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Polymorphous Adenocarcinoma (PAC) Presenting as a Palatal Swelling - A Case Report

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ABSTRACT

BACKGROUND

Polymorphous adenocarcinoma is the second most common intraoral minor salivary gland tumor accounting for 26% of all carcinoma. It is characterized by varied architectural patterns with uniform cytologic picture.

METHODS

We present a case of 45-years-old male who presented with a palatal swelling. neoplastic glandular epithelial cells showing variety of growth patterns and characteristic Indian file pattern was also seen. Microcalcifications were also appreciated.

RESULTS

All these features are suggestive of Polymorphous Adenocarcinoma (PAC). The patient received postoperative radiotherapy in view of close margins for a total dose of 50.4 Gy in 28 fractions. The patient is doing well 33 months post-surgery without any clinical or radiological evidence of recurrence.

CONCLUSIONS

Palatal salivary gland malignancies pose a diagnostic dilemma for the pathologists. Any general practitioner should be skeptical about the palatal swelling and refer the patient to a specialist.

KEYWORDS

Polymorphous adenocarcinoma; Palatal swelling; Radiotherapy; Post-surgery

INTRODUCTION

Palate being rich in minor salivary glands creates a possibility of a wide array of malignancies and poses a diagnostic dilemma [1]. Hence clinicians should be skeptical when a patient presents with palatal swelling. Batsakis first described Polymorphous adenocarcinoma (PAC) as Terminal Duct Carcinoma [2]. Later Freedman and Lumerman described it as Lobular carcinoma in 1983

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[3]. However, Evans and Batsakis suggested the term "Polymorphous Low-Grade Adenocarcinoma" (PLGA). Recently, in 2017 WHO opted for the term "Polymorphous Adenocarcinoma" (PAC). WHO in the recent classification includes "cribriform adenocarcinoma of minor salivary glands" (CAMSG) as a subtype of PAC [4]. Polymorphous adenocarcinoma is the second most common intraoral minor salivary gland tumor accounting for 26% of all carcinoma [5]. PAC shows a female predilection with a wide age range ranging from fifth to sixth decade of life [6]. Most commonly it presents as a painless mass on the palate [5]. PAC s characterized by varied architectural patterns with uniform cytologic picture [7]. On FNAC, cytological features may mimick pleomorphic adenoma (PA), adenoid cystic carcinoma (ACC), mucoepidermoid carcinoma, epithelial myoepithelial carcinoma and papillary cystadenocarcinoma [8]. We present a case of 45-year-old male who presented with a palatal swelling.

CASE REPORT

A 45-years-old male came to our department with the complaint of swelling over the left side of palate since 3 months - 4 months (Figure 1). The swelling increased in size drastically. He visited a private dentist for the same, where medications were prescribed for pain but no relief was seen. Thereafter, patient was referred to our department for further management. During the examination, a well demarked swelling was present over palatal region in 1st, 2nd, 3rd molar region on left side, Swelling was firm, non-tender in nature extending medially from mid palatal raphe to junction of horizontal process of palate and alveolar process (Figure 1). Haematological and biochemical tests were within normal limits. Chest X-ray and ultrasound of abdomen and pelvis were normal. Cone beam computed tomography (CECT) was suggestive of a bulky left palatal lesion with iso to hyperdense lesion. Fine needle aspiration cytology from the parotid swelling was suggestive of pleomorphic adenoma.

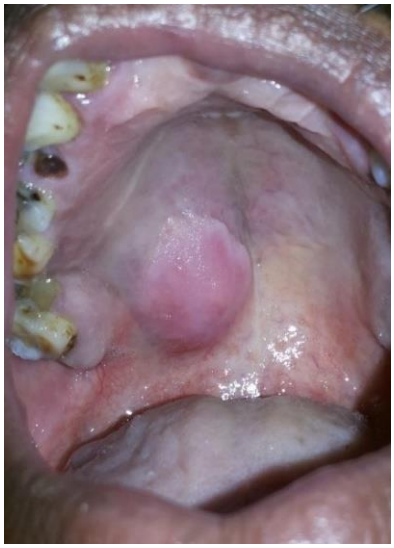

Figure 1: Intraoral photograph of the patient showing palatal swelling on the left side of palate.

The patient underwent surgical excision of the tumor. Gross examination of the specimen revealed a grey white infiltrating tumor measuring 2.5 cm × 2 cm × 2 cm with focal grey brown areas. A histopathological examination was advised.

