CASE REPORT

Florid keratin pearls in pleomorphic adenoma - A mimicker to malignancy

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Abstract

The presence of numerous keratin pearls on microscopic study is a feature commonly seen in well-differentiated squamous cell carcinoma. Pleomorphic adenoma (PA) can show the presence of squamous metaplasia with keratin pearls as a rare finding. Here, we present a case of a male patient in the 5th decade presenting with a mass on the buccal mucosa who smokes tobacco. On microscopic study, the mass showed tumor cells presenting with extensive keratin pearl formation. In this paper, we want to highlight the rare findings of extensive keratin in PA of minor salivary glands, the significance of special stains in diagnosis and differential diagnosis of this uncommon presentation.

Keywords:
Cyst containing keratin, keratin pearls, minor salivary glands, myoepithelial cells, pleomorphic adenoma, squamous metaplasia

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Introduction

Pleomorphic adenoma (PA) involving the minor salivary glands is in the range of 38–44%. As far as minor glands are concerned the palate, upper lip and buccal mucosa are the most common sites for PA. The hallmark of PA is the histologic diversity which has mixed histology and is composed of an epithelial and a stromal/mesenchymal component. Here, we present an unusual case of PA with extensive squamous metaplasia and keratin pearl formation in a minor salivary gland with microscopic features, significance of special stain in diagnosis, and the differential diagnosis of this unusual presentation. Reports of PA presenting with multiple and large squamous epithelium-lined keratin cysts along with squamous metaplasia are sparse.

Case Report

A male patient aged 50 years presented with a slow-growing, asymptomatic left cheek swelling of 3 years duration. History revealed he smokes 4 packs/day for 30 years. On clinical examination, the findings observed were a single, well-defined swelling of size 4 cm x 4 cm firm, mobile mass in the left buccal mucosa extending anteriorly 2 cm distal to the angle of the mouth and posteriorly up to the first permanent molar region [Figure 1]. The mass was excised completely under local anesthesia. While performing the incision, care was taken to avoid injury to the parotid duct opening located on the surface of the buccal mucosa, opposite the upper second molar tooth. As the mass did not involve the facial muscles or the subcutaneous tissue of the cheek, wide local excision with satisfactory margins was performed. Clinically, it was thought to be a benign minor salivary gland tumor, based on its palpatory findings. Differential diagnosis of fibroma, lipoma, dermoid cyst, or a schwannoma was considered.

On gross examination, the mass was observed to be firm with lobulated surface and ovoid in shape. The cut section of the specimen was capsulated, cream to yellow in color with few areas of tan [Figure 2].

On histopathological examination, hematoxylin and eosin stained sections revealed a circumscribed encapsulated lesion composed of mainly epithelial component and fibrous stroma [Figure 3]. The epithelial component was seen mainly in the
form of duct-like areas containing eosinophilic lamellated structures and eosinophilic coagulum; epithelial cells were also seen in the form of nests and cords. The cystic and ductal structures were variable in size and shape and cells lining these cystic spaces showing inner row of columnar cells and outer layer of cells with hyperchromatic nuclei and clear cytoplasm, suggestive of myoepithelial cells. Areas of mucous cells that were observed in the cystic epithelial lining and the eosinophilic substance in the ductal structures were confirmed as mucin by periodic acid-Schiff (PAS) reactions. The cystic spaces of varying sizes containing eosinophilic substance which were lamellated [Figure 4] with squamous metaplasia which was confirmed by Mallory’s keratin stain as keratin pearls [Figure 5]. Stroma consisted of hyalinized eosinophilic areas, few inflammatory cells, and adipose cells intermingled with minor salivary gland acini was also seen. Based on the histopathologic findings of epithelial components, hyalinized areas and the presence of mucin and keratin which was confirmed by special stain the lesion was diagnosed as PA.

Discussion

Willis coined the term PA.\(^1\) It derives its name due to its light microscopy findings presenting with architectural pleomorphism that is variable appearance having both epithelial and connective tissue components. The WHO in 1972 defined PA as “a circumscribed tumor characterized by its pleomorphic or mixed appearance clearly recognizable epithelial tissue being intermingled with tissue of mucoid, myxoid, or chondroid appearance.”\(^2,3\)

Salivary gland neoplasms comprise <1% of all tumors, and 3–5% of all head and neck tumors. Epidemiologically, PA is the most common tumor accounting for 45–75% of all salivary gland neoplasms.\(^4\) Around 70% of these tumors occur in the parotid gland, 10% in the submandibular gland and the remainder in the minor salivary glands. Among the intraoral sites, the hard palate (42.8–68.8%) is reported to be the most commonly affected, followed by the upper lip (10.1%) and buccal mucosa (5.5%).\(^2\) Around 50% of tumors of the minor salivary gland are considered to be malignant in nature\(^5,6\) because of its unencapsulation.

