



Polymorphous low grade adenocarcinoma of the palate a case report

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Abstract

Polymorphous low grade adenocarcinoma (PLGA) is a rare, slow growing malignant neoplasm with a propensity to arise predominantly from minor salivary glands. It is exclusively observed in the soft and hard palate regions, exhibiting an indolent biology. A 31 yr old male who came to the department of Periodontics for a routine cleaning of teeth was incidentally detected with a painless swelling on the palatal 26, 27 region. Histopathological, immunohistochemical, radiographic and CBCT (Cone beam computed tomography) investigations aided in deriving a final diagnosis of Polymorphous low grade adenocarcinoma. The piezoelectric unit was used to excise the mass with no further metastasis or involvement of the palatal vault. The site of excision healed uneventfully and the histopathological report of the excised mass showed no signs of nerve involvement. This tumor is not only a rare lesion but also depicts a similar clinical picture of that of a benign neoplasm, thus poses as a diagnostic dilemma to the clinician.

Key words: Immunohistochemistry, low-grade adenocarcinoma, polymorphous, palate, salivary gland, tumors

Introduction

Polymorphous low-grade adenocarcinoma (PLGA) is a malignancy that predominantly affects the minor salivary glands. Minor salivary gland tumors account for 2- 4% of head and neck malignant neoplasms, 10% of all oral cavity neoplasms and 15- 23% of all salivary gland malignant neoplasms^(1,2). PLGA was described as a distinct entity in 1983⁽³⁾. Freedman and Lumerman⁽⁴⁾ termed it as Terminal Duct Carcinoma and Lobular Carcinoma. It was so named as it was thought to originate from the progenitor cells of the distal/terminal end portions of the salivary gland unit (Intercalated duct reserve cell)⁽⁴⁾. In 1984, Evans and Batsakis proposed the term "polymorphous low-grade adenocarcinoma"⁽⁵⁾. It arises in the middle decades of life, over an age range of 16- 95 years with a mean age of 60 years and generally with a 2:1 female to male ratio⁽²⁾. It has been reported to involve the minor salivary glands located mainly in the palate (40%), lips (20%), buccal mucosa (23%), retromolar mucosa (10%), floor of the mouth (1%), tongue (1%), parotid and rarely the submandibular gland⁽⁶⁾. Its involvement of the non-oral site is rare and has been reported to include the nasal cavity (1%) and nasopharynx (0.5%)⁽⁷⁾. The tumor range in size from 0.4 to 6cm (average of 2cm)^(8,9). It is a slow growing lesion that takes months to years, before it is diagnosed and treated appropriately. In this article, we have reported and discussed the clinical, histopathological and management aspects of an incidentally discovered case of PLGA.

Case Report

A 31 year old male patient reported to the K.L.E Society's Institute of Dental Sciences, Bangalore with a chief complaint of dirty teeth and wanted his teeth cleaned. On routine examination of the oral cavity, a swelling with an insidious onset on the palate was discovered. This had been present for the last five years. History revealed that the swelling had gradually increased in size since its onset. Medical, dental, family and personal histories were not noteworthy. No abnormalities were detected on general physical and extra oral examination. The swelling was not associated with pain, discharge or paresthesia. A detailed intraoral examination revealed a sessile solitary swelling, involving the left postero-lateral region of the hard palate, measuring approximately 15mm × 15mm, extending anteroposteriorly from mesial of 25 to distal of 27, and lateromedially 3-4mm, from the marginal gingiva of 25, 26 and 27 towards the midpalatine raphe (Figure 1). The mass was firm to soft, the overlying mucosal surface of the swelling was smooth, intact and normal in colour without any erythematous or ulcerative changes giving a first impression of a swelling of inflammatory origin. On detailed examination teeth from the involved side were neither carious nor periodontally involved. No regional lymphadenopathy was observed. On palpation, the swelling was nontender, nonpulsatile, and slightly compressible. Patient presented with minimal amount of stains.

Radiographic Findings

Intra-oral periapical radiograph showed a well defined radiolucency associated with the mesial and palatal roots of 27 (Figure2). Occlusal radiograph did not show any significant changes (Figure3). The CBCT findings revealed a spindle shaped soft tissue density lesion with mild enhancement which was seen along the roof of the oral cavity on the left side, bounded superiorly by the hard palate and limited anterolaterally by the maxillary alveolar ridge. The lesion measured 2.2cms wide, 0.9 cm thick and 2.5cms anteroposteriorly. No calcific foci or fluid component was reported and the adjacent bones showed no scalloping/ thinning or erosion (Figure4).

