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Adenosquamous Carcinoma of the Tongue

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Abstract

A 51-year-old white female presented with a painful ulcer of the left ventrolateral tongue. An incisional biopsy confirmed a diagnosis of adenosquamous carcinoma. The adenosquamous carcinoma is an uncommon malignant tumor with histopathological features of a squamous carcinoma and an adenocarcinoma. A definitive diagnosis requires histopathological examination of a deep biopsy involving the submucosal tissue. This malignant tumor shows aggressive behavior with early invasive growth and a poor prognosis. The histopathological findings and differential diagnosis of a case of adenosquamous carcinoma of the tongue are discussed.

Keywords

Oral, Tongue, Carcinoma, Squamous, Adenocarcinoma

History

A 51-year-old white female presented to the dental emergency clinic with a painful ulcer of the left ventrolateral tongue. Reportedly, the ulcer was present for several weeks but had become recently painful. The pain affected tongue mobility, interfering with chewing and speech. There was no history of tobacco or alcohol use. Her medical history was uneventful other than occasional office visits for seasonal respiratory ailments.

Clinical Findings

Extraoral examination was unremarkable and regional lymph nodes were not palpable. On intraoral examination, the left ventrolateral tongue showed an irregular ulcer surrounded by vague leukoplakia-like areas. The ulcer bed was erythematous with a slight fibrinopurulent exudate (Fig. 1). The area was indurated and tender to palpation. The remainder of the oral cavity was within normal limits. The patient elected to undergo an incisional biopsy procedure.

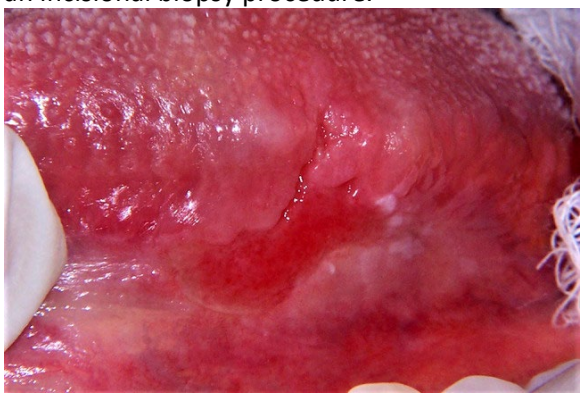

Fig. 1 An irregular ulcer of the left ventrolateral tongue surrounded by a vague leukoplakia-like area

Diagnosis

Formalin fixed hematoxylin and eosin stained sections showed nests and islands of well-differentiated keratinizing squamous cells invading the lamina propria (Fig. 2). A transition to an adenocarcinoma (Fig. 3), with prolific glandular duct-like structures with lumens surrounded by dysplastic cells, many of who showed intracytoplasmic vacuoles was seen in the deeper submucosa. Occasional mucocytes were also seen (Fig. 4). The adenocarcinoma also showed dissection of the extrinsic skeletal muscle fiber bundles (Fig. 5), perineural involvement (Fig. 6) and intravascular tumor islands (Fig. 7). Based on the histopathological findings, a diagnosis of adenosquamous carcinoma was given.

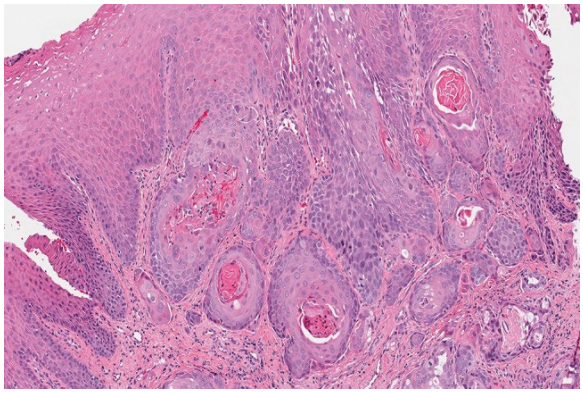

Fig. 2 Well-differentiated, keratinizing squamous nests invading the lamina propria (H&E, 10×)

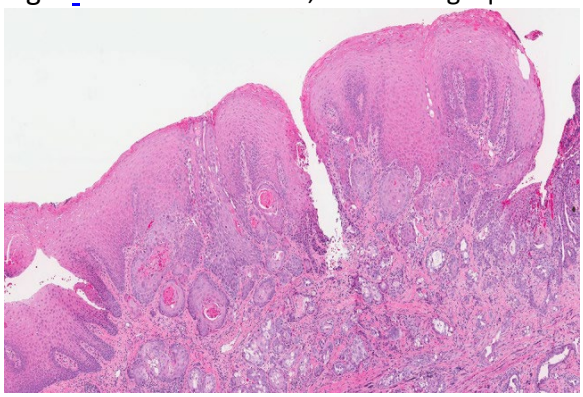

Fig. 3 Transition from a squamous carcinoma to a deeper adenocarcinoma (H&E, 4×)

