

Polymorphous Low-grade Adenocarcinoma of the Palate: Report of a Case and Review of Literature

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ABSTRACT

Polymorphous low-grade adenocarcinoma (PLGA) is a malignancy arising predominantly from minor salivary glands. PLGAs account for 10% of all tumors and 25% of all malignancies of the minor salivary glands. It has been frequently described as occurring in hard or soft palate minor salivary glands; some cases being described in the tongue and in major salivary glands. We report a case of PLGA of the palate extending into the maxillary sinus and nasal cavity diagnosed on the basis of histopathology and treated by subtotal maxillectomy. The review of literature concerning clinical, histological and immunohistochemical features, as well as the proper management concerning this tumor is included.

Keywords: Minor salivary gland tumors, Malignant tumors, Adenocarcinoma, Maxillectomy.

INTRODUCTION

Salivary gland tumors are uncommon and constitute 2 to 6.5% of all head and neck neoplasms affecting predominantly major salivary glands, especially the parotids.^{1,2} Tumors of minor salivary gland origin accounts for 9 to 23% of all salivary neoplasms.³

PLGA was firstly described as a distinct entity in 1983;^{4,5} nevertheless, the terms 'lobular carcinoma' or 'terminal duct carcinoma' was invariably used. PLGA was firstly described as similar to lobular carcinoma of the breast⁴ and Batsakis et al⁵ named it 'terminal duct carcinoma' as presumed origin of this salivary tumor was in the terminal duct. In 1984, Evans and Batsakis⁶ proposed the term 'polymorphous low-grade adenocarcinoma' (PLGA) to refer this tumor in the World Health Organization (WHO) classification of salivary neoplasms in 1990.⁷

Prior to its recognition, it was commonly diagnosed as adenoid cystic carcinoma while over the last two decades there has been substantial data published on the features of PLGA differentiating the two.⁸ It is the second most common primary minor salivary gland malignancy after muco-epidermoid carcinoma, comprising 9 to 26.4% of all salivary malignancies.⁹⁻¹¹

We report a case of PLGA of the palate extending into the maxillary sinus and nasal cavity diagnosed on the basis of histopathology and was treated by subtotal maxillectomy followed by reconstruction of the defect with an obturator.

CASE REPORT

A 52-year-old male patient reported with a complaint of swelling in the palate since 8 years. The swelling developed 8 years back and was static in size, but a sudden increase in the size of swelling was noticed since last 3 months after intake of some homeopathic medication. The patient gave a history of two to three episodes of bleeding through right external nares and increased mucus secretion through left external nares since 3 months and nasal twang in his voice for the past 2 months. He also gave a history of occasional headaches but there was no history of weight loss or decreased appetite. Patient was a known diabetic since 3 years and was under diet control.

A well-circumscribed swelling with an ulcerated overlying mucosa measuring approximately 6 × 5 cm in diameter on the right side of the hard palate extending posteriorly 1cm in the soft palate and crossing the midline (Fig. 1) was present. The swelling was firm in consistency, nontender and nonpulsatile. The right submandibular lymphnode were palpable measuring approximately 0.5 to 1 cm in diameter, firm in consistency, nontender and mobile.

Hematological investigation revealed mild eosinophilia and raised ESR. The serum alkaline phosphate level was raised to 139 IU/L. The patient was tested for Hepatitis B and HIV I and II which were negative.

Maxillary cross-sectional radiograph and CT scan revealed an advanced lesion involving the right maxillary



Fig. 1: Intraoral photograph showing a well-circumscribed swelling with ulcerated overlying mucosa on the right side of the hard palate crossing the midline

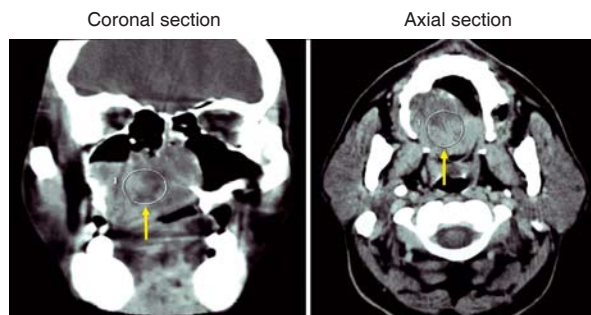


Fig. 2: CT scan revealed an advanced lesion involving the right maxillary antrum, palate and nasal cavity with extensive bony destruction and extension into surrounding structures

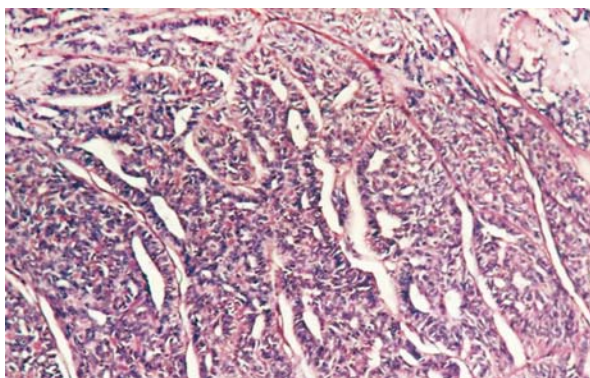


Fig. 3: Pictomicrograph showing the tumor cells as large alveolar masses separated by delicate fibrous septa

antrum, palate and nasal cavity with extensive bony destruction and extension into surrounding structures (Fig. 2). FNAC revealed large sheets of atypical epithelial cells in tight clusters. The cells were round oval to slightly elongated and have scanty cytoplasm with dark-stained nuclei. A wedge biopsy was done and histopathologic section showed bits of tissue lined by stratified squamous epithelium with subepithelial tumor; the cells are seen as large alveolar masses separated by delicate fibrous septa (Fig. 3). At places, glands and vague acini were seen. The

