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Case Report

Florid Squamous Metaplasia and Keratin Cyst Formation in Palatal Minor Salivary Gland Tumor: A Diagnostic Challenge

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ABSTRACT

Pleomorphic adenoma (PA) is a benign epithelial neoplasm of salivary glands. It is the most common salivary gland tumor which accounts for 54-65% of all salivary gland neoplasias and 80% of the benign salivary gland tumors. It mostly affects the parotid gland, followed by the submandibular gland and the minor salivary glands. Myoepithelial cell, being capable of dedifferentiation, metaplasia and transdifferentiation has a key role in the genesis of these tumors. The histopathologic picture may show squamous, mucous, and sebaceous and oncocytic metaplasia, sometimes with the formation of extensive keratin filled cysts lined by squamous epithelium. Metaplastic process is mainly triggered by trauma and probable etiology is ischemia. Extensive metaplasia can be mistaken for malignancy either mucoepidermoid carcinoma or squamous cell carcinoma. An unusual case of pleomorphic adenoma presented as a solitary intraoral palatine mass in a 62 year old male is reported here in which extensive squamous metaplasia and keratin cyst formations was evident microscopically.

Key words: pleomorphic adenoma, squamous metaplasia, keratin cyst, squamous cell carcinoma, salivary gland, palate, salivary gland tumors, myoepithelial cell

INTRODUCTION

Salivary gland tumors are the most common neoplasms of the oral cavity after squamous cell carcinoma and account for a significant proportion of tumors of the oral and perioral regions. [1] Out of all salivary gland tumors, Pleomorphic Adenoma (PA) is most common, and is also known as benign mixed tumor. It accounts for 53-77% of parotid tumors, 44-68% of submandibular tumors and 38-43% of minor salivary gland tumors [2] and presents a female predilection. [3] It occurs over a wide age range, with the peak incidence between 4th and 5th decades of life with the mean age of occurrence being 44 years. [4] It presents as a slow growing, painless, sessile and firm mass which may or may not have an ulcerated surface. [5] the most common site is palate when minor salivary glands are affected. [6]

Histological diversity is the hallmark of PA. Its histological patterns may vary considerably among different parts of the same tumor. [1] Microscopically, it shows varying combinations of epithelial and myoepithelial cells in a mesenchymal background. The duct-like formations exhibit ductal luminal cells in the inner layer and abluminal cells in the outer layer. The capsule varies in thickness and many tumors show finger-like processes projecting into the capsule. [7] The proportion between epithelial and chondromyxoid stroma vary but some metaplastic variations may also occur in the epithelial and mesenchymal components. Thus, diversity in morphology may often

cause a diagnostic problem in surgical pathology. [1] The microscopic finding of squamous metaplasia with the formation of keratin pearls may represent a diagnostic dilemma for the pathologists. [8] Squamous metaplasia can be induced experimentally in the salivary gland following arterial ligation, radiation and carcinogen exposure. [1]

Focal squamous metaplasia may be found in about 25% of the PA, whereas florid squamous metaplasia is known to occur rarely. [1] Extensive squamous metaplastic changes in PA present the potential for its misinterpretation as a squamous cell carcinoma (SCC). SCC as a collision tumor or carcinoma ex PA should be considered in the differential diagnosis. Thus, PA with exuberant squamous metaplasia and keratin filled cysts may cause diagnostic confusion that stresses the need for a guarded approach while interpreting such lesions. [1] This article presents one such case of PA with extensive squamous metaplasia and keratin cyst formation in a minor salivary gland and discusses its pathogenesis and potential diagnostic pitfalls.

CASE REPORT

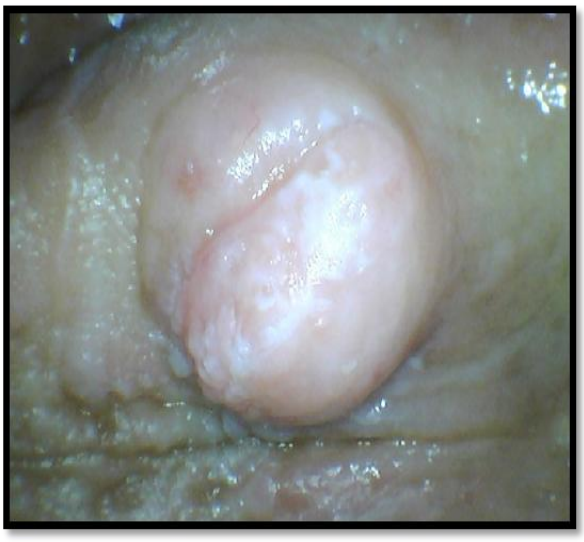

Fig. 1: Intraoral photograph showing a well defined sessile growth on the left posterolateral palate.

