Lymphoepithelial Carcinoma of the Submandibular Gland
- A Case Report -

A case of lymphoepithelial carcinoma occurring in the left submandibular salivary gland is presented. Histologic features of this rare malignancy are described in detail. This unusual carcinoma has been described frequently in Eskimos and is usually located in the parotid gland. The raised serum IgG to Epstein-Barr virus capsid antigen suggests a causal relationship between Epstein-Barr virus and this type of salivary gland carcinoma. *(JKMS 1997; 12: 252~5)*

Key Words : *Lymphoepithelial carcinoma, Malignant lymphoepithelial lesion, Submandibular gland*

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Received : January 6, 1997
Accepted : February 22, 1997

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INTRODUCTION

Lymphoepithelial carcinoma is an unusual squamous cell neoplasm predominantly occurring in upper aerodigestive tracts, and consistently associated with Epstein-Barr virus (EBV) (1). Lymphoepithelial carcinoma arising in salivary glands is very rare and it predominantly occurs in the parotid gland with striking geographic and ethnic distribution (2). We report a case of lymphoepithelial carcinoma occurring in the submandibular gland in a 16-year-old female patient with evidence of EBV infection.

CASE REPORT

A 16-year-old girl was admitted with a painless, gradually enlarging mass in the left submandibular region for six months. Her past history was not contributory. Physical examination disclosed a 3.0×2.5 cm, hard, mobile mass in the left submandibular region, attached with multiple palpable cervical lymph nodes. Under the impression of tuberculous lymphadenitis, fine-needle aspiration cytology was carried out. Cytologic smear showed intermingling of sparse atypical epithelial cells and some lymphocytes. Lymph node biopsy revealed metastatic undifferentiated carcinoma, and we evaluated the nasopharynx, larnyx, and lungs to find out the primary tumor. However, examination failed to reveal any abnormality in those organs. Serum IgG antibody to Epstein-Barr virus capsid antigen was found to be positive. Excision of the left submandibular gland and radical neck dissection were performed. The resected gland contained a gray-yellow and firm mass with a lobulated cut surface, which measured 2.8×2.5 cm in diameters (Fig. 1).

Histopathology of the tumor revealed a malignant lymphoepithelial lesion characterized by intermingling of nests or cords of undifferentiated carcinoma with abundant lymphoid stroma (Fig. 2). The tumor nests consisted of syncytial sheets composed of polygonal or spindle cells.

Fig. 1. Cut surface of the left submandibular gland tumor showed a yellowish-gray, firm and lobulated tumor mass.

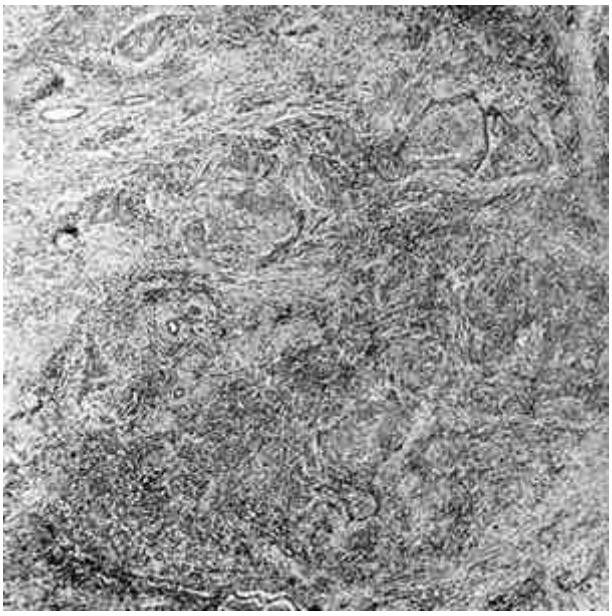

Fig. 2. A low power view of the malignant lymphoepithelial lesion showing intermingling of nests or cords of carcinoma with abundant lymphoid stroma (Hematoxylin-eosin stain, ×20).

