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Adenosquamous Carcinoma Affecting the Maxilla: A Case Report and Review

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Abstract

Adenosquamous carcinoma of the head and neck (ASC) is a rare and aggressive variant of squamous cell carcinoma, a locally aggressive malignancy characterized by the presence of two distinct components: a squamous cell carcinoma and an adenocarcinoma. The purpose of this study was to report an additional rare case of adenosquamous carcinoma affecting the maxilla, with clinical microscopic features and a complex mid-facial rehabilitation.

Keywords

Squamous Cell Carcinoma, Adenosquamous Carcinoma, Implant Supported Prosthesis, Maxillofacial Rehabilitation

1. Introduction

Adenosquamous carcinoma (ASC), first described in 1968 [1], is an unusual and highly malignant neoplasm, which is characterized microscopically by the simultaneous presence of distinct areas of adenocarcinoma and squamous cell carcinoma (SCC) [1] [2]. There are controversies about the exact histogenesis of ASC. One hypothesis is that neoplasm arises from carcinoma *in situ* of minor salivary glands and ductal epithelial tissues. However, recently, authors [3] have strongly suggested that oral ASC is derived only from the squamous superficial epithelium, without the participation of minor salivary glands [3] [4]. The most common clinical feature is a painful mucosal ulceration [1] [2] [3] [4] [5]. Cigarette smoking and alcohol consumption, have been implicated as etiologic agents. There is a male predilection, with a tendency to develop between the sixth and

seventh decades of life [2]. ASC has an aggressive behavior associated with a poor prognosis. The spread to cervical lymph nodes is common and there are frequent reports on loco-regional and distant recurrences after treatment [1]-[8]. Current treatment options include surgery and radiation therapy with or without chemotherapy. A review of the English-language literature, conducted from 1968 to 2016, using the MEDLINE database showed only 24 well-documented cases of the ASC affecting the mid-face site (**Table 1**) [1]-[16]. Therefore, the present article describes an ASC affecting the maxilla with clinical and microscopic features and a complex mid-facial rehabilitation.

Table 1. Cases of adenosquamous carcinoma in the midface.

Case n°	Authors	Year	Age	Sex	Location	Treatment	Recurrence	Follow-up (months)
1	Gerughty *et al.* [1]	1968	76	F	Nose	S + R	Yes	AWD (24)
2			58	M	Nose	S + R	Yes	AWD (36)
3	Sanner [2]	1979	60	M	Maxillary Sinus	S	-	-
4	Minic and Stajcic [3]	1994	72	F	Inferior Turbinate	S	No	AWOD (18)
5	Napier *et al.* [4]	1995	61	F	Maxillary Alveolus	S + R	Yes	DOD (26)
6	Som *et al.* [5]	1997	62	F	Facial Bones, Skull Base and Calvaria	IB	-	-
7	Alos *et al.* [6]	2004	71	M	Nasal Cavity	S	Yes	DOD (24)
8			61	M	Nasal Cavity	S	Yes	DOD (30)
9	Shinhar and Heckathorn [7]	2008	54	F	Nasal Cavity	S + R	No	AWOD (6)
10	Suzuki *et al.* [8]	2009	77	M	Maxillary Sinus	S + C + R + S − 1	Yes	DOD (34)
11	Masand *et al.* [9]	2011	82	M	Paranasal Sinus	-	Yes	DOD (2)
12			52	M	Nose/Hard Palate/Maxilla	S	Yes	DOD (4.5)
13			62	M	Nasal Cavity	S	No	AWOD (26)
14	Kumar and Issing [10]	2011	66	F	Paranasal Sinus	IB	-	-
15	Schick *et al.* [11]	2013	60	-	Maxillary Sinus	S + R	Yes	DOD (39)
16			57	-	Maxillary Sinus	S + R	Yes	AWOD (52)
17			54	-	Nasopharynx	R	Yes	DOD (39)
18	Bishop *et al.* [12]	2013	-	-	Sinonasal Tract	-	-	-
19			-	-	Sinonasal Tract	-	-	-
20			-	-	Sinonasal Tract	-	-	-
21			-	-	Sinonasal Tract	-	-	-
22			-	-	Sinonasal Tract	-	-	-
23			-	-	Sinonasal Tract	-	-	-
24	Thanakappan *et al.* [17]	2015	55	M	Maxilla	-	-	-

-Information not provided; M, Male; F, Female; S, Surgery; R, Radiotherapy; C, Chemotherapy; S-1, A novel oral fluoropyrimidine anticancer agent; IB, Incisional Biopsy; DOD, Dead of disease; AWOD, Alive without disease; AWD, Alive with disease.