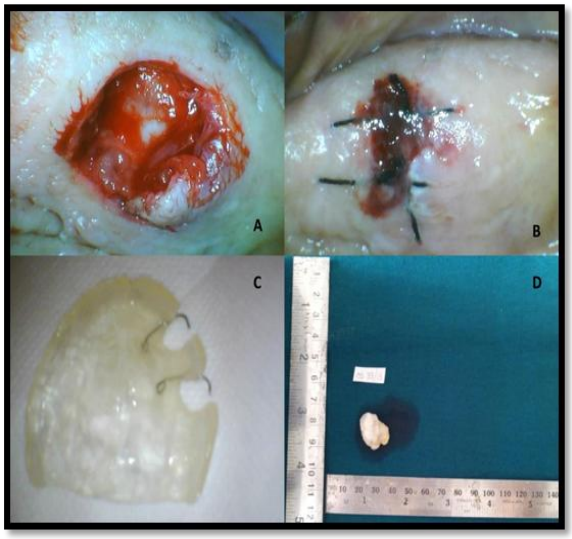

Fig. 2: Intraoral photograph showing incision (A), placement of the sutures after excision of the mass (B), prepared acrylic stent to be placed post surgically (C) and gross excised specimen (D).

A 62 year old male patient walked into the dental clinic with a desire for replacement of missing teeth. On clinical examination, a painless growth was noted on the left side of hard palate. On questioning, the patient revealed that he noticed a small growth 3 to 4 months back which gradually and progressively increased in size. There was no history of trauma and the growth was asymptomatic. The swelling was present at the left posterolateral part of the hard palate which measured approximately 2.5 x 1.5 x 0.8 cm, and the mucosa over the growth was smooth textured. (Fig. 1) It was not tender, firm in consistency, non mobile, non reducible and none emptying. There was no submandibular and cervical lymphadenopathy. FNAC findings indicated a benign salivary gland tumor. Thus, provisional diagnosis of benign tumor of minor salivary gland was given. The standard maxillary occlusal radiograph showed no bony changes or pressure effects. On hard tissue examination, 22 and 25 were present. Complete mass excision was undertaken under local anaesthesia. The surgical excision of the lesion together with the mucosal lining along with a 5 mm safety margin of the adjacent mucosa was done by making elliptical incision around the mass with enough depth to remove the lesion completely. Intermittent 3-0 silk sutures and

acrylic stent with anaesthetic gel was placed. (Fig. 2 A, B, C) Patient was instructed about the usage of the stent. The excised mass was sent for histopathological examination. The excised specimen was creamish brown in colour, roughly circular in shape measuring about 1.8 x 1.7 x 0.8 cm and firm in consistency. (Fig. 2 D) Hematoxylin and eosin stained sections revealed orthokeratinized epithelium with underlying connective tissue stroma consisting of tumor cells arranged in nests, cords and ductal pattern. Individual tumor cells were polyhedral to stellate shaped with eosinophilic cytoplasm. The stroma also showed prominent thick fibrous bands separating extensive squamous metaplasia, areas of keratin pearl formation and cystic degeneration. Areas of mucin pooling and hyalinization were evident. Focal areas of lymphocytic infiltration and blood vessels are also seen. (Fig. 3 & 4)

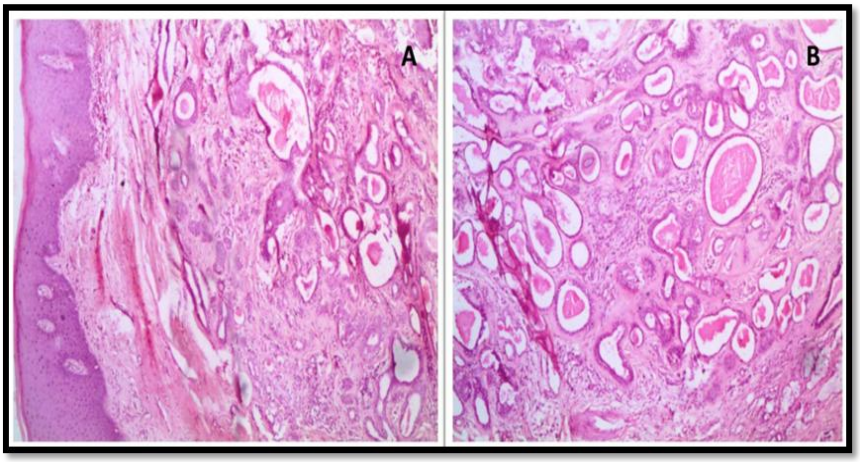

Fig. 3: (4 X magnifications) (A) H & E section reveals stratified squamous keratinised epithelium and connective tissue stroma. The stroma is collagenous consisting of an encapsulated pathology. The lesional stroma shows lot of cystic cavities containing keratin, few ducts and tumor cells arranged in nests and cords. In few areas, the stroma appears hyalinised. (B) (10X magnification) Connective tissue stroma consisting of lot of cystic spaces showing squamous metaplasia and filled with keratin.

