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Case Report

Adenoid squamous cell carcinoma of the oral cavity

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Abstract: Because immunohistochemical features of adenoid squamous cell carcinoma (AdSCC) of the oral cavity is unclear, the author reports herein AdSCC in the gingival with an emphasis on immunohistochemical features. A 73-year-old woman presented with a left lower gingival tumor. The tumor was mildly elevated tumor measuring 1.5 x 1.5 x 0.5 cm. Dentist's diagnosis was granulation tissue, and a biopsy was taken. The biopsy showed proliferation of carcinoma cells arranged in cords, and squamous and tubular differentiations were noted in places. The biopsy diagnosis was adenosquamous carcinoma. Tumor excision with resection of mandibular bone was performed. The resected tissue showed a mixture and squamous cell carcinoma and tubular formation. Gradual merges between the two and acantholytic features of the squamous cell carcinoma element were seen. Both components were free from mucins. Both components were positive for pancytokeratins (AE1/3, CAM5.2) +++, cytokeratin (CK) 5/6 +, CK34βE12 ++, CK7 +, CK14 +++, CEA +, CA19-9 +, CA125 +, p53 +++, p63 +++, KIT + and MUC1 ++. Both components were negative for CK8, CK18, CK19, CK20, EMA, vimentin, TTF-1, desmin, myoglobin, S100 protein, melanosome, smooth muscle actin, CD34, CDX2, CD10, chromogranin, synaptophysin, NSE, CD56, lysozyme, CD68, MDM2, PDGFRA, MUC2, MUC5AC, and MUC6. Since both components were positive for squmaous cell carcinoma markers (CD5/6, CK34βE12, and p63) and adenocarcinoma markers (CEA, CA19-9, CA125, MUC1), this case of AdSCC appears an intermediate form between adenocarcinoma and squamous cell carcinoma. The margins were negative. No metastasis was found by imaging techniques. The patient is now free from tumor and is followed up carefully.

Keywords: Oral cavity, adenoid sqaumous cell carcinoma, immunohistochemistry

Introduction

Adenoid (acantholytic) squamous cell carcinoma (AdSCC) is a squamous cell carcinoma with features of adenoid pattern due to acantholysis of the squamous cell carcinoma [1]. AdSCC is rare, and it is mostly seen in the skin. AdSCC of the oral cavity is very rare [2-6]. Oral AdSCC may show pseudovascular morphology [5, 6]. Adenoid squamous cell carcinoma must be differentiated from adenosquamous carcinoma in which adenocarcinoma element is positive for mucins. Immunohistochemical features of oral AdSCC have been rarely performed [2]. Herein is reported a case of oral AdSCC, with an emphasis on immunohistochemical study.

Case report

A 73-year-old woman complained of a left lower gingival tumor, and consulted to our hospital. The tumor was mildly elevated tumor measuring 1.5 x 1.5 x 0.5 cm in the left gum Dentist's diagnosis was granulation tissue. A biopsy was taken, and it showed proliferation of carcinoma cells arranged in cords (**Figure 1**), and squamous and tubular differentiations were

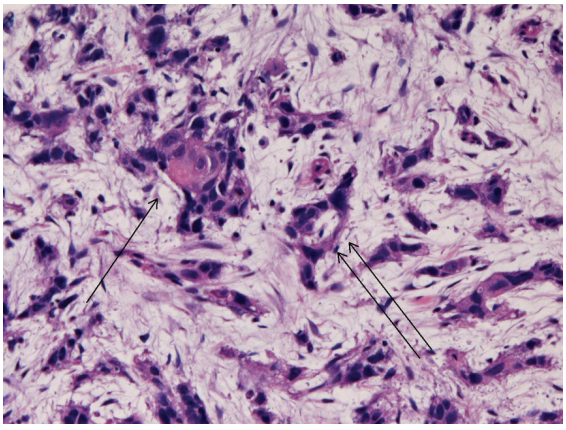

Figure 1. Biopsy features. Carcinoma cells are seen to proliferate in cords. Keratinization (arrow) and tubules (arrows) were scattered. The biopsy diagnosis was adenosquamous carcinoma. HE, x100.