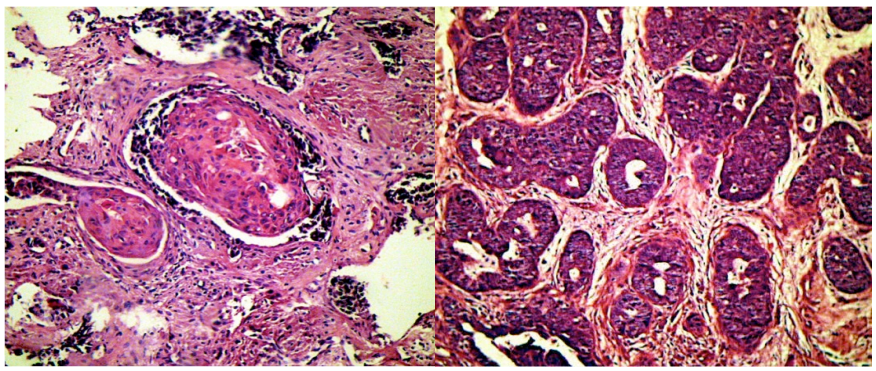
2. Case Report

A 47-year-old Caucasian woman was referred to our Institution complaining of pain in the left maxilla associated with nasal bleeding for the last 6 months. There was nothing relevant in her past medical history and she seemed healthy. Intraoral examination revealed asymptomatic nodular lesion in the left hard palate, covered by mucosa with normal color and resilient palpation. The imaging findings revealed a multicystic radiolucent lesion extending from the right upper lateral incisor to the second upper left premolar with poorly defined margins and causing root resorption of the involved teeth. CT scan showed the lesion in the anterior region of both maxillas, which extended mainly to the left maxillary sinus and nasal cavity (Figure 1).

An incisional biopsy was performed and microscopic examination of the hematoxylin and eosin stained sections revealed infiltrative malignant epithelial neoplasm with areas of squamous and glandular differentiation (Figure 2). The

(a) (b)

Figure 1. Computed tomography showing the involvement of the lesion. Axial reconstruction showing hypodense areas of diffuse osteolysis in the anterior alveolar ridge in both maxillas, with poorly defined margins (a) extending to the left nasal cavity and maxillary sinus (b).

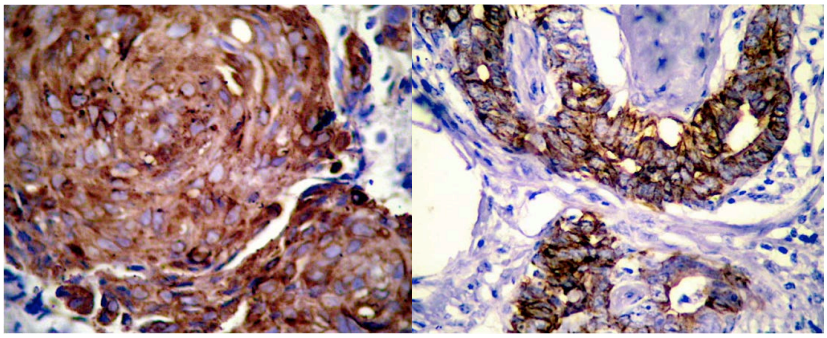


(a) (b)

Figure 2. Histopathological features of the lesion. Invasive neoplastic growth composes of atypical squamous cells arranged in sheets or solids in nests (a). HE 200 ×. Duct-like structures lined by a single or double layer (b). HE 200 ×.

tumor showed atypical cells arranged in sheets or solids in nests. The squamous component showed areas of epithelial dysplasia and carcinoma *in situ*. Perineural and extensive bone invasion were observed. The mucicarmine stain revealed glandular mucus-secreting neoplastic elements. In addition, immunohistochemical evaluation was performed with monoclonal/polyclonal antibodies to cytokeratins 34bE12 and CK7, and against carcinoembryonic antigen (CEA), epithelial membrane antigen (EMA), cErb-B2, chromogranin, estrogen receptor, progesterone receptor, thyroid transcription factor (TTF-1) and actin. The immunohistochemical findings are summarized in Table 2. Sections stained with 34bE12 and EMA showed positive immunoreactivity with both the squamous and adenocarcinoma components (Figure 3(a)). Sections stained with CK7 (Figure 3(b)) and CEA revealed positive immunoreactivity with the adenocarcinoma component only, and negative immunoreactivity with the squamous component. The final microscopic diagnosis was ASC. The patient was staged as having a T4 N1 M0 adenosquamous carcinoma of the maxilla. The treatment consisted of right and left partial maxillectomy and unilateral supraomohyoid neck dissection followed by postoperative radiotherapy with 68 Gy delivered in 35 fractionations. The histopathological examination revealed two positive lymph nodes in level I in the surgical neck specimen.

