Neuroepithelial hamartoma of the oral cavity

Mayra Mesa, DMD, MScD, a Ernest Baden, DDS, MD, b Joseph Grodjesk, DDS, c and Herbert B. Dolinsky, DDS, d Brooklyn, N.Y., and Newark and Jersey City, N.J.
UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY, NEW JERSEY DENTAL SCHOOL, NEW JERSEY MEDICAL SCHOOL, LUTHERAN MEDICAL CENTER, AND CHRIST HOSPITAL

We report a previously undescribed gingival lesion composed of squamous epithelial islands in close association with bundles of nonmyelinated nerves. A review of the pertinent literature is presented and the histologic differential diagnosis is discussed. We suggest the term neuroepithelial hamartoma for this lesion. (ORAL SURG ORAL MED ORAL PATHOL 1994;78:627-30)

Remnants of vestigial or rudimentary epithelial structures that persist into adult life are common in the oral region and include those of both odontogenic and nonodontogenic origin. Examples of odontogenic epithelial remnants that occur in the soft and hard tissues of the oral region include the rests of Serres and the rests of Malassez. Examples of nonodontogenic epithelial remnants include those of nasopalatine duct and thyroglossal duct origin.

These remnants may give rise to cysts, hamartomas, and neoplasms of the jaws or oral soft tissues.1 In addition, the epithelium of the stomodeum possesses a pluripotential spectrum of differentiation as evidenced by the histogenesis of the minor salivary glands, the teeth and mucosal lining of the oral cavity, the thyroid and parathyroid glands, and other structures.2 The diversity of cysts,3 hamartomas,4 choristomas,5,6 and neoplasms7 observed in the gingiva illustrates both the pluripotentiality of the gingival epithelium and the proliferation potential of vestigial embryonal rests. The simultaneous occurrence and close association of epithelial structures and neural elements in the oral cavity has been described as an incidental finding in the microscopic examination of other lesions,8-11 in the juxtaoral organ of Chievitz (or nodular hyperplasia of the organ),12,13 and in perincural spread of an oral carcinoma.14-16

We report herein a gingival lesion that consisted of both squamous epithelial nests and nerve tissue, which could not be classified with anything previously reported. After consultation, we chose to call the lesion neuroepithelial hamartoma.

Fig. 1. Low-power photomicrograph showing lesion composed of islands of squamous epithelium in collagenous stroma (hematoxylin and eosin stain; original magnification x40).
CASE REPORT

A 24-year-old woman was first seen for the removal of "bone" on the lingual aspect of the right mandibular molar teeth. She stated that a ridge was present along the inner surface of the mandible that felt hard and frequently became irritated. Examination revealed what appeared to be an exostosis along the lingual gingival margin of the three right mandibular molar teeth. The area in question was very firm and the mucosa appeared normal. The lesion was located at the level of the lateral border of the tongue and seemed to form a 2 to 3 mm shelf on the lingual gingiva. Radiographic examination showed no osseous changes. Periodontitis was present in all posterior quadrants. The lesion was excised in two portions and the tissue submitted for histologic examination.

Pathologic findings

The surgical specimens were fixed in 10% formalin and processed in the usual manner. Paraffin sections were cut and stained with hematoxylin and eosin, Masson trichrome, and Bodian silver stains.

Immunohistochemistry with the avidin-biotin complex method was done for S-100 protein, neuron-specific enolase, muscle-specific actin, polyclonal cytokeratin, and epithelial membrane antigen markers with suitable controls.

Sections stained with hematoxylin and eosin showed round to oval and irregular islands of squamous epithelium within a collagenized stroma (Fig. 1). The islands consisted of central round to oval epithelial cells with slightly pleomorphic but orthochromatic nuclei. The periphery of the epithelial nests was lined by cuboidal to flattened cells. Some of the islands had intercellular bridges and others a more syncytial structure. Areas of degeneration were
present in the center of some islands, resulting in microcystic changes, whereas few showed keratin pearl formation. Small bundles of nonmyelinated nerves either surrounded or directly collided with the epithelial islands (Figs. 2 and 3). The axons of the nerve bundles stained positively with Bodian stain. On immunohistochemical staining the neural elements found scattered in the stroma, colliding with or cuffed the epithelial islands, strongly reacted with S-100 protein and neuron-specific enolase. Staining for muscle-specific actin was negative except for the venules and arterioles in the stroma. Vimentin marked the endoneurial connective tissue. Staining for polyclonal keratin was positive in the epithelial islands and overlying gingival epithelium. Staining for epithelial membrane antigen was only focally and weakly positive in isolated epithelial islands.