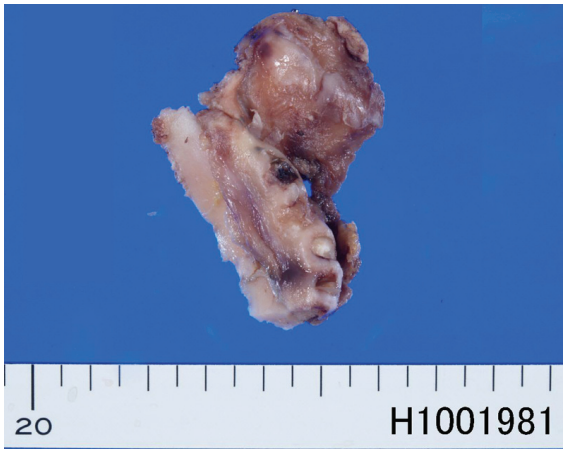

Figure 2. Gross features of the resected tumor and mandible. The tumor (1.5 x 1.5 cm) is somewhat elevated. The margins were negative. and well defined and white. Broad necrosis is present. The tumor measures 12 x 12 cm.

noted in places (**Figure 1**). The biopsy diagnosis was adenosquamous carcinoma. Preoperative imaging modalities including CT and MRI showed no other tumors in the body. Tumor excision with resection of left mandibular bone was performed. During operation, four margins were examined by frozen sections, which showed no invasions. The resected tissue was gingival mucosa containing tumor and left mandibular bone (**Figure 2**). Whole specimen was examined by serial sections. The sections showed a mixture and squamous cell carcinoma and tubular formation (**Figures 3A**, **3B**, **3C** and **3D**). Gradual merges between the two were recognized (**Figure 3A**). The squamous cell carcinoma component was continuous with gingival squamous cells (**Figure 1B**). Acantholytic features of the squamous cell carcinoma element were seen (**Figure 3C** and **3D**). Both components were free from mucins, as revealed by negative PAS, d-PAS, Alcian blue, and mucicar-

