POLYMORPHOUS LOW GRADE ADENOCARCINOMA - CASE REPORT AND REVIEW OF LITERATURE

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Abstract:

Polymorphous low grade Adenocarcinoma (PLGA) is a malignant epithelial tumour that is essentially limited in occurrence to minor salivary gland sites .It has a unique clinical, histomorphologic and behavioural aspects. It is mainly reported as a painless swelling of the hard and soft palate along with symptoms of bleeding, telengiectasia or ulceration of the overlying mucosa occasionally. In this paper, we present a case of Polymorphous low grade Adenocarcinoma with its clincopathological features and immunohistochemistry.

Keywords : Lobular carcinoma , Adenocarcinoma , reserve cells

Introduction:

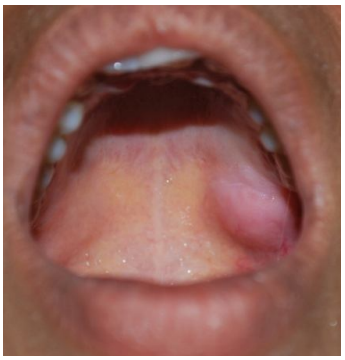
Low grade polymorphous Adenocarcinoma was first reported in 1983 by two different groups under the terms lobular carcinoma of the salivary glands and terminal duct carcinoma[5]. It was later described by Evans and Batsakis in 1984[6].This tumor includes those entities which were previously termed as terminal duct carcinoma, lobular carcinoma, papillary carcinoma and trabeculae carcinoma. Currently the term polymorphous low grade Adenocarcinoma (PLGA) is widely accepted. This tumor is considered to be a low grade malignancy with a relatively indolent course and a low risk of metastasis. It is 2nd in frequency to mucoepidermoid carcinoma and accounts for 26% of all salivary gland carcinomas. It was thought to be originated from the progenitor cell of the distal/terminal duct portions of the salivary gland unit i.e. the intercalated duct reserve cell.

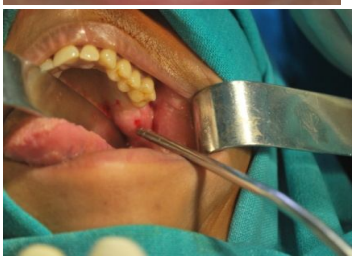
The affected individuals report with a firm, elevated non tender swelling i.e. occasionally associated with bleeding, increase in size/discomfort.Otalgia, odynophagia,

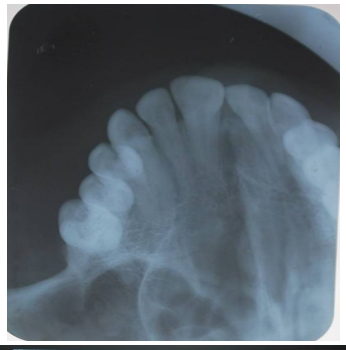
tinnitus and airway obstruction are some of the other less frequently identified symptoms. The involvement of non-oral sites is rare and has included only the nasal cavity (1%) and the nasopharynx (0.5%) [4.This] mainly occurs in the fifth through eight decades of life, with a mean age of 59 years. The female to male ratio is about 2:1.This mostly affects the minor salivary glands located mainly in the palate, lips, buccal mucosa, retromolar mucosa, and floor of mouth, tongue, parotid and rarely the submandibular gland. A wide range size has been noted, but most are between 1 and 4 cm in diameter. It has a slow growth rate which is evidenced by the long duration, from many months to years, before diagnosis and treatment planning. Metastasis to the local nodes only accounts to 10%.The definitive diagnosis only comes after the histopathologic examination.In this article, we report a case of PLGA to discuss and review its clinical and histopathologic features.