Management:

An initial Fine needle aspirational biopsy (FNAC) followed by incisional biopsy was performed. Surgical diathermy (Neosurge 200BD) using both monopolar cautery for excision of the lesion and bipolar cautery for the control of



Figure 1. Pre-operative Clinical picture of the palatal swelling



Figure 2. Intra oral periapical radiograph of the area of the lesion



Figure 3. Occlusal radiograph of the area of the lesion

bleeding was performed (Figure5). The excised mass (Figure 6) was sent for a final confirmatory biopsy which gave similar report and confirmed the diagnosis of Polymorphous low grade adenocarcinoma showing no further infiltration into the nerves. The 3 months follow-up showed satisfactory results (Figure7).

Histopathologic findings

An initial aspirational biopsy was negative. So an incisional biopsy of the growth was performed which showed a covering of orthokeratinised stratified squamous epithelium of regular thickness, which was



Figure 4. CBCT image showing the lesion



Figure 5. Surgical excision being performed



Figure 6. Region of surgery where the surgical excision was performed



Figure 7. 3 month follow-up post-operative clinical picture

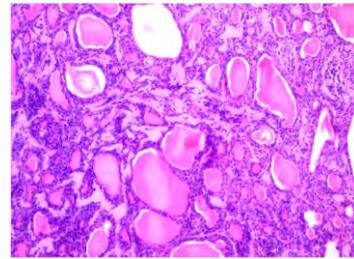


Figure 8b. Ductular growth pattern with eosinophilic coagulum is demonstrated by the tumor cells. Areas of hyalinisation are seen. (H& E 10 X)

proliferating into the connective tissue in an arcading pattern. The underlying connective tissue was composed of dense, thick collagen fibre bundles. A few small blood vessels were observed and mimicked a Localised fibroepithelial hyperplasia. A provisional diagnosis of fibroepithelial hyperplasia was reported.

Considering the rate at which the site of biopsy had filled, and therefore disregarding the provisional diagnosis from the incisional biopsy an excisional biopsy was performed and sent for immunohistochemistry and histopathological analysis.

Excisional biopsy revealed that mucosal aspect of the section was overlined by parakeratinized stratified squamous epithelium (**Figure 8a**). The connective tissue contained strands, cords and duct-like tumour structures of various sizes and small sheet-like areas of tumour cells with indistinct cell membranes and large pale nuclei. Most of the duct-like areas show eosinophilic coagulum, some with developing calcifications. Extensive areas of necrosis were observed in the larger duct-like areas, which also showed papillary extensions into luminal spaces (**Figure 8b, 8c, 8d**). Areas of squamous metaplasia with keratin formation were observed. No mitotic figures were observed. The intervening stromal tissue showed areas of hyalinization, myxoid change and desmoplasia. Perineural and intraneural invasion by tumor cells is seen (**Figure 8e**). A diagnosis consistent with Polymorphous low grade adenocarcinoma was made.

Immunohistochemistry:

The immunohistochemistry report demonstrated tumor cells that expressed calponin, cytokeratin, vimentin and minimal expression GFAP. Tumor cells were negative for

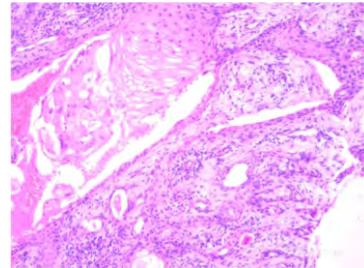


Figure c. Isomorphic tumor cells arranged in cords, strands and cystic pattern in myxoid stroma. Hyperplastic stratified squamous epithelium with acanthosis is seen. (H& E 4 X)

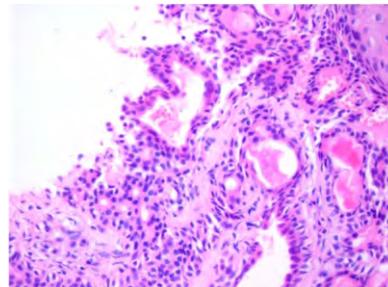


Figure 8d. Isomorphic tumor cells arranged in pseudo cribriform and tubular pattern. (H& E- 10X)

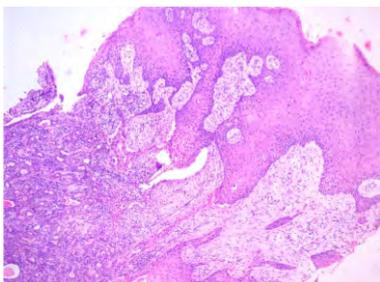


Figure 8a. Stratified squamous epithelium showing secondary pseudoepitheliomatous hyperplasia. The neoplastic lesion is encroaching the surface epithelium. (H& E- 4X)