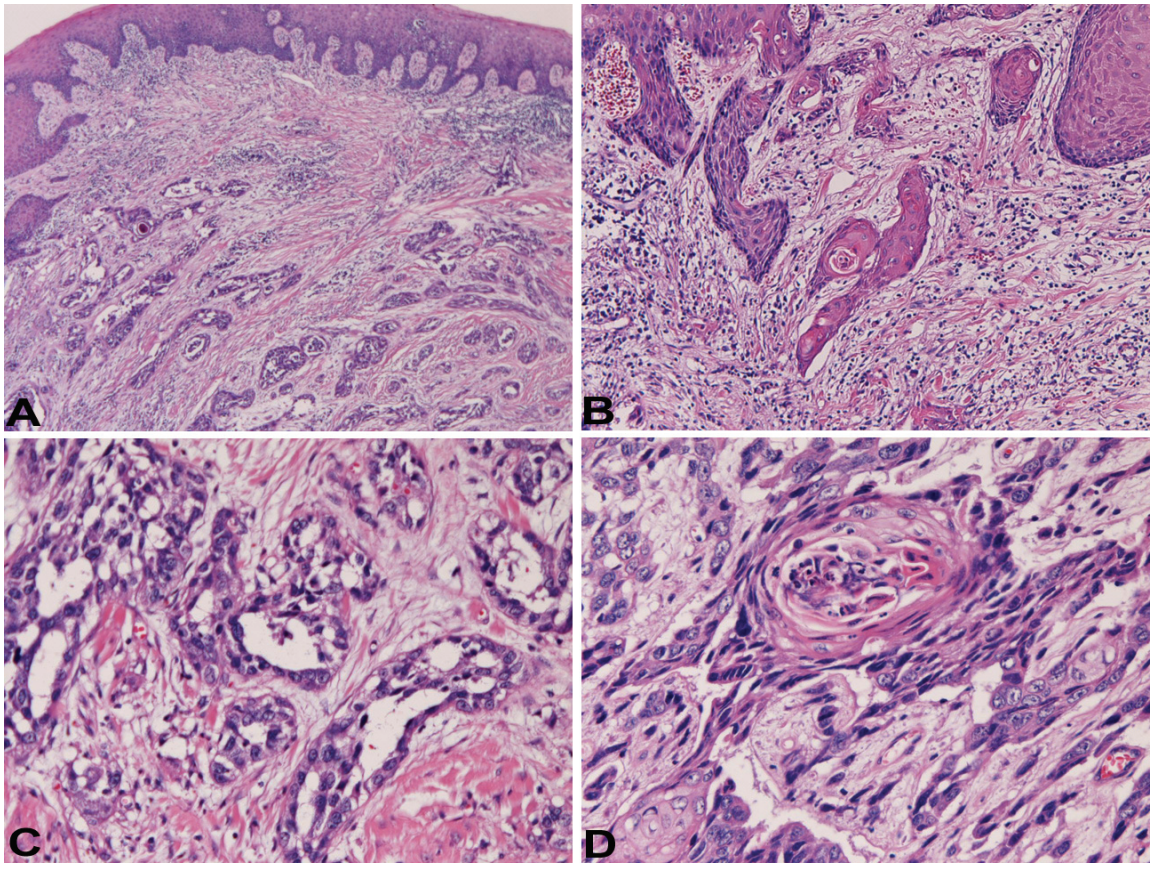

Figure 3. Histological features of the tumor. A: low power view shows proliferation of keratinizing squamous cell carcinoma and tubular structures. HE, x40. B: The squamous cell component shows keratinization and is continuous with gingival mucosal squamous cells. HE, x 200 C: Adenoid component shows tubular formation. HE, x200. D: Squamous cell carcinoma component showing acantholysis. HE, x200.

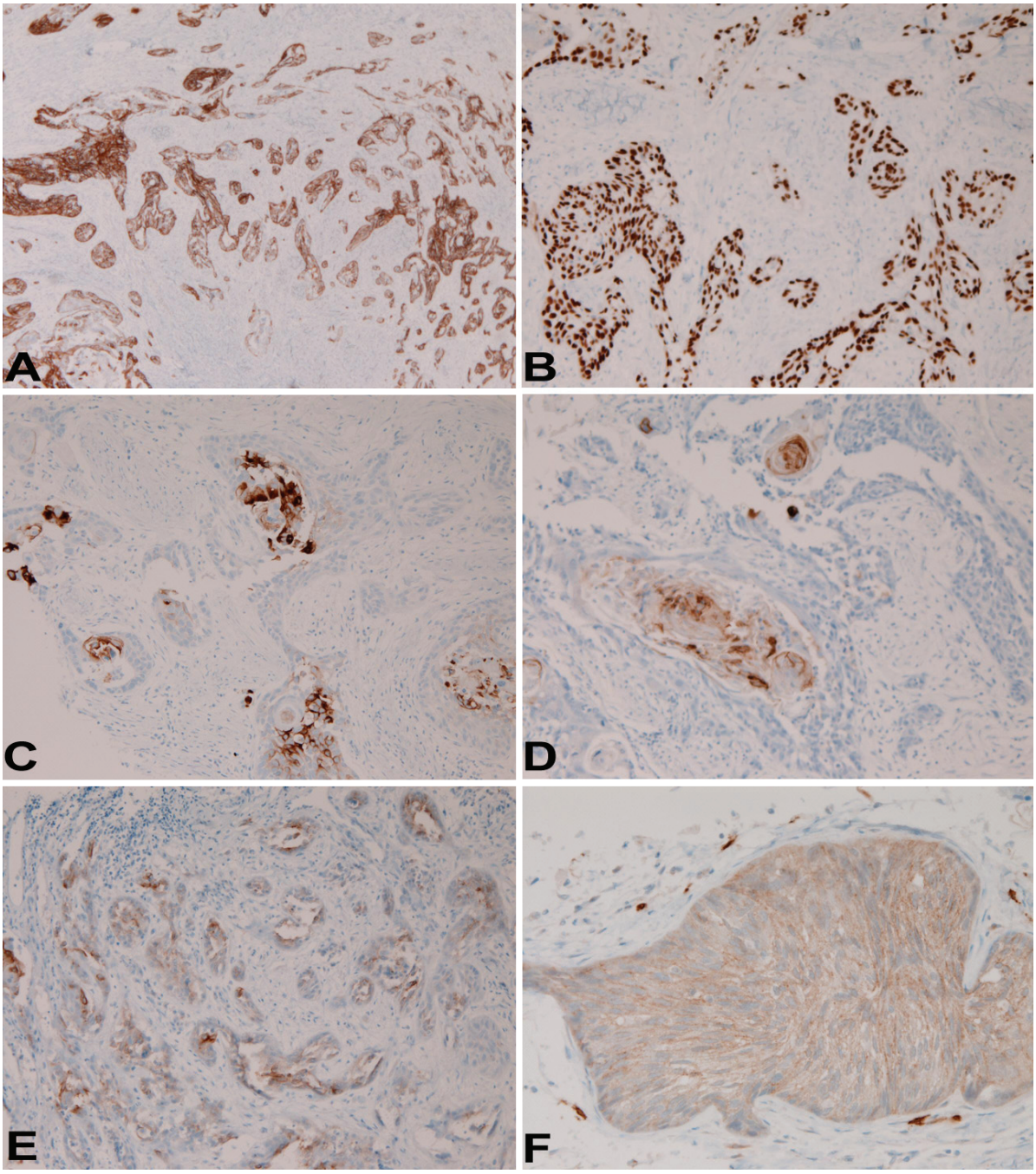

Figure 4. Immunohistochemical features. Both squamous cell component and adenoid component are positive for CK5/6 (A), p63 (B), CEA (C), Ca19-9 (D), MUC1 (E), and KIT (F). Immunostains, x200.

mine stains.

