

CLINICAL NOTE

Lymphoepithelial Carcinoma of the Minor Salivary Gland

N. Knight Worley, MD; Philip J. Daroca, Jr, MD

Undifferentiated carcinoma of the minor salivary glands has been rarely reported in the world literature. Lymphoepithelial carcinoma, which is a variant of undifferentiated carcinoma, is distinguished from small cell and large cell undifferentiated carcinoma by its association with benign lymphoepithelial lesions. We report a case of a lymphoepithelial carcinoma developing in a minor salivary gland of the oral cavity in a 69-year-old woman. To our knowledge, this is the first reported case of a lymphoepithelial carcinoma arising from a minor salivary gland.

Arch Otolaryngol Head Neck Surg. 1997;123:638-640

REPORT OF A CASE

A 69-year-old white woman presented to our clinic with a firm, nontender mass in the left submandibular region that she had had for 3 months. She denied the presence of associated fever, sialadenitis, or a recent head and neck infection. Also, she complained of poorly fitting dentures and irritation to the left buccal mucosa. The patient has never smoked and denied alcohol use. She had recently completed a 2-week course of antibiotics without any change in her symptoms.

On physical examination, a firm subepithelial mass (0.5 cm) was palpated in the left inferior buccal region adjacent to the lateral border of the patient's lower denture. No evidence of mucosal ulceration or inflammation was present. A firm, nontender, non-fluid-filled mass, which was approximately 2×2 cm, was palpated in the left submandibular region. The results of flexible endoscopy of the nose, nasopharynx, oropharynx, and larynx indicated no mucosal abnormalities. The results of the remainder of the physical examination were normal. A fine needle aspirate of the left submandibular mass was not diagnostic. An incisional biopsy specimen of the left buc-

cal space mass was consistent with a benign lymphoepithelial process.

The patient underwent panendoscopy with directed biopsy, the results of which indicated no evidence of a mucosal primary lesion, and an excisional biopsy of the left submandibular mass. The results of histopathologic analysis indicated a normal submandibular gland with metastatic undifferentiated carcinoma of 1 lymph node. A modified radical neck dissection of the left side was performed, and the submucosal buccal mass was completely removed using wide excision, including the overlying mucosa. Postoperative radiotherapy was administered. At approximately 1 year after treatment, the patient had no evidence of recurrent disease.

The submucosal mass in the inferior left buccal region was classified as an undifferentiated carcinoma developing from a benign lymphoepithelial lesion of a minor salivary gland. None of the 22 lymph nodes in the specimen obtained from the modified radical neck dissection of the left side contained metastatic undifferentiated carcinoma. The cytologic features of the metastatic undifferentiated carcinoma found in the previously excised submandibular lymph node were identical to the malignant portion of the minor salivary gland lesion.

The lesion of the mucous accessory salivary gland contained 2 components: a

From the Departments of Otolaryngology, Head and Neck Surgery (Dr Worley) and Pathology (Dr Daroca), Tulane University School of Medicine, and the Department of Pathology, Medical Center of Louisiana (Dr Daroca), New Orleans, La.

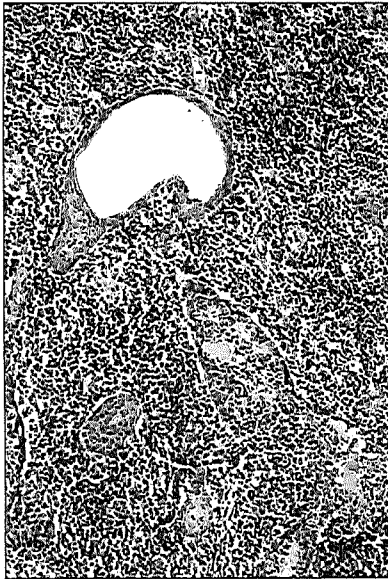


Figure 1. Region of benign lymphoepithelial lesion showing epimyoeptithelial island (right center) and cystic change in duct (top) (hematoxylin-eosin, $\times 100$).

benign lymphoepithelial lesion (BLL) (**Figure 1**) and a lymphoepithelial carcinoma (**Figure 2**). In the BLL, lymphocytes infiltrated the mucous salivary gland acini. Lymphoid follicles were randomly scattered in the BLL. Salivary gland ducts showed microcystic change and regionally formed epimyoeptithelial islands. These islands contained lymphocytes and focal, amorphous, hyaline, acidophilic deposits. The stroma of the BLL contained lymphocytes, plasma cells, and scattered immunoblasts.