In following 6 years, the patient had two relapses, which were treated through maxillectomies and left orbit exenteration (Figure 4). These relapses occurred 4 and 8 months after the end of radiotherapy in the left and right radiotherapy, respectively.



(a) (b)

Figure 3. Presence of immunostaining for cytokeratin 34BE12 protein in the areas of the squamous epithelium. 400 × (a). Presence of immunostaining for cytokeratin CK7 protein in the areas of the epithelium that presented invasive features, indicating a glandular phenotype differentiation 400 × (b).

Table 2. Immunohistochemical findings.

	34bE12	CK7	CEA	EMA	cErbB-2	Chromogranin	Estrogen receptor	Progesterone receptor	TTF-1	Actin
Squamous component	+	–	–	+	–	–	–	–	–	–
Adenocarcinoma component	+	+	+	+	–	–	–	–	–	–

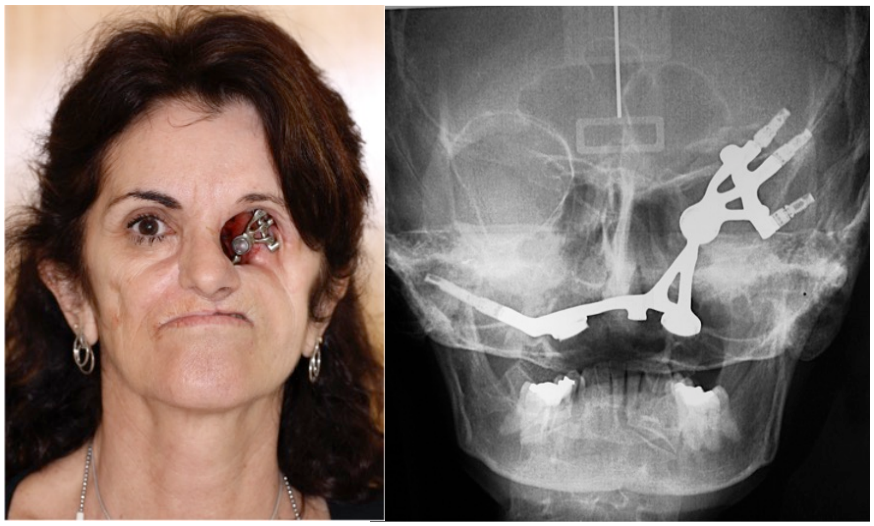
(a) (b)

Figure 4. Extraoral and intraoral clinical presentation after bilateral total maxillectomies and the left orbit exenteration ((a) & (b)).

The oral and maxillofacial rehabilitation of the patient began six months after the end of radiotherapy in the head and neck region. Initially, a diagnosis and treatment plan for implant-supported oral obturator and maxillofacial prostheses was presented to the patient. Implant placement was performed with the patient under general anesthesia and treated according to a 2-stage surgical implant procedure. Osseointegrated implants were installed in the upper left orbital margin and in the right zygoma (**Figure 5**). The planning of maxillofacial rehabilitation consisted of making two implant-supported prostheses. The definitive facial prosthesis was fabricated using silicone elastomer (VST50F; Factor II, Lakeside, AZ) that was colored intrinsically and extrinsically to match the patient's skin tone (**Figure 6(a)**). The obturator prosthesis was made of acrylic resin (**Figure 6(b)**). Magnets were used to provide retention and stability for both prostheses. Currently, the patient is under clinical and imaging follow-up, without any evidence of local recurrence or distant metastasis.

3. Discussion

ASC of the head and neck has been considered to be a very aggressive neoplasm with a poor prognosis. ASC is a rare neoplasm, not only in the head and neck region, but also in other areas [2] [3] [4]. Cases have also been reported in the uterine cervix, pancreas, lung, thyroid and esophagus. In the head and neck region, ASC occurs over a broad age range (34 to 81 years) and is 2 to 4 times more common in men [2] [3] [4] [5]. The most common sites of occurrence appear to be the larynx and the oral cavity [2]. The current case illustrates an ASC involving the maxilla, but the exact origin of this neoplasm could not be asserted due to the identification of maxillary bone invasion at the time of initial clinical examination. This fact led to difficulties in establishing the exact origin of this tumor that included nasal and oral cavities and maxillary sinus [18].



(a) (b)

Figure 5. Osseointegrated implants installed in the upper left orbital margin and in the right zygoma with the metal framework superstructure positioned in the patient ((a) & (b)).

(a) (b)

Figure 6. Final clinical aspect of the patient's facial (a) and oral (b) rehabilitation.