DISCUSSION

The occurrence of a gingival lesion composed of juxtaposed benign squamous epithelial islands and differentiated neural tissue within a connective tissue stroma has not been reported previously. These microscopic characteristics are therefore challenging to the pathologist. The differential diagnosis of a gingival lesion characterized by epithelial proliferation in a connective tissue stroma should include the possibility of a peripheral odontogenic lesion. The present case was initially interpreted as a variant of peripheral squamous odontogenic tumor. Several odontogenic lesions have been reported in a gingival location including peripheral squamous odontogenic tumor. Others include the calcifying odontogenic cyst and tumor, adenomatoid odontogenic tumor, peripheral calcifying epithelial odontogenic tumor, odontogenic gingival epithelial hamartoma (peripheral odontogenic fibroma, World Health Organization type), and peripheral ameloblastoma. Our initial diagnosis of peripheral squamous odontogenic tumor was reconsidered because of the presence of numerous nonmyelinated nerves in close association with the squamous epithelial islands.

The close association of epithelial islands with nerves is characteristic of the juxtaoral organ of Chievitz and of perineural spread of an epidermoid or mucocoeplidermoid carcinoma. This occurrence has also been reported as an incidental histologic finding in other pathologic specimens such as the walls of odontogenic jaw cysts, nasopalatine duct cyst, the maxilla, and within the narrow compartment of an exostosis.

The juxtaoral organ of Chievitz, a normal anatomic structure, is a potential pitfall for the pathologist, having been wrongly interpreted as perineural invasion in patients with oral cancer, thereby resulting in unnecessarily extensive surgery. The anatomic location of the organ of Chievitz is quite specific. It occurs deep to the medial pterygoid muscle, at the level of the pterygomandibular raphe, and is associated with the long buccal nerve. It is a mass of tissue measured in millimeters (0.5 to 2 mm) and not normally palpable. Histologically it is characterized by squamous epithelial islands and duct-like structures in a fibrous connective tissue stroma that contains numerous myelinated and nonmyelinated nerves in close proximity to the epithelial component. Its function has not been established, although it has been thought to have both a neuroreceptoric and a secretory function. Cases of nodular hyperplasia of the organ that were clinically evident have been reported, but all were found in the typical anatomic location. We therefore excluded this diagnosis on the basis of the location of the lesion on the lingual gingiva.

Intraneural epithelial structures have been reported that occurred as incidental findings during the histologic examination of some jaw lesions. Jensen et al. in 1979 reported the occurrence of intraneural epithelial islands with features of odontogenic epithelium that were associated with the inferior alveolar nerve in the walls of a primordial and an odontogenic keratocyst. In 1978, Eversole and Leider described the presence of intraneural epithelial nests within maxillary bone. These islands displayed features in common with odontogenic rests. Wysocki and Wright in 1981 reported the presence of intraneural odontogenic epithelial rests in the buccal aspect of the posterior maxilla within an exostosis. They also described intraneural epithelial structures in the wall of a nasopalatine duct cyst that had morphologic features consistent with remnants of nasopalatine duct. These authors offered three hypotheses on how these epithelial nests become incorporated within peripheral nerves. They suggested that this could occur from entrapment during development of peripheral nerve, entrapment during regeneration after severance of the nerve, or as misdirected benign invasion of peripheral nerves by primordial epithelial structures such as the dental lamina during odontogenesis. George et al. reported the occurrence of intraneural odontogenic epithelium associated with a periapical cyst. All of the cases referred to represented incidental findings in other lesions and thereby were different from our case, which presented as a gingival mass. These reports also differ from the present case in that in most of them the epithelium was found intraneurally and the islands were not typically squamous. In addition, all of these cases were intraosseous and associated with myelinated nerves.
A major consideration in the differential diagnosis of the lesion presented here was the possibility of perineural spread of oral carcinoma (epidermoid or mucoepidermoid carcinoma). The benign nature of the epithelium, the organoid pattern of the stromal and epithelial elements, and the fact that the neural elements surrounded epithelial nests (the converse of perineural infiltration by carcinoma) were all supportive of a benign rather than a malignant process.

Five cases of a new entity designated neurofollicular hamartoma, which showed histologic features similar to those of the present case, have been reported in the skin. The lesions consisted of hyperplastic pilosebaceous units in a spindle cell stroma, with nerve twigs and Schwannian differentiation exhibited. These lesions, as in our case, did not fit into any previously recognized classification of tumors. It is possible that our case represents an analogue of this entity. The histogenesis of the present case is obscure. We believe the lesion represents a hamartomatous process in which the epithelial islands were derived lamina rests (of Serres) and propose the term neuroepithelial hamartoma.

Sincere thanks goes to Mr. Leo Penkovsky, BS, HTL (formerly of the Histology Laboratory, Department of Laboratories and Pathology Lutheran Medical Center, now at Long Island Jewish Hospital) and his staff for the immunohistochemical stains, to Dr. John Doyle (Professor of Clinical Oral Pathology, Biology and Diagnostic Sciences, New Jersey Dental School) for his editorial comments, and to Ms. Gloria Smith for her assistance in the preparation of this manuscript. Special thanks to Drs. John Fantasia, Paul Freedman, John Richardson, Lawrence Schneider, and James Scuibba for consulting in this case.

REFERENCES

Reprint requests:
Mayra Mesa, DMD, MScD
Department of Oral Pathology, Biology and Diagnostic Sciences UMDNJ—New Jersey Dental School
110 Bergen St.
Newark, NJ 07103-2400