Arising out of the milieu of the BLL were nests and cohesive sheets of undifferentiated carcinoma, the second component of this minor salivary gland lesion. The interface of the undifferentiated carcinoma and lymphoid stroma was sharp. At this interface, there were occasional clusters of epithelioid histiocytes. The cells that made up the carcinomatous component were undifferentiated large cells forming syncytial sheets, with inconspicuous cytoplasmic borders. The nuclei were large and vesicular and contained 1 or 2 prominent acidophilic nucleoli. Individual tumor cell necrosis and mitotic figures were identified. The cells that made up the undifferentiated carcinoma were intensely stained with the immunohistochemical stain for cytokeratin (AE1/AE3). On an

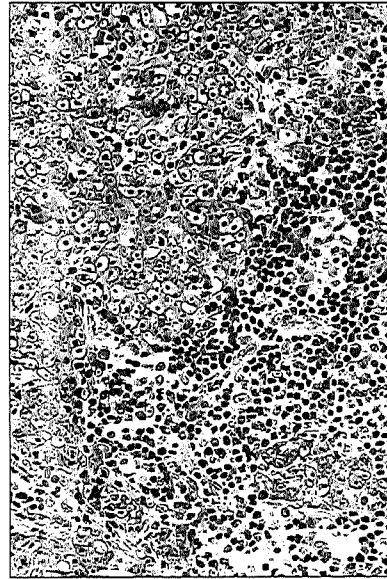


Figure 2. Undifferentiated lymphoepithelial carcinoma component of the minor salivary gland lesion (hematoxylin-eosin, $\times 100$).

immunohistochemical stain for Epstein-Barr virus antigen (LMP-1), the carcinomatous component was not stained even on repeated analysis.

The cytologic features of the metastatic carcinoma in the submandibular lymph node were identical to the carcinomatous component of the minor salivary gland lesion.

COMMENT

In their discussion of undifferentiated carcinoma of the salivary glands, Eversole et al¹ discuss 3 distinct variants of undifferentiated carcinoma: small cell carcinoma, large cell carcinoma, and lymphoepithelial carcinoma. Each variant has a distinct, identifiable, histologic pattern and can be classified accordingly. Lymphoepithelial carcinoma differs in that it exhibits features of and arises in the milieu of a BLL.

In 1952, Godwin² described in detail the histologic features of BLLs. A diffuse lymphocytic or lymphoplasmacytic infiltrate occurs in the parenchyma of the salivary gland and degeneration and atrophy of the acinar parenchyma are seen. Ductal remnants persist and epimyoeptithelial islands are infiltrated by the lymphocytic component. The epithelial component of the lesion is the origin of the malignant cells in lymphoepithelial carcinoma.² Morgan

and Castleman³ have also linked the characteristic histologic pattern seen in BLL to Sjögren syndrome and Mikulicz disease.

The incidence of undifferentiated carcinoma occurring in salivary glands varies from study to study. In the Armed Forces Institute of Pathology study¹ of more than 15 000 salivary gland tumors, only 0.4% were classified as undifferentiated carcinoma. Blanck et al⁴ noted that 4.5% of parotid malignant neoplasms were undifferentiated. In a review of 54 cases of lymphoepithelial carcinoma, Yazdi and Hogg⁵ noted that 51 occurred in the parotid glands and 3 in the submandibular glands. No cases of minor salivary gland involvement by lymphoepithelial carcinoma were noted. The ratio of parotid to submandibular involvement was 16:1 in the review of the literature.⁵ Undifferentiated carcinoma originating in the minor salivary gland has been described in isolated case reports. In these case reports,⁶⁻⁸ the undifferentiated carcinomas of minor salivary glands were classified as small cell carcinomas or large cell carcinomas or unclassified. There were no reports of lymphoepithelial carcinoma originating in the minor salivary gland to our knowledge.

