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EDITORIAL

Pleomorphic Adenoma with Extensive Squamous and Adipocytic Metaplasia Mimicking as Low Grade Mucoepidermoid Carcinoma on FNAC

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Abstract Pleomorphic adenoma (PA) is the most common salivary gland tumor, accounting for 54–76% of all salivary gland neoplasms. Extensive squamous metaplasia in PA can be mistaken for malignancy, including low grade mucoepidermoid carcinoma and squamous cell carcinoma. Here, we present an unusual case of PA with extensive squamous metaplasia and keratin cyst formations in a minor salivary gland, and discuss its microscopic features, including the immunohistochemical characteristics, and differential diagnosis of this uncommon presentation.

Keywords Pleomorphic adenoma · Squamous metaplasia · Low grade mucoepidermoid carcinoma · Keratin cysts

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Introduction

Pleomorphic adenoma (PA) is the most common benign salivary gland tumor, accounting for 54–76% of all salivary neoplasms [1]. The parotid gland is the most common site of PA [1]. Approximately 8% of PA involve the minor salivary glands, whereas palate is the most common site, accounting for 60–65% of cases. The incidence of pleomorphic adenoma in intraoral minor salivary glands is 40–50% [2, 3].

Pleomorphic adenoma (PA) affecting minor salivary glands presents with a female predilection. It occurs over a wide age range, but the mean age is 43.6 years and the peak incidence is between fourth and fifth decades of life. Being pleomorphic, it exhibits the ability to differentiate into epithelial (ductal and nonductal) cells and mesenchyme-like tissue (chondroid, myxoid and osseous) [2]. Thus, it is composed of a mixture of glandular epithelium and myoepithelial cells within a mesenchyme-like tissue, and the proportion of each component varies widely among individual tumors [1].

The variations in epithelial and mesenchyme-like components with or without dysplasia add to this dilemma. The present case-study dealt with a PA of the palate with an extensive squamous and adipocytic metaplasia with giant keratotic lamellae in cyst-like areas.

Case Report

The index case is a 39 years old female who referred to fine needle aspiration cytology (FNA) clinic from ear, nose and throat (ENT) department presenting with chief complaints of soft tissue mass in centre of hard palate since 6–8 years. Swelling was gradually progressive in nature, not

associated with any pain or discharge. There were no complaints of difficulty in swallowing or breathing. On examination, swelling was firm, non-mobile, non-tender measuring 1.5 × 1.5 cm in size (Fig. 1A). CECT revealed a well-defined faintly discernible enhancing lesion of size 1.5 × 1.5 cm at the junction of hard and soft palate suggestive of a benign lesion (Fig. 1B). FNA was done which revealed moderate cellularity comprising of polymorphous population of epithelial cells comprising of ductal epithelial cells, intermediate squamous cells and mucin secreting cells enmeshed in abundant mucin. Background shows giant cells, neutrophils and histiocytes (Fig. 1C–F).

Cell block was prepared which showed scant cellularity (Fig. 1G). Immunohistochemistry (IHC) was applied for EMA and S-100 which were non-contributory. This was followed by core biopsy which showed histological features of pleomorphic adenoma (Fig. 2A). Followed by core biopsy, excision biopsy was done. Grossly, single soft tissue received measuring 2.5 × 2 cm. Cut section was grayish white with areas of hemorrhage (Fig. 2B). Microscopic examination showed tissue lined by stratified squamous epithelium enclosing partially encapsulated tumor arranged in lobules. The lobules are composed of closely packed glands lined by double layer of epithelium enmeshed in chondromyxoid stroma. Abundant areas of squamous and adipocytic metaplasia were noted along with areas of cystic degeneration (Fig. 2C–E). No mitosis or necrosis was noted. Final diagnosis of Pleomorphic adenoma with squamous metaplasia and adipocytic metaplasia was made.

Discussion

PA is clinically characterized by a slow growing, sessile-based, firm painless mass. The most common site for minor salivary gland tumors is the palate. It most frequently affects the parotid gland, followed by the submandibular and the minor salivary glands. Microscopically, mucous, sebaceous, oncocytic and squamous metaplasia, sometimes with the formation of keratin pearls, may be present, but the latter are rare. This extensive squamous metaplasia and keratin brought this tumor's diagnosis close to intracapsular (in situ) PA, muco-epidermoid carcinoma, adenoid or adeno-squamous cell carcinoma, conventional squamous cell carcinoma (SCC), carcinoma ex PA, and necrotizing sialometaplasia [2].