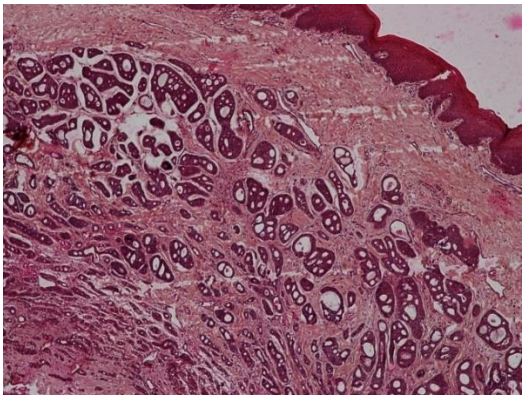

Figure 2: Parakeratinised stratified squamous surface epithelium which is separated at places from the lesional tissue by band of normal connective tissue.

H & E-stained section consists of parakeratinised stratified squamous surface epithelium which is separated at places from the lesional tissue by band of normal connective tissue (Figure 2). The lesional tissue is partially encapsulated and consists of sheets of neoplastic glandular epithelial cells showing variety of growth pattern which includes cord like, duct like arrangement, cribriform pattern (Figure 3 and Figure 4) peripheral part of section shows Indian file type of arrangement (Figure 5).

These neoplastic glandular epithelial cells are round to oval in shape with scanty cytoplasm and pale staining vesicular nuclei. At one focus cells are arranged in a concentric pattern forming 'targetoid' appearance (Figure 6).

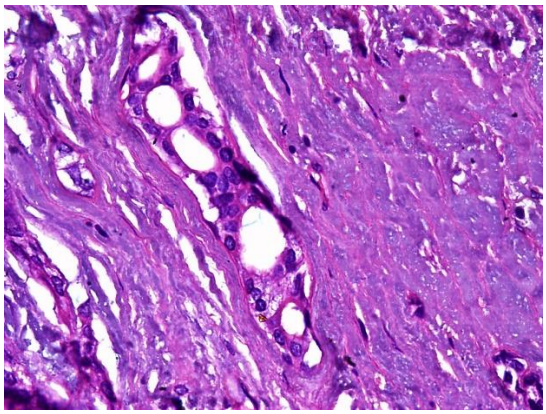

Figure 3A: Duct like arrangement of neoplastic glandular cells (40x magnification).

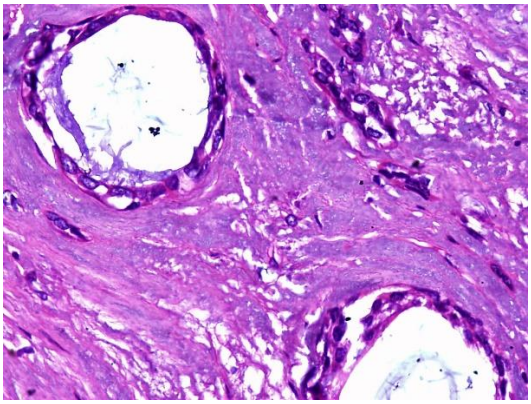

Figure 3B: Opening up and channelization of tubules.

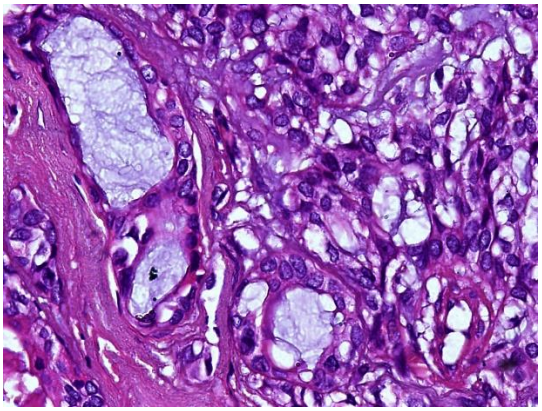

Figure 4: Cribriform arrangement resembling adenoid cystic carcinoma.

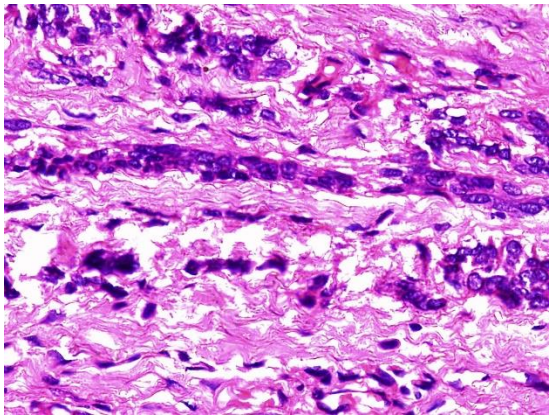

Figure 5: Single file/ Indian file arrangement of neoplastic cells.