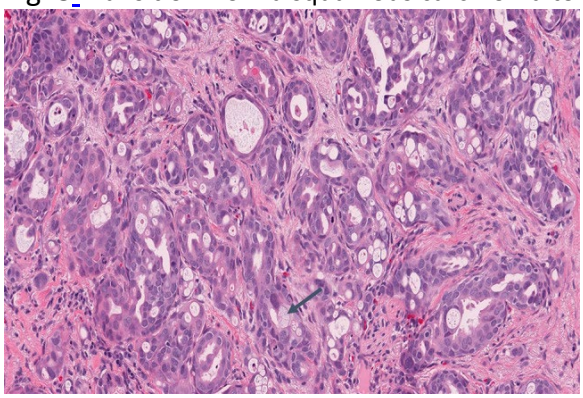

Fig. 4 Numerous nests of adenocarcinoma with ducts surrounded by cells with intracytoplasmic vacuoles. Occasional mucocytes (arrow) are also seen (H&E, 10×)

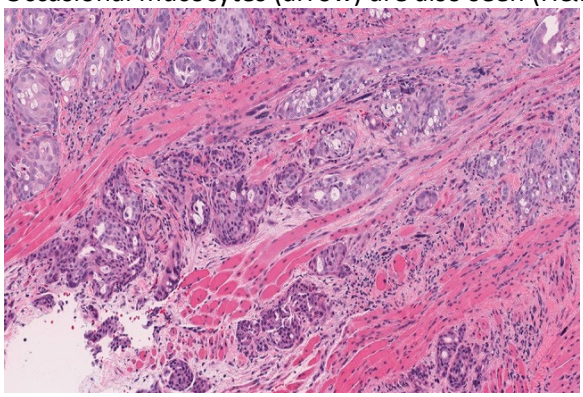

Fig. 5 The adenocarcinoma is dissecting between the muscles of the tongue (H&E, 10×)

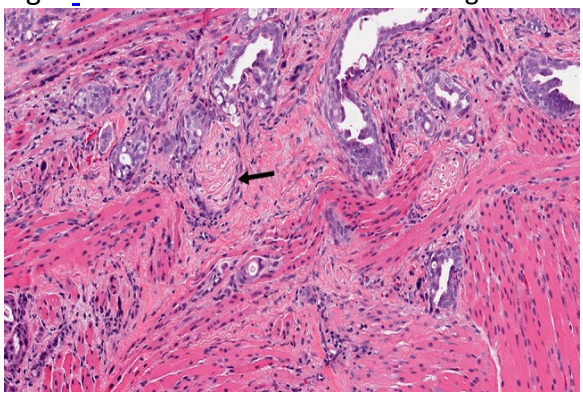

Fig. 6 A focus of perineural involvement (H&E, 10×)

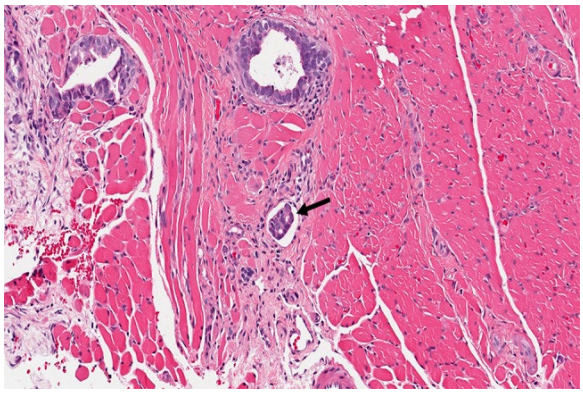

Fig. 7 Intravascular tumor nest (H&E, 10×)

Discussion

The adenosquamous carcinoma is a tumor that demonstrates the presence of a true adenocarcinoma and overlying squamous cell carcinoma. It was described first by Gerughty et al., who postulated that the tumor arises from the excretory ducts of the minor glands of the upper respiratory tract and spreads by contiguity to the surface epithelium [1]. On the other hand, Ellis et al. hypothesized that the tumor arises simultaneously from both malignant transformation of the surface epithelium and glandular excretory ducts [2].