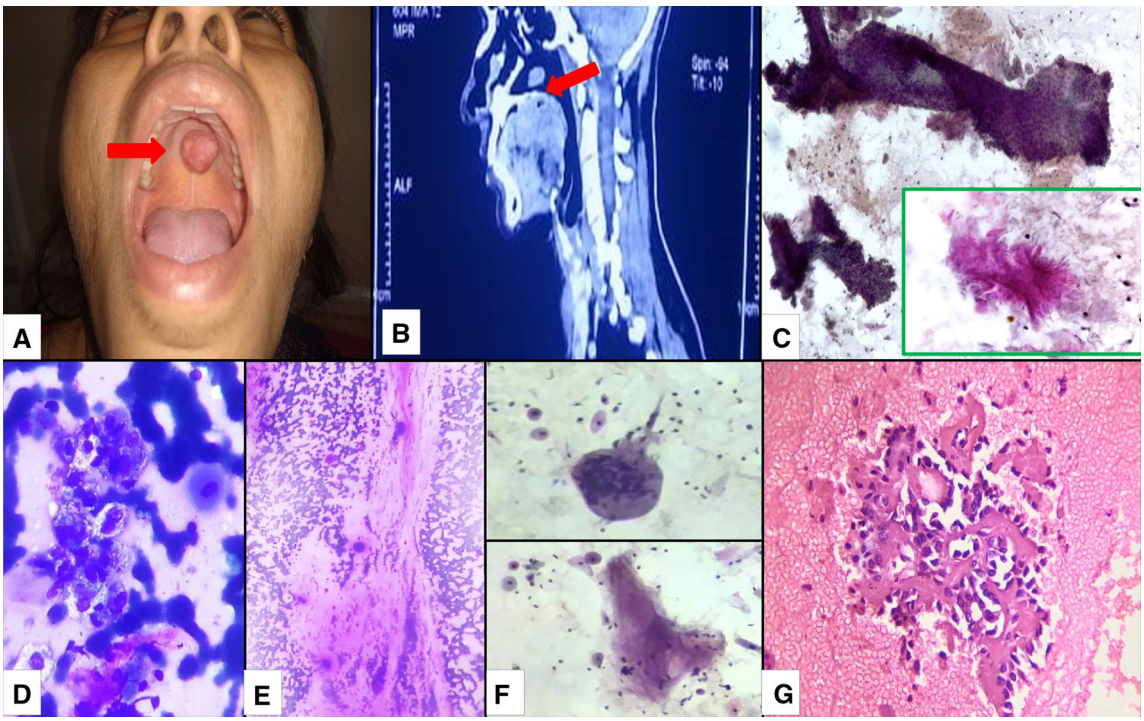

Fig. 1 **A** Depicting a mass over hard palate. **B** CECT showing well-defined faintly discernible enhancing lesion of size 1.5 × 1.5 cm at the junction of hard and soft palate suggestive of a benign lesion. **C** Fine needle aspiration showing intermediate squamous cells showing mild atypia, mild anisonucleosis and hyperchromatic nucleus and keratin flakes depicting troll hair appearance. **D**, **E** Giemsa stained smear showing muciphages and abundant mucin. **F** Showing giant cells and keratinous material. **G** Cell block preparation showing keratinous material with intermediate squamous cells

