Squamous Cell Carcinoma of Parotid Gland Associated with Concurrent Lymphoepithelial Cysts and Lymphoepithelial Lesion: Case Report and Proposed Histogenesis

Jane H. Zhou · F. Christopher Holsinger

Received: 28 June 2014 / Accepted: 27 September 2014 / Published online: 5 October 2014
© Springer Science+Business Media New York 2014

Abstract Lymphoepithelial cyst and lymphoepithelial lesion have similar histologic features and an affinity for the parotid gland. Though considered as different entities, both conditions arise from heterotopic salivary epithelial rests or inclusions in intra- or peri-parotid lymph nodes. We present a case of squamous cell carcinoma of parotid gland associated with concurrent lymphoepithelial cyst and lymphoepithelial lesion in a patient who was not infected with human immunodeficiency virus. We propose that lymphoepithelial cyst and lymphoepithelial lesion have a similar histogenesis.

Keywords Lymphoepithelial cyst · Lymphoepithelial lesion · Histogenesis

Introduction

Lymphoepithelial cyst, a rare benign lesion of the parotid gland, is most commonly reported in patients infected with human immunodeficiency virus (HIV) [1]. Lymphoepithelial lesion, another rare lesion of the parotid gland, is

frequently associated with Sjögren's syndrome and other autoimmune connective tissue disorders [2]. Both lymphoepithelial cyst and lymphoepithelial lesion are histologically characterized by an epithelial and a lymphoid component. Both entities are believed to originate from heterotopic salivary epithelial rests or inclusions in either intra- or peri-parotid lymphoid tissue [3, 4]. Although malignant transformation of lymphoepithelial lesion in the parotid glands into lymphoma [5, 6], or into carcinoma has been well documented [7, 8], squamous cell carcinoma of parotid gland associated with concurrent lymphoepithelial cyst and lymphoepithelial lesion has not been described. Herein, we report such a case, and discuss the histogenesis.

Case Report

A 58-year-old otherwise healthy American-Indian woman presented with a mass in the left upper neck. Physical examination revealed a well-defined but hypomobile cystic mass without tenderness in the left parotid. The patient had intact bilateral facial nerve function. Computed tomography of the neck revealed a 4.6-cm multilocular cystic mass with a solid component (Fig. 1). Fine needle aspiration biopsy revealed atypical squamous cells, benign lymphoid cells, and cystic fluid. The patient had no history of skin cancer in the head and neck region or any other head and neck cancers. Detailed clinical and radiological examination ruled out the possibility of a nasopharyngeal carcinoma, and she was not infected with HIV. The patient underwent left superficial parotidectomy.

A well-encapsulated cystic mass with a rim of solid area measuring 5.0 cm in greatest dimension was in the resection specimen. Microscopic examination revealed a large cystic space (Fig. 2) lined largely by stratified or attenuated

J. H. Zhou
Department of Pathology, The University of Texas MD
Anderson Cancer Center, 1515 Holcombe Blvd., Houston,
TX 77030, USA

J. H. Zhou (✉)
Human Genome Sequencing Center, Baylor College of
Medicine, One Baylor Plaza, Houston, TX 77030, USA
e-mail: jhzhou211@gmail.com

F. Christopher Holsinger
Department of Otolaryngology-Head and Neck Surgery,
Stanford University School of Medicine, 875 Blake Wilbur Dr.,
Stanford, CA 95305, USA

Fig. 1 High-resolution computed tomography revealed a multilocular cystic mass with a solid component

Fig. 2 Shows a large cystic space with squamous cell carcinoma in the wall. The lining squamous cells show dysplastic changes in transition to squamous cell carcinoma

squamous cells (Fig. 3), and islands of basoloid squamous carcinoma cells in lymphoid stroma (Fig. 4). Focally cuboidal cells were seen lining the cyst (Fig. 5). We also observed focal dysplastic changes of the squamous epithelium in transition to the squamous carcinoma cells (Fig. 2). Foci of benign lymphoepithelial lesion were within the remaining parotid tissue (Fig. 6). Squamous cell carcinoma is adjacent to the lymphoepithelial cysts (Fig. 7). The lymphocytes are small resembling a normal lymph node. Histological features of a lymphoma are not present.

