CASE REPORT

Ultrastructural evaluation of intraductal papilloma: report of a case

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Summary
Intraductal papilloma is an extremely rare benign salivary gland tumor. The tumor was evaluated by electromicroscope. There were numerous secretary granules that were located predominantly in the luminal portion of the cells. Rough endoplasmic reticulum, many golgi apparatus and mitochondria in the cytoplasm were thought to reveal active production of secretary granules. A specific ultrastructure known as annulate lamellae was found in the cytoplasm of the tumor epithelial cells. This structure is believed to relate to cell proliferation and is important for consideration of tumorigenesis of intraductal papilloma.

KEYWORDS
Intraductal papilloma; Salivary gland tumor; Minor salivary gland; Ultrastructure

Introduction
Intraductal papilloma, that Abbey \textsuperscript{1} primarily reported, is one of monomorphic adenoma and is an extremely rare benign tumor, which commonly arises from minor salivary glands. In previous reports, intraductal papilloma was found in small tumor form, making it usually impossible to evaluate by electromicroscope.

We report here a patient with an intraductal papilloma of the upper labial minor salivary gland, and describe interesting findings of the ultrastructure of intraductal papilloma.

Case report
A 65 year old man was referred to the Oral and Maxillofacial Surgery of Shimane Medical University Hospital with a several-year history of a slowly growing painless tumor at the upper lip. On physical examination, a smooth elastic soft swelling measuring approximately 22 × 15 mm was noted in the area of right side of upper lip. The lesion was totally excised under local anesthesia.

The structure of the tumor showed papillary proliferation of tumor epithelial cells with numerous intricately branching fronds into a cystically dilated duct lumen. The tumor epithelia was predominantly composed of single-layered cuboidal cells. Mitoses were virtually absent. Thus, histological examination revealed the typical characteristics of intraductal papilloma (Fig. 1).
For ultrastructural examination, tumor tissues obtained from operation were immediately fixed in 2.5% glutaraldehyde and 2.0% paraformaldehyde in 0.1 M phosphate buffer (pH 7.2) and washed in 0.1 M phosphate buffer, and then underwent post fixation with 1% osmium tetroxide. After dehydration in a graded series of ethyl alcohol, the specimens were embedded in epon 812. 70 nm sections of the specimens were stained with uranyl acetate–lead citrate, followed by electron microscopic observation. There were many microvilli on the luminal surfaces, numerous secretary granules located in the luminal sides of the tumor cells, rough endoplasmic reticulum, many golgi apparatus and mitochondria (Fig. 2A and B). We also detected structures termed annulate lamellae which form intracytoplasmic membrane system composed of parallel arrays of cisternae bearing at regular intervals small annuli or fenestrae (Fig. 2C).

**Figure 1** Histopathologic appearance of tumor. Microscopic examination shows papillary proliferation of tumor epithelial cells with numerous intricately branching fronds into a cystically dilated duct lumen. The tumor epithelia was predominantly composed of single-layered cuboidal cells (hematoxylin-eosin, A × 40, B × 200).

**Figure 2** Electron microscopic findings. (A) There are many organelle including of secretary granules, rough endoplasmic reticulum, many golgi apparatus and mitochondria. (B) Microvilli on the luminal surface of the epithelia cells seem to have high secretory ability. (C) Annulate lamellae composed of parallel arrays of cisternae bearing at regular intervals small annuli or fenestrae.
Discussion

Histologically, intraductal papilloma, an extremely rare salivary gland tumor is a luminal papillary proliferation characterized by numerous intricately branching fronds. Based on microscopic examination, the tumor appeared to arise from within one of the main excretory ducts, as was described in previous reports. Such prior reports, however, were not based on immunohistochemical and or electromicroscopical observation of the tumor. Ishikawa et al. described an epithelial origin from the excretory salivary gland ducts and the secretory potential of the tumor cells, based on immunohistochemical results. Nagao et al. reported two cases of intraductal papilloma of the major salivary gland and the potential of malignant transformation of the tumor.

Discussion of the ultrastructure of intraductal papilloma was found in only one previous report. This prior report noted that the tumor epithelia was composed of single-layered, double-layered or multi-layered columnar or cuboidal epithelial cells. Luminal cells were usually covered with slender microvilli or apical protrusions characteristic of apocrine differentiation. Beneath these structures, there usually were numerous secretory granules located predominantly in the apical portion of the cells. In our present case, the tumor epithelia was composed of single-layered cuboidal epithelial cells and many microvilli on the luminal surface of the epithelia cells seemed to demonstrate the high secretory potential. Rough endoplasmic reticulum, many golgi apparatus and mitochondria in cytoplasm were also thought to reveal active production of secretory granules. In addition to these findings, which lend support to an active secretory ability of the tumor, we found structures termed annulate lamellae in the cytoplasm of the epithelial cells. Embryonic cells and some types of tumor cells have frequently been documented intracytoplasmic annulate lamellae and this organelle has been seen in a few human neoplasms such as solid and cystic acinar cell tumors of the pancreas, adenoid cystic carcinoma and clear cell odontogenic tumor. In solid and cystic acinar cell tumors of the pancreas, electron microscopic findings, which the tumor cells had numerous mitochondria, zymogen-like granules, and annulate lamellae were considered showing acinar cell differentiation.

Hara et al. also suggested that intraductal papilloma tumor cells appear to have a tendency toward acinar differentiation, based on immunohistochemical and electron microscopic observations.

From these significant findings, it may be necessary to reevaluate our thinking about the tumorigenesis of intraductal papilloma.

References