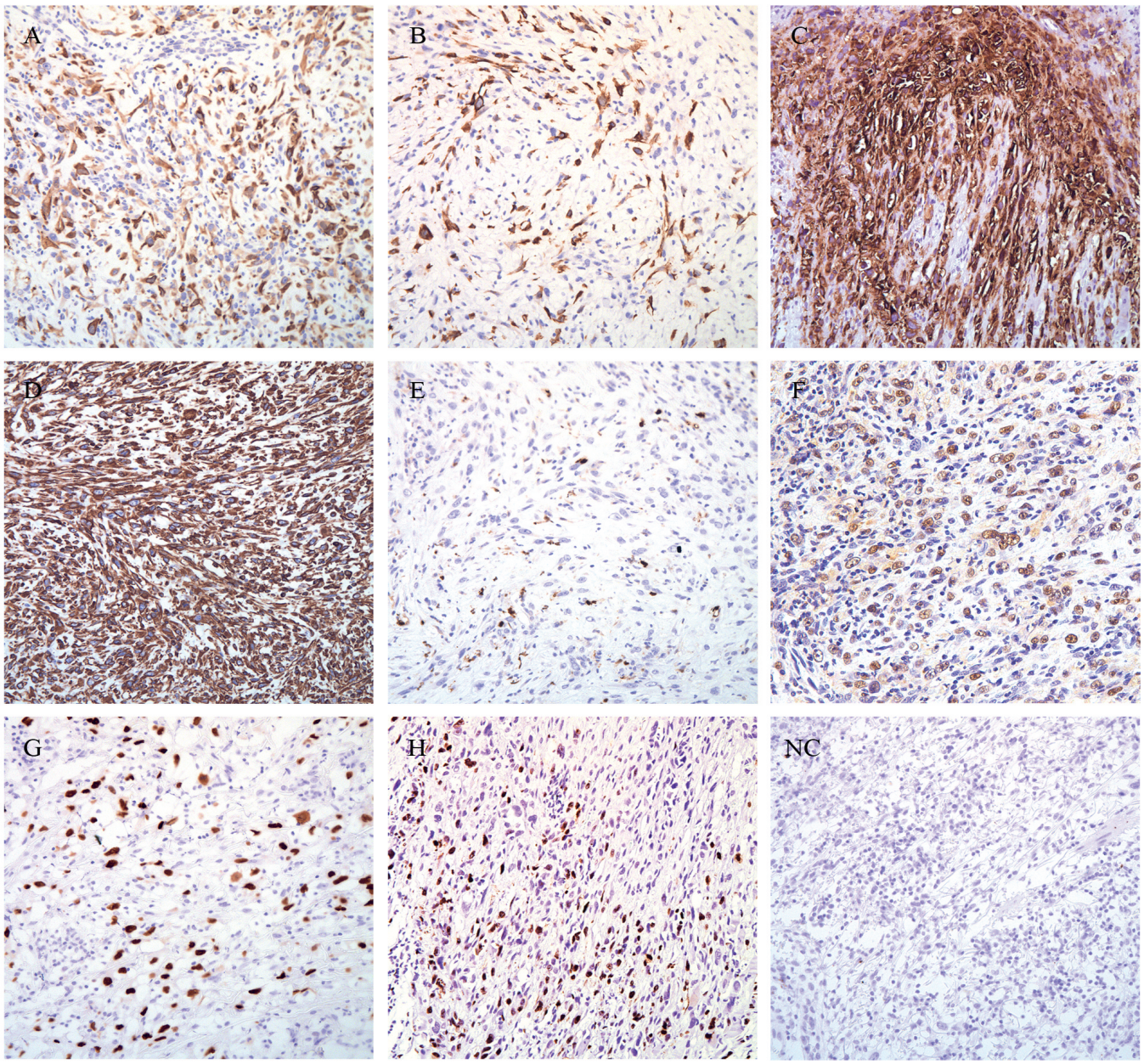

Fig. 3. mmunohistochemical characteristics of OSSCC. Representative images of the cases positively immunoreactive for AE1/AE3 **(A)**, CKH **(B),** EMA **(C)**, Vimentin **(D)**, p53 **(F)**, p63 **(G)**, p40 **(H)**, and Negative control **(NC)**. Negative immunoreaction was observed for S-100 **(E)**. x 200.