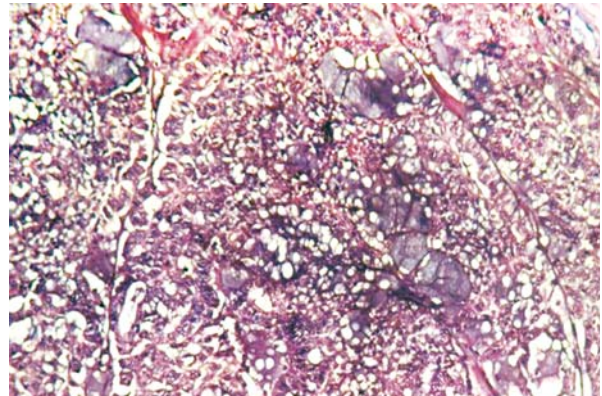


Fig. 4: Pictomicrograph showing large, round to oval tumor cells with moderate cytoplasm and vesicular nuclei with prominent nucleoli

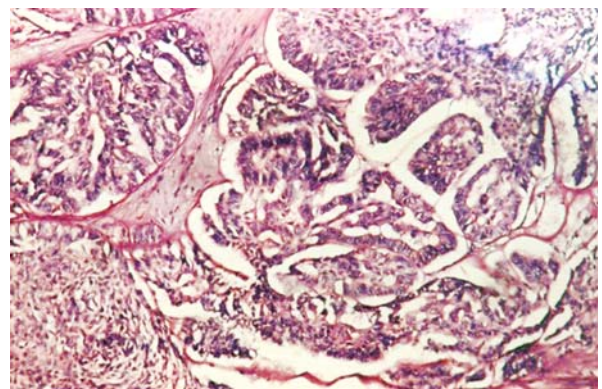


Fig. 5: Pictomicrograph showing glands lined by cuboidal to columnar epithelial cells at the periphery and the central area showed spindle shaped cells in whorls, papillary patterns

cells were large, round to oval with moderate cytoplasm and vesicular nuclei with prominent nucleoli, and occasional mitosis was seen (Fig. 4). Many large glands were seen lined by cuboidal to columnar epithelial cells at the periphery, and the central area showed spindle shaped cells in whorls, papillary pattern (Fig. 5). Based on the clinical presentation, radiological findings, FNAC and histopathology, the diagnosis of polymorphous low-grade adenocarcinoma (PLGA) was suggested. The patient's PLGA was localized close to the nasal fossa and maxillary sinus, although neither perinervous nor perivascular invasion was histopathologically encountered.

The subtotal maxillectomy was done for the patient and the defect was restored with an obturator (Fig. 6). The postoperative course was uneventful and on follow-up no recurrence was observed as evidenced by physical and radiographic examination.

DISCUSSION

PLGA is a well-defined neoplasm characterized by architectural diversity, cytological uniformity and indolent clinical behavior.¹² The myriad of histologic types of minor salivary gland tumors makes this the most heterogeneous

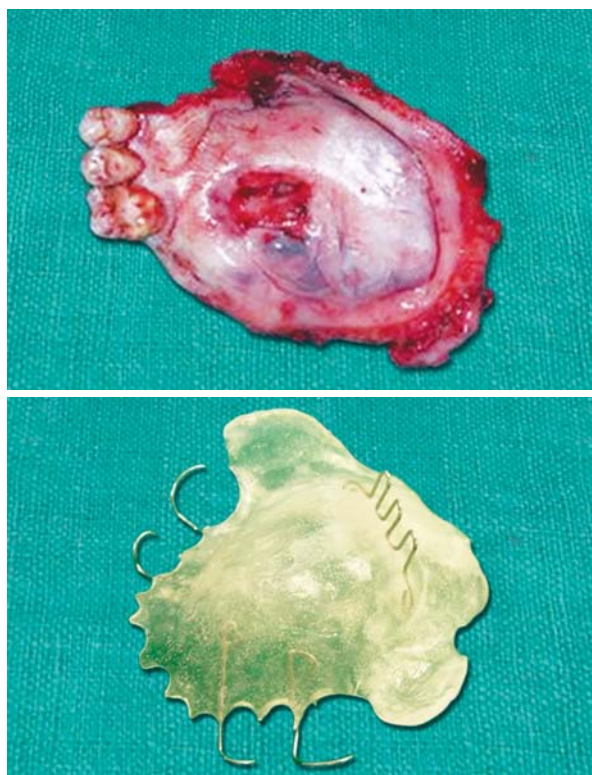


Fig. 6: Resected tumor mass following subtotal maxillectomy and obturator for reconstruction of the maxillary defect

group of neoplasms. Although some tumors of minor and major salivary glands may arise from the same progenitor cells, they may exhibit different biologic behavior related to anatomic site of occurrence.¹¹