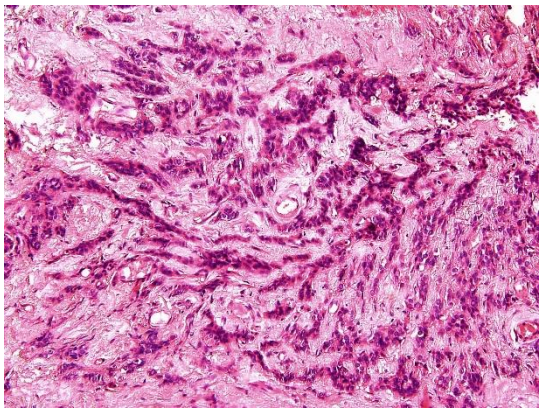

Figure 6: Targetoid arrangement of cells in concentric layers.

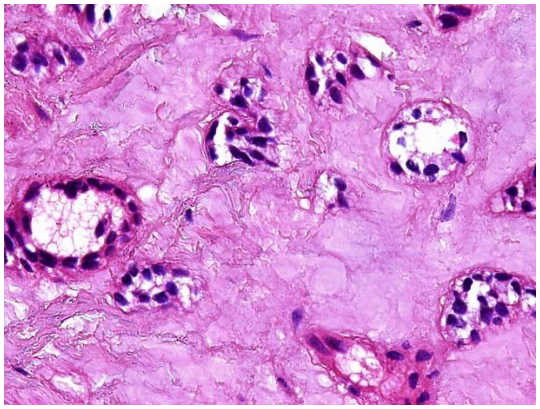

Figure 7: Clear cells resembling mucoepidermoid carcinoma like areas.

At places, the cells are arranged in nests with intervening connective tissue septae resembling alveolar pattern. The cells are round to oval with granular eosinophilic cytoplasm and hyperchromatic nuclei. Clear cell differentiation is evident at places (Figure 7).

The intervening connective tissue shows numerous areas of hyalinisation and few areas of mucous. (Figure 8 and Figure 9) At places areas of microcalcifications were seen (Figure 10).

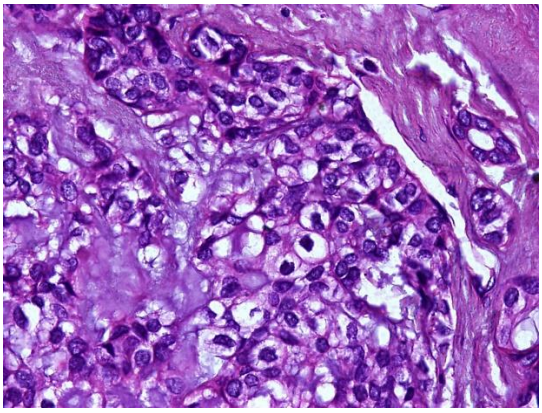

Figure 8: Hyalinised stroma.

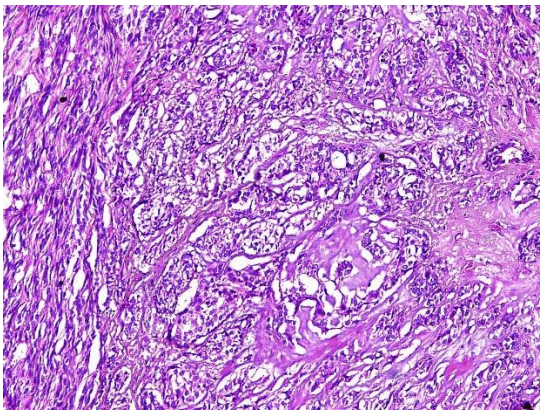

Figure 9: Mucoid stroma.

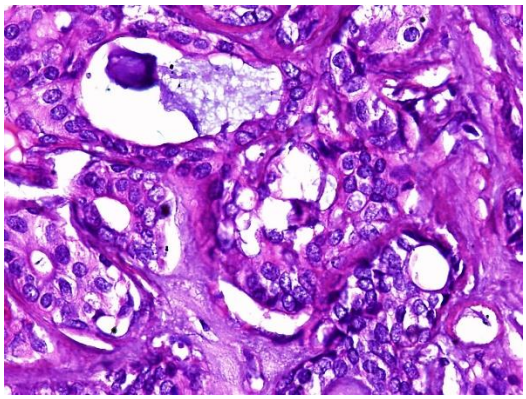

Figure 10: Microcalcifications resembling psammoma bodies.