PA can occur in individuals of all ages; it is commonly seen in third to sixth decades of life with the mean age between 43 and 46 years\(^4\) in accordance with our case which is shown at 50 years of age. PA occurs more frequently in women than men (2:1),\(^7\) unlike the present case which is seen in a male patient. Since this patient had smoking habit, it was more in favor of malignancy.

The exact etiology of PA is not known; however, radiation exposure (after 20 years) and simian virus (SV40) may play an important role. Genetic changes in PA gene (PLAG1) are consistently rearranged in PAs, activated by chromosomal translocations involving 8q12, the chromosome region that is most frequently affected in these tumors.\(^8\)

The tumor commonly presents as a unilateral, painless, slow-growing mass of many years duration. Few cases can present with pain and ulceration. Our case presented with a painless swelling
of 3 years duration which is in accordance with the benign tumor presentation.

Histopathologically, PA of minor salivary gland is usually unencapsulated. The epithelial components are seen forming ducts, small cysts, cellular nests, sheets of cells, anastomosing cords, and foci of keratinizing squamous or spindle cells. Myoepithelial cells appear as angular or spindled, while some cells are round with eccentric nuclei and hyalinized eosinophilic cytoplasm. Its histological patterns may vary considerably among different parts of the same tumor. Among the varied patterns, this case showed extensive squamous metaplasia with keratin pearl formation. Although the present case gave an appearance of adenexal structures, the given diagnosis was confirmed in reference to the location of the lesion and the use of special stains.

The presence of numerous keratin pearls is frequent presentation of well-differentiated squamous cell carcinoma and also may be seen in high-grade mucoepidermoid carcinoma and trichoadenoma. Keratin pearls are seen extensively in squamous cell carcinoma; however, there is the absence of cytologic atypia, invasion, and necrosis in PA. In mucoepidermoid carcinoma, there is the presence of mucus cells, epidermoid cells, and intermediate cells. Keratin pearls may be evident in high-grade mucoepidermoid carcinoma but were ruled due to the absence of epidermoid cells, intermediate cell, and dysplastic features.

Trichoadenoma is a benign tumor of the hair follicles. Microscopic study of this lesion also shows the presence of numerous keratin pearls and keratin present in cyst, but the cells lining these spaces contain keratohyaline granules and are made up of basaloid cells. This was ruled out due to the presence of myoepithelial-like cells lining the duct-like areas and absence of keratohyaline granules and basaloid cells which is not a feature of PA.

Pathogenesis of squamous metaplasia and keratin pearl formation in PA has been proposed as the dedifferentiation of the acinar cells and subsequent hyperplasia of acinar, duct luminal, and myoepithelial cells. A study conducted on the rat by ligation of the artery supplying the salivary gland parenchyma caused metaplasia of the acinar-intercalated duct cell complex and keratin formation. However, there was no history of trauma nor ischemia in our case. Keratin pearls in PA are frequently seen involving the minor salivary glands than the major glands. Hence, we suggest that the epithelium of the minor salivary gland duct exposed to various source of irritants may be responsible for the presence of keratin pearls in PA. The source of irritation was the habit of smoking in our case. However, the exact mechanism is not clear.

The importance of special stains in diagnosis of salivary gland tumors needs to be emphasized. PAS and Mallory’s keratin stains for confirmation of mucin within the ducts and keratin within the cystic spaces, respectively, have contributed to great extent in diagnosis without the necessity to undergo expensive immunohistochemical procedures.

PAs may occasionally display focal squamous metaplastic changes; when extensive, it presents the potential for misinterpretation of the histology as indicative of well-differentiated squamous cell carcinoma. Misdiagnosis can lead to overtreatment of these lesions using more aggressive surgical approach and/or radiation therapy.

Conclusion

PA presenting with numerous keratin pearls with squamous metaplasia and keratin-containing cyst along with the presence of habits in the patient can pose diagnostic dilemma. The use of special stains in histopathology can significantly solve this challenge instead of the expensive immunohistochemistry procedures. Hence, it is important to be aware of the presence of keratin pearls in PA and the need to distinguish it from malignant lesions to avoid unnecessary aggressive therapy. Although PAs arising from the minor salivary glands not uncommonly affect the cheeks, it should be considered in the differential diagnosis of cheek masses. This case was also published to add on to...
of the existing literature on histopathologic findings in PA with extensive keratin in the form of pearls and cystic contents.

References


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