Fig. 3 Shows the squamous cells in the cyst lining with dysplastic nuclear features

Fig. 4 Shows islands of squamous cell carcinoma with necrosis in lymphoid stroma

The squamous carcinoma cells stained positive for p63, epidermal growth factor receptor, BCL-2, and negative for p16 by immunohistochemistry. Both the carcinoma and the benign lymphoepithelial components were negative for human papilloma virus and Epstein–Barr virus by in situ hybridization.

Discussion

We present a case of squamous cell carcinoma of parotid gland associated with concurrent lymphoepithelial cyst and lymphoepithelial lesion in a patient who was not infected with HIV. In light of the rarity of primary squamous cell carcinoma of parotid gland, other more common carcinomas or mimics that can occur in parotid gland need to be

Fig. 5 Shows the cuboidal cells in the cyst lining

Fig. 6 Shows benign lymphoepithelial lesion

ruled out. We also discuss the histogenesis of lymphoepithelial cyst and lymphoepithelial lesion.

Differential Diagnosis

The differential diagnosis in this case includes metastatic squamous cell carcinoma from the skin or scalp and the nasopharynx, necrotizing sialometaplasia, mucoepidermoid carcinoma, salivary duct carcinoma, Warthin tumor, and keratocystoma.

The most common squamous cell carcinoma in parotid gland is metastatic squamous cell carcinoma from the skin or the scalp above parotid gland, the orbital region, nose, and external auditory canal. The patient in our case did not have any skin lesion in the head and neck region, neither any lesion in the nasopharynx upon detailed clinical and radiological examination.

Fig. 7 Shows squamous cell carcinoma adjacent to lymphoepithelial cysts

Distinguishing squamous cell carcinoma from necrotizing sialometaplasia can be difficult. In necrotizing sialometaplasia, the lobular architecture of the gland is preserved. The metaplastic squamous cells replace the acinar cells but maintain the configuration of acini, the cytologic atypia is reactive in nature, and the lymphoid infiltrate is inflammatory accompanied by granulation tissue. In our case, the lobular architecture is not present, the squamous cells are in large islands with basoloid appearance, and the lymphoid component is much more pronounced resembling a lymph node.

In this case, the lymphoepithelial cyst needs to be differentiated from low-grade mucoepidermoid carcinoma, and the squamous cell carcinoma from high-grade mucoepidermoid carcinoma. Low-grade mucoepidermoid carcinoma is usually cystic lined by mucous cells; a prominent lymphoid component resembling a lymph node is not a usual feature. We did not see any mucous cells either in the cystic or the carcinoma component in our case. High-grade mucoepidermoid carcinoma can show nests of squamous cells, but close examination reveals a more prominent population of intermediate cells, and keratinization is rare. The intermediate cells are not usually as hyperchromatic as in basoloid squamous cell carcinoma. In our case, we see basoloid squamous cells with necrosis. There is focal keratinization. We did not see any intermediate cells or mucous cells.

Salivary duct carcinoma can have an squamoid appearance. However, salivary duct carcinoma usually shows sheets of malignant epithelial cells resembling ductal carcinoma of the breast. There may be lymphoid infiltrate, but a prominent lymphoid component resembling a lymph node is not usually the feature.

Warthin tumor, characterized by both an epithelial and a lymphoid component, can rarely give rise to squamous cell

carcinoma. However, some residual Warthin tumor should be present. Our case can be easily distinguished from a Warthin tumor by the lack of double-layered oncocytic epithelium.

The extremely rare entity, keratocystoma, should also be excluded. Keratocystoma is a benign cystic lesion of the parotid gland, characterized by cystic spaces lined by stratified squamous cells and filled with lamellated squames. Cytologic atypia, necrosis, or invasion should be absent. Although in our case we see focal cystic spaces lined by bland squamous cells and filled with lamellated squames, the presence of malignant squamous cell carcinoma with necrosis in its close vicinity argues against such a diagnosis.