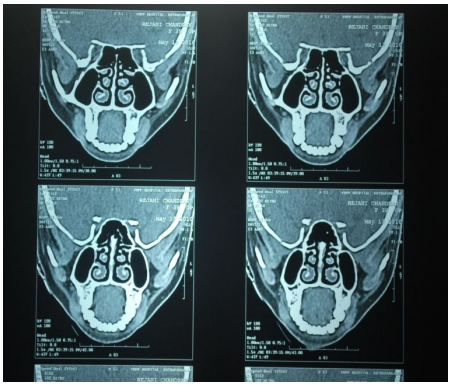
Case report:

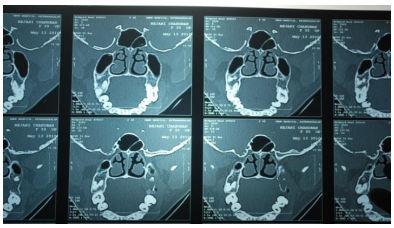
A 38 yr old female reported with a painless swelling on the hard palate extending to retro molar region, distal to 26 of 5yr duration. Intraoral examination revealed a 2X 2 cm smooth bony hard, non tender swelling which was not fixed. Occlusal radiograph showed a radiolucent lesion 2.5 cm in diameter with a sclerotic border present in hard palate & in relation to the distal aspect of 26.. CT scan revealed a infiltrating lesion on the tuberosity region. Incisional biopsy was done, which show mucosa lined by hyperplastic stratified squamous epitheliumand the connective tissue shows areas of anaplastic salivary gland epithelial cells arranged in solid, cystic and Indian file arrangement. Stroma shows areas of hyalinised materials. Areas of neural tropism seen. The epithelial cells show vesicular, washed out as well as hyperchromatic nuclei. Cystic areas show hyalinised secretary materials. Connective tissue septa shows plump as well as spindle shaped fibroblasts and fibrocytes. Areas of ductal structures and blood vessel are also seen in the tumour area.

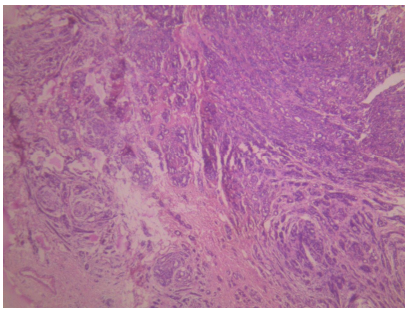


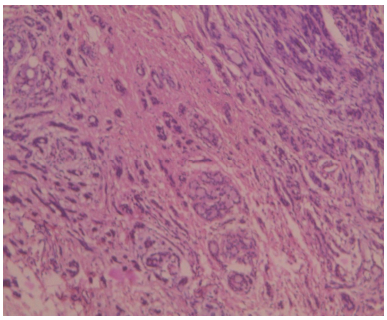


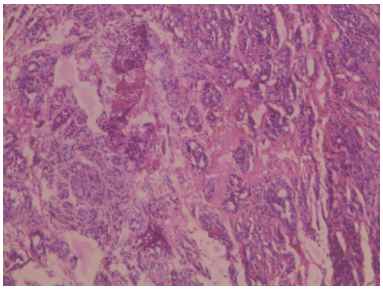


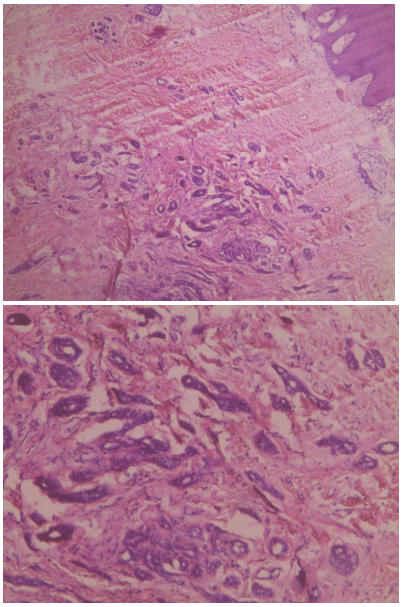












Discussion:

Polymorphous low grade Adenocarcinoma (PLGA) is believed to be originated from the reserve cells in the most proximal portion of the salivary duct[5]. Myoepithelial differentiated cells appear in the tumor, but only in slight to moderate numbers. It is generally considered to be a low grade malignancy with a relatively indolent course and low risk of reccurrence and metastasis. Incidence of PLGA is reported to be palate [40%], lips[20%], buccal mucosa[23%], retromolar mucosa[10%], floor of the mouth[1%] and tongue[1%]. A few cases of involvement of Parotid gland and Nasal/ Nasopharynx have been reported. Submandibular gland lesion is rare[5].

PLGA is a common malignancy of minor salivary gland; second in frequency to mucoepidermoid carcinoma. It usually present as an asymptomatic submucosal mass.