The recognition of ASC of the head and neck, as a distinct entity, was controversial for many years. Differential diagnosis should be specially done from squamous cell carcinoma, mucoepidermoid carcinoma, and other metastatic tumors. Histological diagnosis of ASC is often difficult for the pathologist because of the small biopsy specimens that lack either component, particularly the adenocarcinomatous one, which often exists in the deeper portion of the lesion. The SCC component which can be *in situ* or invasive usually predominates, and the adenocarcinoma component can have a tubular, alveolar and/or glandular morphology. In the present case, ASC is an appropriate diagnosis because of the com-

bination of distinct areas of adenocarcinoma and SCC in both biopsy and resection specimens. This appearance contrasts with the intimate intermingling of glandular and squamous components commonly seen in mucoepidermoid carcinoma, a tumor that may arise in the oral cavity from minor salivary glands and that also exhibits a dual histomorphology [19]. Mucoepidermoid carcinoma is also characteristically associated with intermediate or transitional cells, and these are also lacking in ASC. Further evidence to support a diagnosis of ASC may be obtained using immunohistochemistry, which demonstrates distinctive staining patterns in each of the two components. Thus, in the present case, the phenotypical characteristics of the adenocarcinomatous component were emphasized by the immunoreactivity with 34bE12, CK7, CEA and EMA, while the phenotypical characteristics of the squamous component were demonstrated by the positive immunoreactivity with 34bE12 and EMA and the negative immunoreactivity with CK7 and CEA.

ASC is an aggressive tumor characterized by local recurrences, early lymph node metastasis and distant disseminations after treatment. The treatment of choice for ASC has not yet been standardized, but it seems a consensus that the best treatment option should be surgical resection with an adequate safety margin. Additional post-operative therapies, such as radiotherapy and chemotherapy, are not yet consensus on the handling of this clinical entity. Most of the reported cases in the oral cavity and maxillofacial area have been locally and extremely aggressive showing marked infiltration and destruction of the adjacent hard tissue, regardless of the radical surgical treatment and postoperative adjuvant therapies. The poor outcome of ASC of the head and neck region has been reported in the literature. Schick et al (2013) reported a 3-year overall survival rate of 52% and a mean survival time of 39 months [5]. Keelawat *et al.* (2002) reported a 5-year survival rate of 20% among a series of 12 patients with adenosquamous carcinoma of the larynx, oral cavity and oropharynx [20]. Yoshimura *et al.* (2003) found a 5-year overall survival rate of 61% in patients who underwent an active treatment [21]. The reasons for the aggressive behavior of ASC are unclear; however it could be explained by an apparent propensity to spread by perineural invasion [17]. This histopathological feature has been reported to be present in 6 of the 12 cases in Keelawat's series [20], and in 75% of the patients reported by Sheahan *et al.* The current case showed a local extreme aggressive behavior with infiltration and destruction of the maxilla and regardless of radical surgical approach and post-operative radiation therapy the patient presented 2 relapses in the first year of follow-up.

Prosthodontic rehabilitation of head and neck cancer patients is a challenging and demanding procedure. Radiation and aggressive surgical resection frequently result in functional disabilities and esthetic deformity. Oral and maxillofacial rehabilitation using conventional prostheses may be compromised or impossible to achieve due to impairment or absence of supporting tissues after surgery. Since Brånemark and Albrekttsson introduced percutaneous craniofacial implants to be used with bone conduction hearing aids, implants have also

acquired an important role in the prosthetic rehabilitation of patients with craniofacial defects. We have previously reported our experience with implant-supported craniofacial prostheses for the management of patients with head and neck cancer. In this study, the survival rate of implants placed in the orbital region was 100%. Some clinical studies have also reported survival rates higher than 90% for orbital implants, which seems to be a predictable result [22]. However, in the current case the implants were installed outside of the primary tumor irradiation field, which allowed more predictable implants and prostheses outcome. The optimal timing of implant placement in head and neck patients is controversial. Some authors recommend the installation of implants during ablative tumor surgery. Insertion of implants at this time would be of great advantage because the initial implant healing occurs before irradiation and, thus, minimizes the risk of late oral complications, such as the development of osteoradionecrosis. The rehabilitation of maxillofacial deformities in head and neck cancer patients using implant-supported prostheses allows direct access to the cavities for searching an eventual tumor local recurrence. Fortunately, the use of cosmetic and restorative therapy has improved the quality of life of patients with disfiguring diseases.

4. Conclusion

In conclusion, ASC is an aggressive tumor characterized by local recurrences. Although ASC rarely affects the maxilla, the dentist also has an important role in the diagnosis, rehabilitation treatment and patients' follow-up of patients, improving their quality of life.

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