Proposed Histogenesis

Although lymphoepithelial cyst and lymphoepithelial lesion have been described since the late 1800 and early 1900 [2, 9], the histogenesis of both entities is still not well elucidated. The similarity of the histology of these two entities and their shared affinity for the parotid gland raise the possibility that they are different manifestations of the same lesion. Bernier et al. [3] indicated that cyst could form in the diffuse type of benign lymphoepithelial lesion, although they considered that this cyst was different from lymphoepithelial cyst. However, they did not give much explanation for such a conclusion even though both conditions were thought to be reactive in nature. Kojima et al. [10] reported three cases of lymphoepithelial cyst with lymphoepithelial lesion-like features in HIV-negative patients, suggesting that the two conditions may have a similar histogenesis in this patient population. The findings in our case lend support for this notion. Wu et al. [11] studied 64 cases of lymphoepithelial cyst in HIV-negative patients and noted dysplastic changes in the squamous epithelial lining in two cases of their series. We also noticed that some of the squamous cells lining the cyst exhibit dysplastic changes in our case. These findings suggest that lymphoepithelial cyst may be capable of malignant transformation, although we cannot definitively determine that the squamous cell carcinoma arose from the lymphoepithelial cyst in our case. We propose that epithelial rests or inclusions within the parotid lymphoid tissue, under certain antigenic or mechanic stimuli, may

develop into lymphoepithelial cyst, or undergo squamous metaplasia to become lymphoepithelial lesion, and are capable of malignant transformation. Both entities may share a common histogenesis. Whether these two entities are the same disease with different manifestations need further study.

Acknowledgments We thank Dr. Adel El-Naggar for providing Figure 2. JHZ is supported by NIH Grant T32CA163185.

References

1. Uccini S, D'Offizi G, Angelici A, Prozzo A, Riva E, Antonelli G, et al. Cystic lymphoepithelial lesions of the parotid gland in HIV-1 infection. *AIDS Patient Care STDS*. 2000;14(3):143–7. doi:[10.1089/108729100317920](https://doi.org/10.1089/108729100317920).
2. Godwin JT. Benign lymphoepithelial lesion of the parotid gland adenolymphoma, chronic inflammation, lymphoepithelioma, lymphocytic tumor, mikulicz disease. *Cancer*. 1952;5(6):1089–103.
3. Bernier JL, Bhaskar SN. Lymphoepithelial lesions of salivary glands; histogenesis and classification based on 186 cases. *Cancer*. 1958;11(6):1156–79.
4. Fujibayashi T, Itoh H. Lymphoepithelial (so-called branchial) cyst within the parotid gland. Report of a case and review of the literature. *Int J Oral Surg*. 1981;10(4):283–92.
5. Azzopardi JG, Evans DJ. Malignant lymphoma of parotid associated with mikulicz disease (benign lymphoepithelial lesion). *J Clin Pathol*. 1971;24(8):744–52.
6. Sato K. Malignant lymphoma in the head and neck associated with benign lymphoepithelial lesion of the parotid gland. *Auris Nasus Larynx*. 2002;29:209–14.
7. Gravanis MB, Giansanti JS. Malignant histopathologic counterpart of the benign lymphoepithelial lesion. *Cancer*. 1970;26(6):1332–42.
8. Hilderman WC, Gordon JS, Large HL Jr, Carroll CF Jr. Malignant lymphoepithelial lesion with carcinomatous component apparently arising in parotid gland. A malignant counterpart of benign lymphoepithelial lesion? *Cancer*. 1962;15:606–10.
9. Camilleri AC, Lloyd RE. Lymphoepithelial cyst of the parotid gland. *Br J Oral Maxillofac Surg*. 1990;28(5):329–32.
10. Kojima M, Nakamura N, Matsuda H, Kaba S, Itoh H, Masawa N. HIV-unrelated benign lymphoepithelial cyst of the parotid glands containing lymphoepithelial lesion—like structures: a report of 3 cases. *Int J Surg Pathol*. 2009;17(6):421–5. doi:[10.1177/1066896908328575](https://doi.org/10.1177/1066896908328575).
11. Wu L, Cheng J, Maruyama S, Yamazaki M, Tsuneki M, Lu Y, et al. Lymphoepithelial cyst of the parotid gland: its possible histopathogenesis based on clinicopathologic analysis of 64 cases. *Hum Pathol*. 2009;40(5):683–92. doi:[10.1016/j.humpath.2008.10.012](https://doi.org/10.1016/j.humpath.2008.10.012).