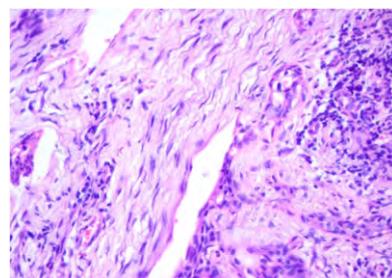


Figure 8e. Invasive Polymorphous low grade adenocarcinoma showing intra neural and perineural invasion. (H& E- 20X)



SMA and bc12. Ki67 proliferation index was <1%. A definitive diagnosis of polymorphous low grade adenocarcinoma was therefore made.

Discussion

The polymorphic nature of the PLGA displays a striking mixture of a variety of growth patterns which includes solid lobules, cystic, ductal, tubular, trabecular, glandular profiles, cribriform nests, and linear, single cell "Indian-file" infiltration usually seen at the periphery of the tumor⁽¹⁰⁾. Generally the diagnosis of PLGA is not difficult, however diagnostic difficulties can be encountered with frozen sections, small biopsy samples or due to overlapping of histopathologic features of mixed tumors (Pleomorphic adenoma), Adenoid cystic carcinoma (ACC) and Adenoid carcinoma. Hence differential diagnosis is a very important aspect for the clinician in deriving a final diagnosis. Similarly in the case reported, due to the size of the sample, the initial incisional biopsy gave an impression of Localised fibroepithelial hyperplasia.

The differentiation between PLGA and Pleomorphic adenoma can be made by identifying the presence of neurotropism. The typical plasmacytoid myoepithelial cells are seldom seen in PLGA⁽¹¹⁾.

Immunohistochemistry is an important tool when dealing with salivary gland neoplasms⁽¹²⁾. Pleomorphic adenoma shows immunoreactivity for GFAP (Glial fibrillary acid protein) which is normally present in nervous system cells, specifically in glial cells. However the presence of this antibody has been described in tumors of non-glial origin. PLGA has minimum or no reactivity to GFAP which is a distinct difference from pleomorphic adenoma⁽¹³⁾. Other immunohistochemical studies have shown that PLGA expresses large amounts of vimentin, which is absent in canalicular adenoma⁽¹⁴⁾.

ACC can show similar growth patterns identified in PLGA, especially the proclivity for perineural invasion. However differences in nuclear morphology are particularly striking and nearly pathognomonic. In contrast with PLGA, the cells of ACC tend to be smaller with hyperchromatic nuclei, less cytoplasm, a higher nuclear-to-cytoplasmic ratio, and coarser nuclear chromatin. ACC lacks the slate-gray background matrix of PLGA.

The immunohistochemical profile of ACC demonstrates high positivity than that of PLGA for Ki-67, p53 and bcl-2. S-100 protein was found to be quite weak in ACC relative to PLGA and CD17 was found to be strong in ACC.⁽¹¹⁾ ACC is very aggressive with faster growth and metastasis rate in comparison to PLGA, which shows low grade of malignancy and slow growth.

The case described in the report corresponds to the established features of PLGA such as, slow growth, higher incidence in palate and similar histopathologic and immunohistochemical aspects.

Complete surgical excision is the treatment of choice and usually it is done during an excisional biopsy or a wide local excision. The extent of surgery may at times be larger than what it is planned for a low grade neoplasm, but this is due to the frequent association with perineural invasion. Uncommonly, post-operative radiation therapy has been suggested for recalcitrant recurrences, but it is more of a palliative rather than a curative option. The overall survival for PLGA is generally excellent with conservative management, with more than 95% of patients alive after a

mean follow-up of 10 years⁽¹⁰⁾. Tumors associated with the hard palate are more likely to have a higher incidence of recurrence or persistence. The recurrence rate is about 10% emerging upto 14 years after initial presentation (mean 7 yrs)⁽⁶⁾ which is mainly attributed to the incompleteness of the excision. Women are more likely to present with recurrences and the initial size of the primary lesion does not influence the disease progression or the patient outcome.⁽¹⁰⁾

Conclusion

Polymorphous Low Grade Adenocarcinoma is a rare malignant neoplasm with low symptomatology which may go undetected or eventually determine a late diagnosis, and having various similarities with that of different salivary gland tumors and benign neoplasms, it is of primary importance to carry out the appropriate radiographic, histopathologic and immunohistochemical analysis to arrive at the final diagnosis amidst an array of differential diagnosis for an effective treatment plan.

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