recommendations for these tumors were still based on those of SCC in our hospital. Table 4 shows a summary of the treatment strategies and prognosis outcomes. A total of 14 patients underwent extensive resection of the mass (pathological confirmation for the resection margins as R0), and 5 of them combined with one-stage neck dissection. Seven patients were treated with adjuvant radiotherapy (intensity-modulated radiotherapy, range from 60-72 Gy) and chemotherapy (5-FU and/or Cisplatin). In addition, cases 3 and 6 received adjuvant radiotherapy, and cases 10 and 13 received adjuvant chemotherapy only. Generally, the prognosis for patients with OSSCC was not encouraging, and the responses to radiotherapy and/or chemotherapy were poor. Complete follow-up data were available for 12 patients, and at the last follow-up, all 12 of the patients had died. Statistically, the mean overall survival was 11.67 months (range: 3-24 months). For the 8 cases with more sarcomatoid components, the average survival time was 10.43 months (range: 3-17 months). For the 6 cases with more SCC components, the average survival time was 13.4 months (range: 6-24 months). Of the 14 cases, 5 developed recurrence. In addition, 2 patients without one-stage neck dissection developed lymphoid metastasis. Two patients developed metastatic disease in the lung (Fig. 4), and one developed brain metastasis one month later. Histopathological, perineural invasion was observed in all 5 recurrent cases. For the 2 patients with distal metastasis, more sarcomatoid components, vascular invasions, and perineural invasions were observed.

Table 3. Immunohistochemical characteristics for the OSSCC cases.

Case	AE1/AE3	CKH	p63	p40	EMA	Vimentin	S-100	p53
1	+	+	/	+	+	+	+	/
2	+	-	-	-	+	+	-	+
3	+	-	-	-	+	+	-	+
4	+	+	+	+	-	+	+	+
5	+	+	+	+	+	+	+	+
6	+	-	-	-	-	-	+	+
7	+	+	-	-	+	+	-	+
8	+	+	/	+	+	+	+	/
9	-	+	+	+	+	+	-	+
10	+	+	/	+	+	+	+	/
11	+	+	+	+	+	+	-	+
12	+	+	/	+	+	+	+	/
13	+	+	+	+	-	+	-	+
14	+	+	-	-	+	+	-	+

Discussion

Herein, we retrospectively summarized and analyzed 14 cases of OSSCC. We learned that OSSCC is a rare and aggressive variant of OSCC, most commonly occurring in gingiva. An accurate, thorough morphological evaluation is still essential for the final diagnosis of OSSCC. The cytopathological features reveal a malignant neoplasm with a mixture of SCC components and spindle cell neoplastic components. The use of the IHC markers AE1/AE3 and Vimentin are more indicative of the confirmation of OSSCC. More sarcomatoid components, vascular invasion, and perineural invasion may indicate a worse outcome for the patients with OSSCC. In particular, lymph node involvement, distant metastasis, and recurrence occurred at a high proportion in OSSCC.

From the reported Caucasian sarcomatoid carcinoma cases in head and neck areas, the incidence rate for men and women was close to 5:1 with an average age 65 years (Perrone et al., 2016). From the reported 78

Table 4. Treatment and prognosis for patients with OSSCC.

Case	Surgery	Neck dissection	Radiation	Chemotherapy	Prognosis
1	Extensive Resection	RND	No	No	Died at 3 m
2	Extensive Resection	L RND+ R SOND	Yes	Yes	Lung metastasis at 9 m - brain metastasis at 10 m - Died at 12m
3	Extensive Resection	-	No	No	A history of extensive resection of R buccal SCC and R SOND for 13 y -- Recurrent at 6 m - Died at 9 m
4	Extensive Resection	R SOND	Yes	Yes	Recurrent at 15 m - Died at 20m
5	Extensive Resection	-	No	No	Lymphoid metastasis at 12m (Extensive Resection + L RND) - Died at 16 m
6	Extensive Resection	-	Yes	No	Died at 8 m
7	Extensive Resection	-	No	No	Lost
8	Extensive Resection	R SOND + L RND	Yes	Yes	Died at 5 m
9	Extensive Resection	-	Yes	Yes	A history of extensive resection of SCC in mouth floor - Recurrent at 7 m (Extensive Resection + R RND and L SOND) - Died at 17 m
10	Extensive Resection	-	No	Yes	Died at 6 m
11	Extensive Resection	-	Yes	Yes	Lymphoid metastasis at 12m - Died at 24m
12	Extensive Resection		Yes	Yes	Recurrent at 6 m - Lost
13	Extensive Resection	-	No	Yes	A history of extensive resection of R post-molar SCC + SOND and radiation for 6 y – Recurrent at 1 m, 2 m, and 5 m - Died at 14 m
14	Extensive Resection	L SOND	Yes	Yes	Lung metastasis at 4 m- Died at 6m