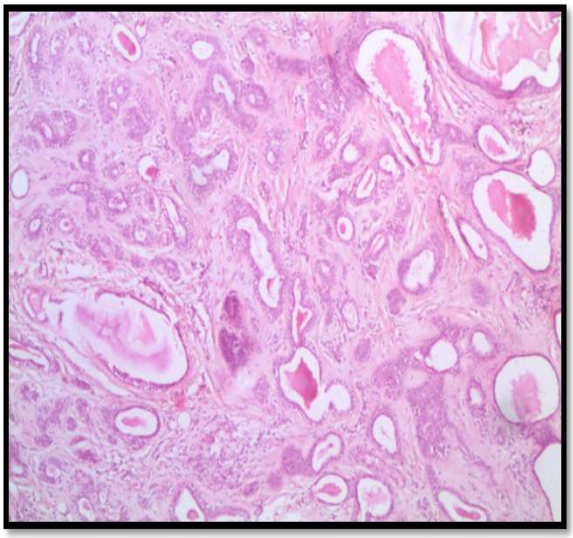

Fig. 4: (10X magnification) H & E section reveals connective tissue stroma which is collagenous and hyalinised in few areas. Tumor cells which are polyhedral with dark stained nuclei are seen in nests, cords and ductal pattern. Extensive areas of cystic spaces filled with keratin and lined by squamous epithelium are also evident.

DISCUSSION

Salivary gland neoplasms are unique entities and perhaps have the most complex histopathology of any organ system. [9] Pleomorphic structure of the tumor is determined by two types of cells, an inner row of the epithelial cells and an outer layer of myoepithelial cells. In PA, the presence of great diversity of cytological differentiation can be explained by the metaplastic potential of the neoplastic myoepithelial cells. [10] Myoepithelial cells are the result of the differentiation of the pluripotent cells from the salivary ducts during the 10th week of intrauterine life. But in adult life they may proceed from the reserve cells of the intercalated and striated salivary ducts. The myoepithelial cells have the ability to transdifferentiate into cells of the mesenchymal line. The modified myoepithelial cells are derived from the neoplastic myoepithelial cells as a result of metaplasia, differentiation and transdifferentiation processes. [10,11] PA presenting extensive squamous metaplasia is uncommon and an incidental microscopic

finding which signifies a potential pitfall in the histopathological diagnosis. [8,12] But squamous metaplasia has also been noted in non neoplastic pathologies like chronic sialadenitis, necrotizing sialometaplasia and lymphoepithelial cyst. This change is commonly associated with repair following infarction and necrosis of the salivary glands. The metaplastic process might occur spontaneously or be triggered by minor trauma. The most probable etiology for this change is ischemia. This etiology is supported experimentally by the induction of squamous metaplasia in rat salivary glands by arterial ligation. [11] The varying degree of squamous metaplasia is because of rapidity and ease of the switch in genetic programming of cytokeratin filaments induced by ischemia in salivary glands. [13] The squamous differentiation in mucoepidermoid carcinoma is either by the luminal epithelial or modified myoepithelial cells. [14-16] The marked ability of acinar units in rat salivary gland to undergo squamous metaplasia lends further support to this premise and provides new evidence for histogenic pathways in human salivary gland tumors. It has been observed that squamous metaplasia may be a finding in almost any salivary gland tumor that has been exposed to preoperative FNAC. [15] However, in the present case we could not elicit any history of trauma and hence the cause for extensive squamous metaplasia remains unexplained.

Extensive squamous metaplastic changes seen in PA might lead to difficulties in diagnosis through FNAC and intraoral frozen section, simulating malignant neoplasm probably high grade mucoepidermoid carcinoma (MEC) and SCC. The probable reasons are the squamous cells often reveal nuclear atypia and the presence of scanty mesenchymal component in such pleomorphic adenomas. This may have direct effect on preoperative and intra operative surgical planning of these tumors. [17,18] Glandular cells transformed into squamous cells resulting in multiple squamous epithelium-lined cysts containing keratotic lamellae, and some solid squamous cell islands containing keratin pearls posed difficulty in diagnosis.

It is important to discuss the diagnostic pitfall of this unusual presentation of a common benign entity, since malignant lesions are considered in its differential diagnosis. Microscopically, MEC presents mucous, intermediate and squamoid (epidermoid) cells and is usually multicystic with the cystic spaces generally lined by mucous cells. Further, prominent epidermoid cells associated with keratin production including keratin pearl formation is rare in MEC. The absence of cytological atypia, necrosis, invasion, as well as minimal cellular proliferation helps in ruling out SCC. [8] Based on the histopathological features in the present case, we could rule out both MEC and SCC and arrive at a final diagnosis of pleomorphic adenoma, even though the epidermoid areas mimicked other lesions.

CONCLUSION

To conclude, the gender, location and microscopic features of the presented case are unusual. PA with extensive squamous metaplasia poses diagnostic challenge as the feature of extensive squamous metaplasia raises the possibility of carcinoma. Ischemia has proven to cause extensive squamous metaplasia in salivary glands. It is important to be aware of these changes in order to prevent over interpretation of benign salivary tumors while excluding other malignancies and to avoid unnecessary aggressive therapy.

Consent: The patient has given his informed consent for the case report to be published.

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