Several studies¹ have examined the incidence and clinical features of lymphoepithelial carcinoma of the salivary glands. Eskimos and Asian individuals have the greatest incidence of lymphoepithelial carcinoma at a rate 15 times greater than whites of North America. The female-male ratio is approximately 2:1. The peak incidence is between the fourth and fifth decades of life at the time of diagnosis. The most common symptom is pain in the salivary gland involved, and a mass is usually palpated during the initial examination. Paralysis of the facial nerve has been reported infrequently. The parotid gland is usually involved, with rare cases of submandibular gland involvement.⁹

The differential diagnosis of lymphoepithelial carcinoma of the minor salivary glands includes mucoepidermoid carcinoma, squamous cell carcinoma, large cell carcinoma, and small cell carcinoma. The patient described herein had the

classic histologic pattern of lymphoepithelial carcinoma as described by Eversole et al,¹ which developed in a minor salivary gland. There was no mucinous or squamous differentiation in the carcinoma. An associated BLL was present, and the features of small cell carcinoma were absent. Therefore, the case reported herein fulfills the criteria for a lymphoepithelial carcinoma developing in a minor salivary gland.

Povah et al¹⁰ further classified lymphoepithelial carcinoma into low-grade and high-grade tumors. The classification is based on cellular pleomorphism, mitotic activity, and the degree of lymphocytic infiltration. Patients with high-grade lymphoepithelial carcinoma have a greater incidence of local recurrence, distant metastasis, and poorer survival. The regional nodal metastases consist of undifferentiated carcinoma. The stromal lymphocytic component seen at the primary site is not easily discerned in nodal parenchyma. The 2-year survival rate is approximately less than 10% for patients with high-grade lesions.¹⁰ In a review of the literature, Bosch et al¹¹ found an incidence of regional nodal metastases in 41.3% of the patients with lymphoepithelial carcinoma of a major salivary gland.

Distant metastases to the lung and lumbar spine have been reported.¹¹ Eskimos have a 30% to 50% incidence of regional metastases, while Asian patients have a 10% incidence of regional metastases. The 5-year survival rate for all stages and grades of lymphoepithelial carcinoma was 66% in the results of the study by Bosch et al.

Postoperative radiotherapy was administered to the patient described herein, since undifferentiated carcinoma of the salivary glands can have a propensity for further metastasis and local recurrence. Previous reports⁴ indicate that the lesions are radiosensitive.

In conclusion, lymphoepithelial carcinoma is a variant of undifferentiated carcinoma that has rarely been reported in studies of major salivary glands. To our knowledge, we describe the first reported case of a lymphoepithelial carcinoma developing in a minor salivary gland of the oral cavity.

Accepted for publication December 9, 1996.

Reprints: N. Knight Worley, MD, 3525 Prytania St, Suite 606, New Orleans, LA 70115.

REFERENCES

1. Eversole LR, Gnepp DR, Eversole GM. Undifferentiated carcinoma. In: Ellis GL, Auclair PL, Gnepp DR, eds. *Surgical Pathology of the Salivary Glands*. Philadelphia, Pa: WB Saunders Co; 1991;25:422-440.
2. Godwin JT. Benign lymphoepithelial lesion of the parotid gland. *Cancer*. 1952;5:1089-1103.
3. Morgan WS, Castleman B. A clinico-pathologic study of 'Mikulicz's disease.' *Am J Pathol*. 1953; 29:471-489.
4. Blanck C, Backstrom A, Eberoth CM, Jakobsson PA. Poorly differentiated solid parotid carcinoma. *Acta Radiol*. 1974;13:17-31.
5. Yazdi HM, Hogg GR. Malignant lymphoepithelial lesion of the submandibular salivary gland. *Am J Clin Pathol*. 1984;82:344-348.
6. Ishii T, Tanaka T, Koizumi M, et al. A case of undifferentiated carcinoma arising in the mandible. *J Nihon Univ Sch Dent*. 1990;32:93-98.
7. Hayashi Y, Nagamine S, Yanagawa T, et al. Small cell undifferentiated carcinoma of the minor salivary gland containing exocrine, neuroendocrine, and squamous cells. *Cancer*. 1987;60: 1583-1588.
8. Koss LC, Spiro RH, Hajdu S. Small cell carcinoma of minor salivary gland origin. *Cancer*. 1972; 30:737-741.
9. Seifert G, Donath K. Classification of the pathohistology of disease of the salivary glands: a review of 2600 cases in the salivary gland registry. *Beitr Pathol*. 1976;159:1-32.
10. Povah WB, Beecroft W, Hodson I, Yazdi H. Malignant lymphoepithelial lesion: the Manitoba experience. *J Otolaryngol*. 1984;113:153-159.
11. Bosch JD, Kudryk WH, Johnson GH. The malignant lymphoepithelial lesion of the salivary glands. *J Otolaryngol*. 1988;17:187-190.