Lost, lost to follow-up; RND, radical neck dissection; SOND, supraomohyoid neck dissection; R, right; L, left; m, months; y, years.

sarcomatoid carcinoma cases in head and neck areas of Taiwan, the incidence rate for men and women was close to 12:1 with an average age 55 years (Chang et al., 2013). Comparatively, we observed that the incidence rate of OSSCC for women was higher (the incidence rate for men and women was close to 4:3) with a younger average age (57.1 years for men, and 50.3 years for women). Accordingly, in head and neck areas, sarcomatoid carcinoma more frequently occurred at larynx in Caucasian patients, and more frequently occurred at oral mucosa in Asian patients (Viswanathan et al., 2010; Chang et al., 2013; Perrone et al., 2016). As compared and summarized in Table 5, the common affected sties for OSSCC were lip, tongue, gingiva, and buccal mucosa. In this study, we observed that the most common affected site was gingiva, followed by mouth floor.

Sarcomatoid carcinoma is characterized by the presence of both carcinomatous and sarcomatoid components. Therefore, it is important to distinguish sarcomatoid carcinoma from other spindle cell neoplasms. A diagnostic algorithm has been proposed for different sarcomatoid carcinomas from other spindle cell neoplasms based on 171 cases of mucosal spindle cell tumors of the head and neck (Viswanathan et al., 2010). Nevertheless, a combination of HE and IHC staining is still essential. However, the tumor's origin and nature have been a matter of debate for many years