PLGA occurs more frequently in females than in males with a male-to-female ratio ranging from 1:1.02 to 1:2.0.¹³ It affects mainly adult patients from the 3rd through the 7th decades, with a peak prevalence from the 5th to 6th decades of life.^{6,11}

It commonly arises in the palate (49-77.8%), followed by either the buccal mucosa or upper lip (7.4-13.4%) and can also involve the floor of the mouth, lower lip, alveolar ridge and tongue.^{6,9,14,15} Additionally, PLGA can arise in the lung,¹⁶ parotid gland,¹⁷ submandibular gland¹⁸ and maxilla,¹⁹ and two case reports describe it transforming into higher grade neoplasms.^{20,21} The presenting symptom in PLGA is a lump, may or may not associated with discomfort and/or pain.²² In our case, PLGA presented as an asymptomatic swelling with an ulcerated mucosal surface on the right side of hard palate and crossing midline extending into the right maxillary sinus and nasal cavity.

Fine-needle aspiration cytology is a useful aid to diagnosis. PLGA cytology is characterized by the presence of cuboidal cells with abundant cytoplasm, round to oval nuclei and inconspicuous nucleoli. Mitotic figures are rarely seen. Histopathology of malignant minor salivary gland

tumors is well-established important diagnostic aid. On gross examination, PLGA appears as a well-circumscribed, nonencapsulated, firm, homogeneous, tan mass. Infiltration of the surface epithelium may give the tumor an ulcerated appearance, but central necrosis is rare.¹⁴ At low magnification, a central lobulated portion with islands and columns of cells extending into surrounding salivary gland or connective tissue are observed. At high magnification, the cells are cuboidal to columnar with slightly enlarged nucleoli, the cytoplasm being eosinophilic or amorphous or even clear, mitotic figures are scant and necrosis does not occur and the stroma often varies from mucoid to hyaline. PLGA unified several histologic patterns: Solid, trabecular, glandular, cystic, ductal, spindled, fascicular, cribriform and papillary. Transoral open biopsy is not recommended prior to definitive treatment because of the risk of seeding the oral mucosa.²³⁻²⁵

Immunohistochemical staining can assist in making a diagnosis of PLGA, as 90% of cells stain positively with S-100 protein and epithelial membrane antigen (EMA).²⁴ The results of staining with high molecular weight keratin are somewhat more variable as 75 to 95% of the cells stain positively. Muscle-specific actin and carcinoembryonic antigen are poor markers of PLGA because of their high variability in staining.²⁴ PLGA may stain with glial fibrillary acidic protein (GFAP) but this is usually less consistent than GFAP staining of pleomorphic adenomas. Most PLGAs stain poorly with proliferation markers p53 and Ki-67, which supports the clinical observation that PLGA are slowly growing tumors.¹⁴

Because PLGA share many of the histologic characteristics of pleomorphic adenomas, monomorphic adenomas, adenoid cystic carcinomas (ACC), and low-grade papillary adenocarcinomas (LGPA), these tumors should be considered in the differential diagnosis of PLGA.¹⁴ Pleomorphic adenoma and monomorphic adenoma can be easily distinguished from PLGA by its lack of infiltration and by the presence of PLGA characteristics, such as poor circumscription, peripheral infiltration, and the tendency for perineural invasion.^{14,24} The need to distinguish PLGA from ACC arises more often as there are overlapping histologic features (i.e. cribriform, tubular and solid patterns), local infiltration and perineural invasion, but they can be distinguished from one another by cytology; ACC exhibit basaloid cells with scant cytoplasm.^{14,15} In addition, PLGA show spindling, and ACC do not.^{23,24} Finally, while PLGA stain widely with S-100 protein and EMA, ACC stain much less diffusely.²⁴ A distinction should be made between PLGA and LGPA because the latter displays a more aggressive behavior; their rates of both local recurrence and regional lymph node metastasis are higher.^{14,15} Most authors agree that if the histologic features are predominately papillary, the tumor should be identified as a low-grade papillary adenocarcinoma.^{14,15,24}

The treatment of choice for PLGA is wide local excision with clear margins. Postoperative radiation therapy is reserved for cases of positive or close surgical margins, but it has not been shown to alter outcome in patients without lymph node metastasis. The presence of cervical metastasis is considered an indication for adjuvant radiation therapy. For the treatment of recurrences, radical excision is warranted.¹⁴ In the present case, subtotal maxillectomy was performed followed by reconstruction of the defect with obturator.

CONCLUSION

Minor salivary gland tumors are relatively uncommon lesions encountered in the daily practice. PLGA is the second most common minor salivary gland malignancy, characterized by architectural diversity, cytological uniformity, and indolent clinical behavior. The understanding of the site, gender, age and prevalence, and histological typing aids in proper diagnosis and appropriate management of PLGA.

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