The tumours are well circumscribed but unencapsulated and infiltrate into adjacent structures. The polymorphic nature of the lesion refers to a variety of growth patterns which includes solid, cystic, ductal, glandular, cribriform, trabecular and tubular types. A single file arrangement is usually seen at the periphery of the tumour.Tumour consists of cuboidal/columnar isomorphic cells with spindle shaped nuclei. Nucleoli appear small and inconspicuous. The chromatin varies from vesicular to stippled. The tumor stroma varies from mucoid to hyaline .Perineural invasion is common.

On electron microscopy, cuboidal/polygonal cells with high nuclear to cytoplasmic ratios, dispersed chromatin and small nucleoli that were often in direct contact with the nuclear membrane. The cytoplasm contains abundant intermediate filaments. Scanty mitochondria, inconspicuous Golgi complexes with variable amount of rough endoplasmic reticulum are also seen. The cells were joined by desmosomes and apical tight junctions.Pseudoglands consisted of cells with similar ultra structural features[4]

On immunochemistry, this showed a positivity with epithelial markers (cytokeratins, EMA), S-100, and sometimes CEA, SMA and vimentin.PLGA showed a significantly weaker expression of c-kit,Ki-67 and bcl2 when compared to ACC showing better prognosis that ACC[1].Intraluminal mucin can be identified by PAS after diastase digestion.

The differential diagnosis between PLGA and ACC and other tumors are very important in deciding treatment. In adenoid cystic carcinoma, the nuclei are more hyper chromatic and more angular. There is the accumulation of basophilic pools of GAG in the cribriform areas, which is not typical of PLGA.The cytoplasmic staining of ACC is pale to clear staining unlike in PLGA which is eosinophillic to amphophilic.The staining qualities of EMA and CEA in the luminal cells were in equal proportion and intensity whereas in PLGA, it was dissimilar. The exuberant myoepithelial component of ACC resulted in stronger staining with SMA and MSA.ACC showed galectin-3 immunostaining mainly in the nuclei which was responsible for its aggressive nature; while PLGA revealed a positive mostly cytoplasmic reaction to galectin-3. The distinction between the two is crucial as ACC has a much more aggressive course.

Benign mixed tumour can be differentiated from PLGA as these are not infiltrative and do not exhibit neurotropism.The GFAP immunoreactivity is present in benign mixed tumour and absent in PLGA.

The treatment modality will include a conservative wide surgical excision.Even though this has varied from wide Excisional biopsy to wide local excision to a more radical procedure(including maxillectomy,hemimandibulectomy and orbital excenteration).The role of radiotherapy in the primary treatment has to be fully assessed in the absence of regional nodal spread.Perineural invasion does not apparently affect the prognosis.The prognosis is good.The reccurence rate is about 10% which is mainly attributed to the incompleteness of the excision.

Conclusion

The origin of PLGA is proposed as arising from the intercalated duct system. This finding supports the muticellular theory of salivary gland tumour histogenesis. PLGA is a slow growing, indolent, malignant tumour that can recur over long period of time and may even metastasize to regional cervical lymph nodes; however distant metastases do not occur, and death attributable to PLGA is extremely rare. Neurotropism is found in majority of tumour along with perivascular invasion. Some authors suggest PLGA as a low grade variant of ACC which is still controversial.

References:

1.*David Beltran,William .C.Faquin,George Gallagher and Meredith August(2006):Selective Immunohistochemical comparison of polymorphous low grade Adenocarcinoma and adenoid cystic carcinoma,J Oral Maxillofacial Surgery:64:415-423*

2.Antonio Cardesa,Pieter .J. Slootweg:Pathology of the Head & Neck:149-150

3.K.L Ferrazzo,M.M.Neto,E.dos Santos,D.dos Santos Pinto,S.O.M de Sousa(2009):Differential expression of galectin -3,Beta-catenin and cyclin DI in

adenoid cystic carcinoma and polymorphous low grade Adenocarcinoma of salivary glands,J Oral Pathology Medicine 38:701-707

4.Gary .L.Ellis,Paul L.Auclair,Douglas R.Guepp:Surgical Pathology of the salivary glands:Volume 25 in the series,W.B Saunders company,390-410

5.Regezi,Sciubba,Jordan:Oral pathology-Clinical pathologic correlations:Saunders- Elsevier;5th edition,205-207

6.Shafer,Hine,Levy:Shafer's Textbook Of Oral Pathology:6th edition,235-236