This tumor has been documented in epithelial tissue of the entire gastrointestinal tract, skin, lung, pancreas, hepatobiliary system, female reproductive system and genitourinary system. Head and neck tumors have been described in the thyroid gland, nasal cavity, oral cavity, pharynx and the larynx [1, 2]. Tumors of the larynx and hypopharynx are the most common involving the head and neck [3, 4].

The adenosquamous carcinoma is diagnosed most commonly in the 6th and 7th decades of life with a male dominance [3, 5, 6]. Tobacco use and alcohol consumption have been implicated in its causation. The role of gastric acid reflux has been suggested but not established [3]. One case of the floor of the mouth was diagnosed following radiation treatment for a previous conventional squamous carcinoma [7].

Symptoms are related to the site affected and include painful ulcers, hoarseness, dysphagia, stuffiness, obstruction, and hemoptysis [3, 4]. Oral tumors present as painful ulcers and/or swelling. Tongue and floor of mouth involvement is most common [8–11]. The majority of tumors present as T4 stage lesions [4, 5, 12] and in two series of cases of the upper aerodigestive tract approximately 75% of cases exhibited nodal spread on initial presentation [4, 13].

The histopathological features show an epithelial malignancy with squamous and glandular differentiation. While the two patterns may be distinct but in close proximity, most lesions demonstrate blending, intermixing or an area of transition from a superficial squamous cell carcinoma to a deeper adenocarcinoma. The squamous component may show varying grades of differentiation. The adenocarcinoma shows tubular/ductal structures with intraluminal or intracellular mucin. Mucin production and perineural invasion is typically present but not required for diagnosis [1–5, 7–11, 13, 14]. Immunohistochemistry is typically not necessary to make a diagnosis. The tumor, however, expresses high molecular weight cytokeratins in both the squamous and glandular components. The

adenocarcinoma expresses CEA and CK7. CK20 is negative. The squamous component expresses CK5/6 and p63 [3, 5]. CAM5.2 is expressed only by the glandular component of the tumor [8, 14].

The histopathological differential diagnosis includes mucoepidermoid carcinoma, adenoid squamous cell carcinoma, metastatic adenocarcinoma, necrotizing sialometaplasia, and squamous cell carcinoma. Mucoepidermoid carcinomas lack a surface component and true squamous differentiation. Adenosquamous carcinomas with poor squamous differentiation may be impossible to differentiate from high-grade mucoepidermoid carcinomas if the lesion is largely ulcerated and histopathologically the two components are blended. Unlike the mucoepidermoid carcinoma, the adenosquamous carcinoma lacks MAML2 translocation making it a useful tool in their differentiation [12].

Adenoid (acantholytic) squamous cell carcinomas are a result of acantholysis of the cells thereby creating pseudoglandular spaces. These spaces do not show mucin production. Oral lesions of adenoid squamous carcinoma are most common on the vermillion of the lower lip [2]. Metastatic adenocarcinomas do not show a squamous carcinoma component. While necrotizing sialometaplasia may show a pseudoepitheliomatous hyperplasia on low power, the lobular architecture of the glands is preserved and acinar necrosis is seen [15]. Squamous cell carcinomas may extend down glandular ductal units but the glands themselves are benign.

Adenosquamous carcinomas are treated with an aggressive surgical approach including neck dissection irrespective of detectible nodal disease. Tumors diagnosed at an older age, large and extensive tumors all portend a decreased survival rate [6]. Surgical resection improves survival in patients with localized or regional disease, whereas radiation therapy confers survival benefit in patients with distant spread. Prognosis is generally poor with 5-year survival rates in the range of 15–25% [1, 3, 4, 16]. However, a recent survival comparison study of patients with head and neck adenosquamous carcinoma and those with conventional squamous carcinoma found no significant difference in median survival times, irrespective of matched tumor sizes (T) and nodal status. The authors caution about the small sample size in their study [12].

The role played by the human papilloma virus (HPV) in the etiology of adenosquamous carcinoma is uncertain. One study found 25% of cases of adenosquamous carcinoma of the head and neck to be associated with HPV. This study also noted that the HPV-associated adenosquamous carcinomas had a response to therapy equal to those patients with HPV positive conventional squamous carcinomas [17].

Compliance with Ethical Standards

Conflict of interest

This case was presented at the Continued Competency Examination of the 2014 Annual Meeting of the American Academy of Oral and Maxillofacial Pathology.

Research Involving Human and Animal Participants

This article does not contain any studies with human participants or animals performed by any of the authors.

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