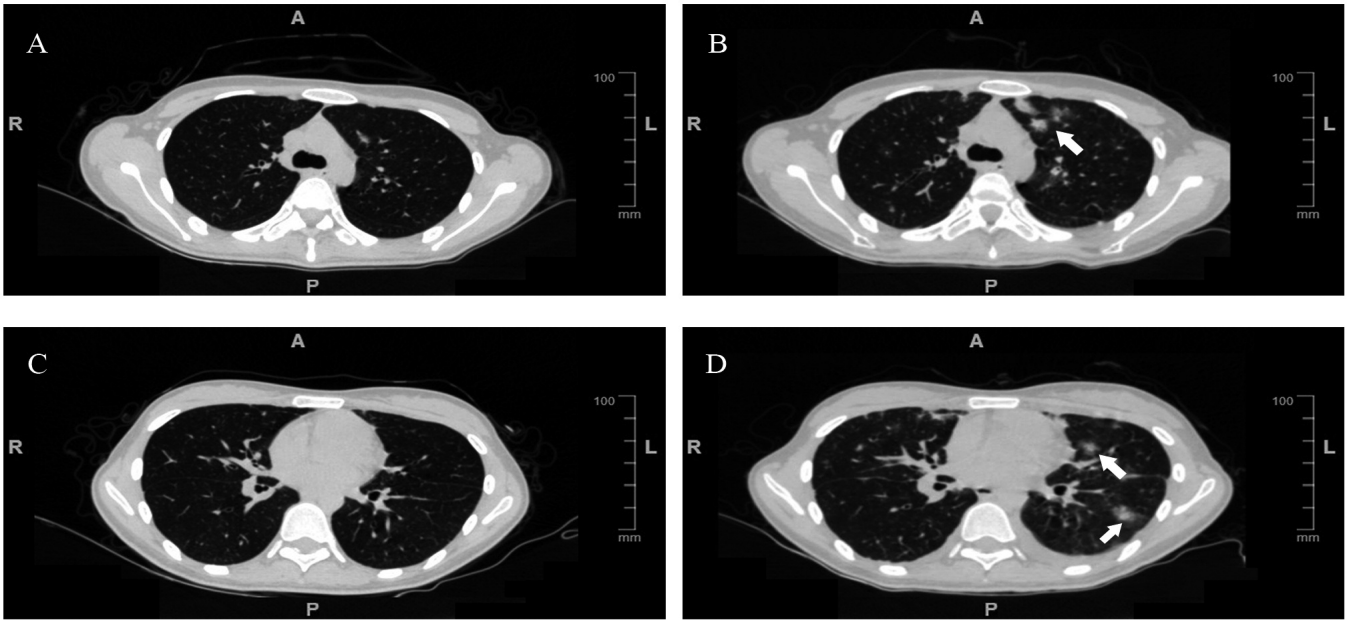

Fig. 4. Representative computed tomography (CT) imaging for lung metastasis of sarcomatoid carcinoma. **A-B.** Paired CT imaging of chest indicated multiple pulmonary nodules (White arrow) at 9 months post-operation, which further identified as lung metastasis in Case 2. **C-D.** Paired CT imaging of chest indicated multiple pulmonary nodules (White arrows) at 4 months post-operation, which further indicated lung metastasis in Case 14.

Table 5. Review and comparison the anatomic sites of the reported OSSCC cases.

Study	This study	Chang et al.*	Viswanathan et al.*	Ellis and Corio*	Leventon and Evans*	Other case repots*
Total cases	14	55	65	57	8	19
Lip	1	0	2	26	1	8
Tongue	1	21	13	12	1	4
Gingiva	8	11	20	13	1	4
Buccal mucosa	0	19	25#	2	2	1
Palate	1	3	5	1	1	0
Mouth floor	3	1	0	3	1	2
Labial vestibule	0	0	0#	0	1	0

*: cited from: Chang et al., 2013; Viswanathan et al., 2010; Ellis and Corio, 1980; Leventon and Evans, 1981; Chang et al., 2013; respectively. #: 25 cases located at the buccal mucosa and labial vestibule.

(Padberg et al., 2005). Recently, studies based on molecular and genetic characteristics have proposed that sarcomatoid carcinoma is a monoclonal epithelial neoplasm, and the sarcomatoid features represent a subclonal dedifferentiation or transformation from the carcinomatous components (Bi et al., 2016; Akhtar et al., 2017). The evolution of sarcomatoid carcinoma from the conventional epithelial-type has been demonstrated by a comparative analysis of matched micro-dissected epithelial and sarcoma-like components from 11 primary sarcomatoid carcinomas using microsatellite markers in head and neck squamous carcinoma (Choi et al., 2003). In this study, 11 patients were primarily diagnosed with OSSCC, and 3 patients had a history of OSCC. We proposed that OSSCC might occur separately or develop from previous OSCC, which should be confirmed with additional studies.

In our study, we observed that the proportion of sarcomatoid components ranged from 10-80% in the 14 cases, and more sarcomatoid components were observed in 8 cases. Comparatively, the cases with more sarcomatoid components seemed to experience a worse prognosis, indicating that the sarcomatoid components might play important roles in the malignant development of OSSCC. Sarcomatoid morphologic changes have been demonstrated to correspond with epithelial-mesenchymal transition (EMT) from squamous epithelia (Akhtar et al., 2017; Boland et al., 2017). During the EMT process, cells lose epithelial polarity, experience massive reorganization of the cytoskeleton, acquire mesenchymal traits, and become motile and invasive (Al-Ismaeel et al., 2019). Sarcomatoid carcinoma seems to be irreversible and permanent changes during the EMT transition and various EMT pathways have been reported (Sung et al., 2013). The realization of the roles of EMT greatly promoted the diagnosis of OSSCC. The uses of pan-CK, EMA, and vimentin have been reported to be practical markers for the diagnosis of sarcomatoid carcinoma of the head and neck (Viswanathan et al., 2010). Accordingly, p40 is highly sensitive and specific for squamous cell carcinoma and is considered the best marker for this cancer (Nakajima et al., 2019). Besides, transcription factor p63 has been termed as a key mediator for epithelial tumorigenesis, especially for controlling tumor metastasis and cancer cell stemness (Gatti et al., 2019). In our study, combined with the routine epithelial markers AE1/AE3, CKH, and EMA, the markers p63 and p40 were also included in the panel to evaluate the epithelial characteristics of OSSCC. Recently, the association between EMT and S100 protein has been demonstrated in several cancer types (Al-Ismaeel et al., 2019). In our study, combined with the routine EMT marker Vimentin, the expression level of S-100 was also evaluated in OSSCC. Comparatively, positive IHC staining with AE1/AE3 and Vimentin may be helpful in achieving the diagnosis of OSSCC.