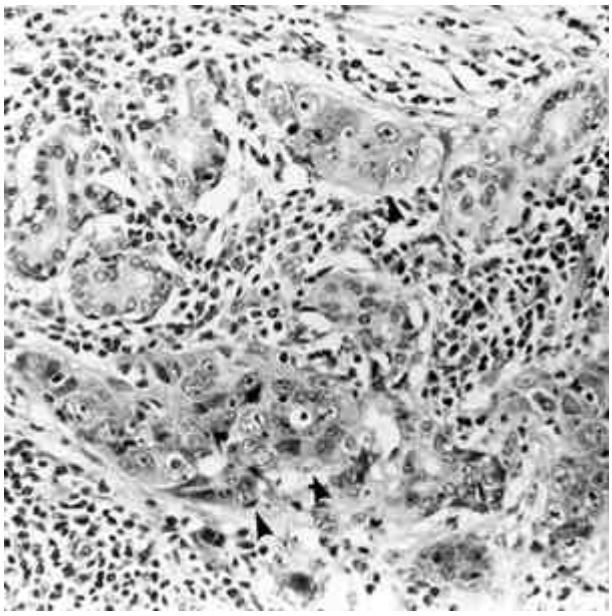

Fig. 3. The malignant epithelial components arising from ductal epithelial cells (arrow heads). The stroma was composed mainly of lymphocytes and plasma cells (Hematoxylin-eosin stain, × 200).

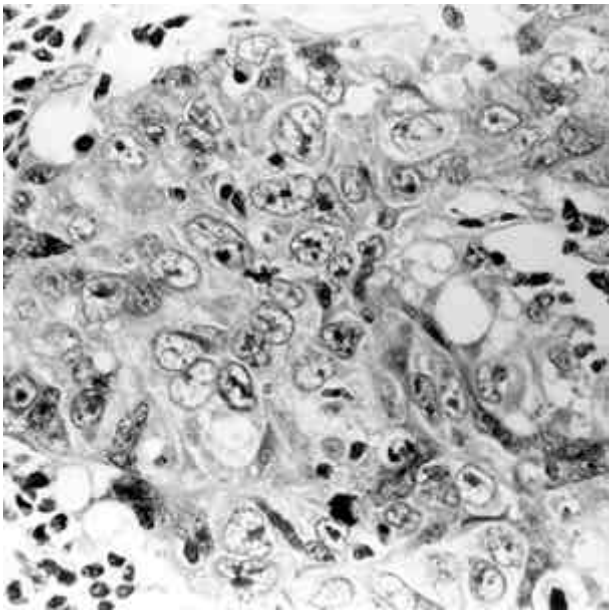

Fig. 4. The tumor showed nests of syncytial pattern. The tumor cells are arranged in nests of syncytial pattern, and have large pleomorphic nuclei with prominent nucleoli (Hematoxylin-eosin stain, ×400).

There was no evidence of keratinization or luminal formation. The lymphoid stroma was composed of a polymorphic mixture of T and B-lymphocytes, and a few plasma cells (Fig. 3). Tumor cells are made up of large, pleomorphic, and vesicular nuclei with prominent eosinophilic nucleoli (Fig. 4). The residual salivary gland lobules showed atrophy with fibrosis and lymphocytic infiltrates. There were no epimyoepithelial islands, seen in benign lymphoepithelial lesion. The cervical lymph node showed a tumor metastasis with the same histologic features that mentioned above in the salivary tumor. There was no evidence of recurrence during the ten-month follow-up.