An immunohistochemical study was performed with the use of Dako Envision method, as previously described [7-10]. Both components were positive for pancytokeratins (AE1/3, polyclonal wide, CAM5.2) +++, cytokeratin (CK) 5/6 + (**Figure 4A**), CK34βE12 ++, CK7 +, CK14 +++, p63 +++ (**Figure 4B**), CEA + (**Figure 4C**), CA19-9 + (**Figure 4D**), CA125 +, MUC1 ++ (**Figure 4E**), p53 +++, and KIT + (**Figure 4F**) (**Table 1**). Both components were negative for CK8, CK18,

Table 1. Immunohistochemical reagents and results

Antigens	Antibodies (clone)	Sources	Results	
			SCC	Ade
Pancytokeratin	AE1/3	Dako Corp, Glostrup, Denmark	+++	+++
Pancytokeratin	CAM5.2	Beckson-Dickinson, CA, USA	-	+
HMWCK	35BE12	Dako	++	++
CK5/6	D5/6	Dako	+	+
CK7	N1626	Dako	-	-
CK8	DC10	Dako	+++	+++
CK14	LL002	Novocastra, Newcastle upon tyne, UK	-	-
CK18	DC8	Dako	-	-
CK19	RCK108	Progen, Heidelberg, Germany	-	-
CK20	K20.8	Dako	-	-
EMA	E29	Dako	-	-
Vimentin	Vim 3B4	Dako	-	-
TTF-1	8G7G3/1	Dako	-	-
CEA	Polyclonal	Dako	+	+
CA19-9	NS19-9	TFB-Lab, Tokyo, Japan	+	+
CA125	NS125	TFB-Lab	+	+
Desmin	D33	Dako	-	-
Myoglobin	Polyclonal	Dako	-	-
S100 protein	Polyclonal	Dako	-	-
Melanosome	HMB45	Dako	-	-
ASMA	1A4	Dako	-	-
CD34	NU-4A1	Nichirei, Tokyo, Japan	-	-
CDX-2	AMT28	Diagnostic Byosystem, CA, USA	-	-
P53 protein	DO-7	Dako	+++	+++
P63	4A4	Dako	+++	+++
Ki-67	MIB-1	Dako	30%	30%
Chromogranin	DAK-A3	Dako	-	-
Synaptophysin	Polyclonal	Dako	-	-
NSE	BBS/NC/VI-H4	Dako	-	-
CD56	UJ13A	Dako	-	-
Lysozyme	Polyclonal	Dako	-	-
CD68	KP-1	Dako	-	-
KIT	Polyclonal	Dako	+	+
PDGFRA	Polyclonal	Santa-Cruz, Santa Cruz, CA	-	-
MDM2	IF2	Invitorogen, Camarillo, CA, USA	-	-
MUC1	MA695	Novocastra	++	++
MUC2	Ccp58	Novocastra	-	-
MUC5AC	CLH-2	Novocastra	-	-
MUC6	CHL-5	Novocastra	-	-

SCC, squamous cell carcinoma area. Ade, adenocarcinoma area. +++, 67-100% positive. ++, 33-66% positive. +, 1-33% positive. -, negative. HMWCK, high molecular weight cytokeratin. CK, cytokeratin. TTF-1, thyroid transcriptional factor-1. EMA, epithelial membrane antigen. CEA, carcinoembryonic antigen. CA19-9, carbohydrate antigen 19-9. CA125, carbohydrate antigen 125. ASMA, α-smooth muscle antigen. SA-A, Surfactant apoprotein A. NSE, neuron-specific enolase. PDGFRA, platelet-derived growth factor receptot-α.

CK19, CK20, EMA, vimentin, TTF-1, desmin, myoglobin, S100 protein, melanosome, smooth muscle actin, CD34, CDX2, CD10, chromogranin, synaptophysin, NSE, CD56, lysozyme, CD68, MDM2, PDGFRA, MUC2, MUC5AC, and MUC6 (**Table 1**). Since both components were positive for squmaous cell carcinoma markers (CD5/6, CK34βE12, and p63) and adenocarcinoma markers (CEA, CA19-9, CA125, MUC1), this case of AdSCC appears an intermediate form between adenocarcinoma and squamous cell carcinoma. The margins were negative. Postoperative imaging techniques showed no metastasis, and the patient is now free from tumor and is followed up carefully.