Tobacco use, alcohol consumption, and radiation exposure seem to be risk factors for sarcomatoid transformation (Viswanathan et al., 2010). The driving factors for this process have not been well elucidated, which might result from its rarity and heterogeneous morphology. It has been reported that the sarcomatoid spindle cell component might be transformed from cancerous precursors with the loss of heterozygosity involving multiple cancer-associated chromosomal arms (Kwon et al., 2003). In addition, a high rate of tumor protein p53 (TP53) mutations has been reported in sarcomatoid carcinoma (Boland et al., 2017). In our study, we observed that p53 protein was highly expressed, indicating that the TP53 mutant might be an important biological event during the sarcomatoid transformation of OSSCC. Some molecular-level studies have reported that this tumor occurs along with certain genetic diversity (Boland et al., 2017). Since these patients have a dismal response to conventional chemotherapy, the discovery and description of potential genetic driver mutations is critical for the improvement of therapeutic options (Boland et al., 2017). Therefore, a better understanding of the biological nature of OSSCC is still needed.

In this study, patients with OSSCC were treated based on the treatment experiences from OSCC. There are no standard recommendations for the management of OSSCC owing to its rarity. The current concept for the treatment of sarcomatoid cancer is surgical tumor ablation (Chang et al., 2013). The high mortality rate for sarcomatoid cancer in head and neck area is reported to be due to the lower resistance to tumor-spreading along tissue planes and extensive lymph drainage system with resultant lymphatic and distant metastases (Chang et al., 2013). OSSCC patients might have distal micro-metastases even at the initial examination (Shigeta et al., 2015). Accordingly, lymph nodal metastasis and distant metastasis to lung, brain, and other soft tissues might be present during the progression of sarcomatoid carcinoma in head and neck areas (Viswanathan et al., 2010). A thorough PET-CT scan might be valuable for evaluating these patients. Adjuvant radiotherapy, chemotherapy, and/or immunotherapy should be provided synergistically (Gadre et al., 2009; Chang et al., 2013). In the 14 involved cases, the average survival time was only 11.67 months after treatment. So, effective systemic therapies for individuals with OSSCC are still an unmet need.

A growing understanding on the molecular pathogenesis of sarcomatoid carcinoma has yielded novel approaches for the treatment of this deadly malignancy (Shum et al., 2016). Molecular targeted therapy based on next-generation sequencing might be a useful treatment strategy (Li et al., 2017). The recent identifications of frequent genetic alterations in mesenchymal to epithelial transition factor (MET), Kirsten rat sarcoma viral oncogene homolog (KRAS), and TP53 genes have yielded actionable targets for intervention with available inhibitors for a subset of patients with pulmonary sarcomatoid carcinoma (Lococo et al., 2016; Pelosi et al., 2016; Shum et al., 2016). Previous studies have also identified that anaplastic

lymphoma kinase (ALK) translocation might serve as a potent oncogenic driver in sarcomatoid carcinoma of the head and neck, and the clinical benefits of crizotinib for cases with ALK translocation have been demonstrated (Kim et al., 2015). Therefore, understanding the molecular and genetic events of OSSCC is critical to discovering new treatment options. Another promising new therapy for sarcomatoid carcinoma is the group of immune checkpoint inhibitors (Raychaudhuri et al., 2017). Recently, Programmed death 1 (PD-1) and Programmed Death Ligand-1 (PDL-1) overexpression has been found in half of sarcomatoid carcinomas, raising the possibility that these tumors might be responsive to immune checkpoint inhibitors (Bi et al., 2016; Boland et al., 2017). Clinical evidence should be harvested for OSSCC cases treated with immunotherapy against immune checkpoints, such as anti-PD1/PD-L1 agents in the near future.

Summarily, a consensus for the therapeutic options of OSSCC has not been achieved, and patients with OSSCC respond poorly to the strategies solely referring to experiences from OSCC treatment. The effective diagnosis and treatment for OSSCC at an early stage is absolutely necessary. Besides, a tight and regular follow-up is essential for all the cases with OSSCC. Concerning the high rate of lymph metastasis and distal metastasis, comprehensive examinations are necessary during follow-up. Herein, we would like to share our diagnostic and treating experiences of OSSCC for clinical communication. Overall, the treatment for OSSCC still poses a great challenge for clinical oncologists, and further studies are still needed to identify more effective strategies for this rare disease.

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Competing interests. The authors declare that they have no competing interests.

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