DISCUSSION

Lymphoepithelial carcinoma or malignant lymphoepithelial lesion of the salivary gland is a rare neoplasm, predominantly occurring in the parotid gland with striking geographic and ethnic distribution (3~6). In 1952, Godwin introduced the term 'benign lymphoepithelial lesion' to designate several cases reported in the literature with different names but showing a similar histologic feature, that is, the presence of epithelial and lymphoid elements in variable proportions (7). In 1962, Hilderman et al. described an epithelial malignancy of the parotid gland that to some degree emulated benign lymphoepithelial lesion (2). Since this initial report, the malignant lymphoepithelial lesion has become recognized as a distinct entity with well-defined histopathologic features. But the term malignant lymphoepithelial lesion

is obfuscatory, since it does not imply which cell type, lymphoid or epithelial, is malignant. Electron microscopic study carried out by Kott et al. confirmed the squamous epithelial origin of the neoplastic cells (4). Therefore, Eversole et al. prefer the term lymphoepithelial carcinoma to clarify that the epithelial component is malignant (3). Immunostaining for cytokeratin may prove helpful for confirming the epithelial nature of the tumor in difficult cases (5). The significance of lymphoid infiltrates is poorly understood, but there is evidence of interaction between these two constituent cells-each cell population appears to produce factors that support the growth of the other (1).

There have been over 100 cases of lymphoepithelial carcinoma reported in the world literature (3). The vast majority have occurred among North American and Greenland Eskimos, and Asian Orientals. Clinically, the overall female to male ratio is slightly less than 2 to 1. The tumor developed at a younger age than the other salivary gland malignancies. The mean age is 44 years for males and 36 years for females. Cancer development at unusual young age was also reported (8). The parotid gland is involved in over 90% of Eskimo and White patients with lymphoepithelial carcinoma, whereas a submandibular localization is rare. The ratio of the parotid gland to submandibular gland in accumulated cases of lymphoepithelial carcinoma is 17 : 1 (6). Submandibular localization is more frequent in Oriental patients and encountered among one third to one half of the patients.

Most tumors measure less than 5 cm in maximum diameter (5). Gross features of these tumors have been variably described as grossly encapsulated, partially circumscribed, multinodular, and infiltrative. The cut surface varies from gray-tan to yellow-gray. Zonal necrosis and hemorrhage are not typical features. Histologically, lymphoepithelial carcinomas consist of islands of syncytial epithelial cells with pleomorphic vesicular nuclei and prominent eosinophilic nucleoli, intermingled with numerous lymphocytes and plasma cells (3, 5).

Of major significance in the cases of lymphoepithelial carcinoma is the issue regarding any relationship with preexisting benign lymphoepithelial lesion or any association with Sjögren's syndrome (3). The classic histopathologic feature of the benign lymphoepithelial lesion is composed of acinar atrophy, lymphocytic sialadenitis and ductal epithelial hyperplasia and metaplasia leading to the formation of epimyoepithelial cell islands. Many authors have implied that lymphoepithelial carcinoma arises from the epithelial component of a preexisting benign lymphoepithelial lesion (9~11). No association with Sjögren's syndrome has been found, and none of the affected patients have presented with any of the stigmata characteristic for the syndrome (12, 13).

Recent studies showed that EBV is consistently associated with a high proportion (80~90%) of lymphoepithelioma-like carcinomas from the stomach, salivary gland, lung, and thymus. EBV expression is generally restricted to Asian patients with lymphoepithelial carcinoma of the lung and salivary glands. Whereas it is independent of race in stomach and thymic lymphoepithelial carcinoma (14). To date, the presence or absence of EBV in lymphoepithelial carcinoma does not appear to be of prognostic significance (1). The nasopharynx, salivary gland, and thymus are all derived from the primitive pharynx, and lymphoepithelial carcinomas occurring in these sites, all possibly related to Epstein-Barr virus, are histologically indistinguishable (5). Although the presence of benign lymphoepithelial lesion adjacent to the tumor is a helpful finding, the distinction between primary lymphoepithelial carcinoma and metastatic nasopharyngeal carcinoma in a salivary gland is difficult and depends on careful clinical evaluation. Multiple-site biopsies of the upper aerodigestive tract are mandatory to rule out nasopharyngeal carcinoma.

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