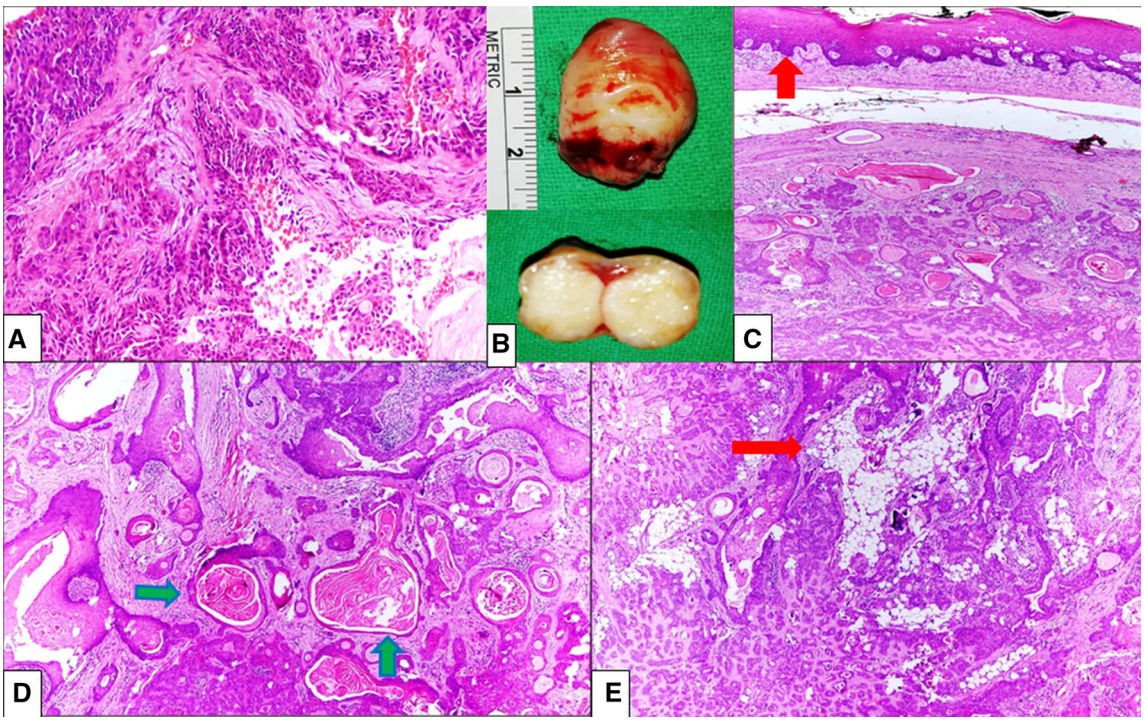

Fig. 2 **A** Core biopsy showing features of pleomorphic adenoma. **B** Gross specimen of excision biopsy showing a tumor measuring 2.5 × 2 cm. Cut surface is greyish white with areas of hemorrhage. **C** Microscopy shows tissue covered by stratified squamous epithelium enclosing tumor cells arranged in lobules. **D** These lobules were composed of closely packed glands lined by double layer of epithelium alternating with sheets of polygonal epithelial cells along with chondromyxoid stroma and keratin pearl formation. **E** H & E 40 × showing adipocytic metaplasia

Pleomorphic adenomas, particularly of minor salivary glands of palate, may contain large areas of squamous and mucinous metaplasia, arising the suspicion of mucoepidermoid carcinoma. It is usually distinguished from mucoepidermoid carcinoma by at least focal presence of characteristic ductal and myoepthelial proliferation and myxochondroid stroma [2, 4, 5]. In mucoepidermoid carcinoma, prominent keratinization and keratin pearl formation are rare. In our case, there was extensive squamous metaplasia and these cells had bland morphology. In addition, a tiny area of chondromyxoid stroma was identified. Thus, the morphological features must be carefully evaluated in order to confirm the diagnosis. The treatment of choice is wide local excision [6, 7]. The recurrence rate is around 5–30% and is associated with incomplete surgical excision. There is also a risk of malignant transformation, usually giving rise to carcinoma ex pleomorphic adenoma. A close postoperative follow-up is essential [4, 5, 8].

As per review of literature, similar case reports by Sharma et al., Brisebois et al., Lam et al., Lim et al., Goulart et al. and Takegawa et al. have been provided by various authors with or without application of immunohistochemistry (IHC) markers. One case Lam et al., Lim et al. and Goulart et al. described a 32-year-old patient with 45% of the tumor consisting of squamous cells, wherein IHC helped distinguish the squamous metaplastic cells from SCC [2, 4, 7–10].

The presence of low molecular weight cytokeratin and p63 in squamous cells helps rule out SCC or even reactive squamous hyperplasia in such PA cases [10]. Multiple IHC markers are used to ascertain differences between glandular cells or metaplastically formed squamous cells. Although no conclusive differences have been established using cytokeratin or even MIB-1 (a proliferative marker), Ki-67 as used by Goulart et al. [8] had a higher proliferative index in the epithelial lining of a large keratin cyst.

Brisebois et al. [4] have published one such case with extensive squamous metaplasia and adipocytic metaplasia. They performed immunohistochemistry with markers such as epithelial membrane antigen which was positive in the luminal cells, smooth muscle actin, and S100 highlighting the myoepithelial cells. In their case, keratin 5/6 were all positive for the entire specimen. In an article by Lim et al., the authors have opined that the pattern of cytokeratin expression can be helpful in determining squamous metaplasia. According to them, the cells that express high molecular weight cytokeratin (HMW CK) have undergone squamous metaplasia, but those expressing low molecular

weight cytokeratin (LMW CK) and p63 have not yet undergone squamous metaplasia [10].

Tonofilaments and desmosomes begin to appear in the luminal and abluminal myoepithelial cells, and thus keratinization of central cells materializes [2]. The presence of squamous metaplasia is also a prognostic pitfall, as its transition into SCC has been further emphasized by Takegawa et al. in the submandibular glands of rats by the application of potassium iodide. Takegawa et al. [7] observed the development of squamous metaplasia in proliferative ductules and interlobular ducts that apparently transited to SCC, and emphasized that this occurred via a non-genotoxic, proliferation-dependent mechanism.

In the index case till last follow up; 4 months after surgery, patient is doing well and post operative site is healthy and clean. The awareness of this entity of pleomorphic adenoma with extensive squamous metaplasia is important as it can mimic low grade mucoepidermoid carcinoma on cytology. PA with extensive squamous metaplasia poses a diagnostic challenge. Therefore, it is important to be aware of this possibility to distinguish it from malignant lesions and to avoid unnecessarily aggressive therapy.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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