Discussion

The present tumor is morphologically malignant. The strong expression of p53 and high Ki67

labeling support this. The present tumor must be differentiated from squamous cell carcinoma, adenosquamous carcinoma, basaloid squamous cell carcinoma, pseudovascular AdSCC, and some salivary gland tumors such as adenoid cystic carcinoma and mucoepidelmoid carcinoma. The current tumor is different from ordinary squamous cell carcinoma because the tumor showed glandular lumen. This tumor is different from adenosquamous carcinoma because the adenoid elements were negative for mucins and also because anatholytic features of squamous cell carcinoma were present. This tumor is different from vasaloid squamous cell carcinoma because of no basaloid cells. The present tumor is also different from pseudovascular AdSCC because the adenoid elements show no features of vasculatures. The current tumor is not adenoid cystic carcinoma because no cribriform patterns were noted and no immunohistochemical features of myoepithelial cells (S100 protein and α-smoooth muscle actin) were found. The current tumor is not mucoepidermoid carcinoma because no mucous cells or mucins were found.

Immunohistochemical study of oral AdSCC is very scant. However, Kusafuka et al [4] describe that an AdSCC of the oral cavity was positive for CK7, CK8, CK19, E-cadherin, and p53 but negative for vimentin, CK20, and S100 protein. The Ki-67 labeling was 50% [4]. In the present case, the AdSCC was positive for p53 but negative for CK8, CK19, CK20, S100 protein. The Ki-67 labeling 30%; thus the present case somewhat is different from the case of Kusafuka et al [4].

In the present case, the squamous cell carcinoma element and adenoid elements showed the same immunohistochemical profiles, suggesting that both components are the same in nature. The present case was positive for pancytokeratins, high molecular weight cytokeratin 34βE12, CK5/6, CK7 and CK14, but negative for CK8, CK18, CK19, and CK20. Namely, high molecular weight CKs were positive, and low molecular weight CKs were negative. Since squamous cell carcinoma express mainly high molecular weight cytokeratin [11]. The present case is basically squamous cell carcinoma. CK7+/CK20- pattern is consistent with oral squamous cell carcinoma [12]. CK14 is known to be expressed in squamous cell carcinoma [13]. The present case expressed p63. P63 is well known to be expressed in squamous cell carcinoma but not adenocarcinoma [14]; therefore the present case has characteristics of squamous cell carcinoma.

Interestingly, the present case expressed CEA, CA19-9, CA125, and MUC1, all of which are well known markers of adenocarcinoma. This finding suggests that the present tumor has adenocarcinoma characteristics. Namely, the present case shared squamous cell carcinoma and adenocarcinoma immunohistochemical characteristics.

It is very interesting that the present case expressed KIT. PDGFRA was negative. Although it is well known that adenoid cystic carcinoma express KIT, the present case is not adenoid cystic carcinoma. Therefore, oral AdSCC should be included as KIT-positive tumor such as germ cell tumor, myeloid malignancies, GIST, and mast cell neoplasm [15-22].

The present case was negative for EMA, vimentin TTF-1, myoglobin, S100 protein, melanosome, ASMA, CD34, CDX2, and CD10. The data suggest that EMA, a marker of epithelial cells, was negative in oral AdSCC. The data also suggest that TTF-1 (marker of thyroid carcinoma and pulmonary adenocarcinoma) and CDX2 (markers of colon carcinoma) were negative in oral AdSCC and indicate that the present tumor is not a metastatic tumor from the thyroid, pulmonary and colorectal malignancies. Negative S100 protein and melanosome indicate that the present tumor is not malignant melanoma. Negativity of other mesenchymal antigens indicates that this tumor is epithelial malignancy and not carcinosarcoma or sarcoma.

The present case was negative for neuroendocrine markers such as chromogranin, synaptophysin, NSE, and CD56, suggesting that the present tumor does not have neuroendocrine features. The present tumor was negative for lysozyme and CD68, suggesting that the tumor does not have histiocytic characters. MDM2 was negative, suggesting that MDM2 is not associated with the tumorigenesis and progression of the present AdSCC. MUC2, MUC5AC and MUC6 were negative, indicating that these genes are not operative in oral AdSCC.

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