These neoplastic glandular epithelial cells have invaded the surrounding capsule and adjacent minor salivary gland tissue at places.

All these features are suggestive of Polymorphous Adenocarcinoma (PAC).

The patient received postoperative radiotherapy in view of close margins for a total dose of 50.4 Gy in 28 fractions. The patient is doing well 33 months post-surgery without any clinical or radiological evidence of recurrence.

DISCUSSION

As early as 1983, Freedman and Lumermann published very first description of PAC when they termed it as lobular carcinoma to emphasize the similarity with single-file (Indian file) pattern seen in breast lobular carcinoma [3]. Simultaneously, Batsakis et al reported a series of similar tumors and proposed the term “terminal duct - adenocarcinoma” to denote their origin from terminal segment of salivary gland ducts [2]. It was in 1984 that Evans and Batsakis emphasized that this group of salivary gland tumors are characterized by bland uniform cytology but diverse architectural pattern and coined the term “Polymorphous Low-Grade Adenocarcinoma” (PLGA) [8]. However, with experience it was understood that PLGA is not as indolent as was thought [9]. High grade transformation was also noted [10]. It was on these grounds that in 2017, WHO dropped out “Low Grade” and opted for the term “Polymorphous Adenocarcinoma” (PAC) and defined it as “a malignant epithelial tumor characterized by cytological uniformity, morphologic diversity and an infiltrative growth pattern” [11].

PAC is the second most common salivary gland malignancy after Mucoepidermoid Carcinoma [12]. This tumor like any other salivary gland tumor affects women with F:M ratio of 2:1 [9]. More than 90% PACs occur in more than 40 years of age with incidence rates between 40 years - 79 years and mean age of diagnosis is 61.3 years affecting whites more than the people of color [12]. PAC is most commonly located on the posterior hard palate and soft palate. Buccal mucosa, labial mucosa may also be involved [12,13]. Up to 9% of PAC originate from major

salivary gland predominantly parotid gland [14]. Most PACs present with approximately 2 cm size [12]. Few cases show pain, ulceration, bleeding or ill-fitting dentures. Our case was also in line with these findings except patient was a male.

PAC has non-specific findings on imaging but can be an adjunct in assessing the local extent in the bone [15]. In our case Cone Beam Computed Tomography (CECT) was suggestive of a bulky left palatal lesion with iso to hyperdense lesion. Additional chest, abdominal radiographs are required to rule out metastasis [16,17] in our case both were normal.

For evaluation of salivary gland lesions, Fine needle aspiration cytology (FNAC) is very informative [18]. In our case the aspirate showed round basaloid cells and a diagnosis of pleomorphic adenoma was proposed with a differential diagnosis of Adenoid cystic carcinoma, Mucoepidermoid carcinoma [19].

Diagnosis of PAC relies on incisional biopsy with margins of normal tissue [20]. Macroscopically, PAC is firm to solid with no capsule but circumscribed tumor mass lying just below the epithelium. The cut surface appears white or tan [20]. Tumor mass is adjacent to normal salivary gland lobules and flood the lamina propria just reaching the surface epithelium [21]. PAC is characterized by uniform appearance, round or polygonal shaped small to medium cells with indistinct boundaries. All dysplastic features like increased nucleo-cytoplasmic N:C ration, vesicular nuclei with inconspicuous nucleoli are seen. These cytologic features contribute to the pale appearance of the tumor and was useful diagnostic criteria in the past [5,9,21,22]. Nuclear atypia and mitoses are not common.

PAC is famous for its varied architectural patterns ranging from solid islands & chords, tubules, pseudo-cribriform aggregates and Indian-file pattern.

These pseudo-cribriform patterns which exhibits true lumina should be differentiated from classic cribriform pattern in Adenoid cystic carcinoma wherein they result from stromal cores trapped in tumor parenchyma and thus outlined by basement membrane [22]. Targetoid pattern i.e., cells arranged concentrically around a nerve bundle is a common finding [11,9].

Tyrosine rich crystals and microcalcifications can also be seen [23]. In our case also calcific bodies were seen.

For cytoskeleton and cytoplasmic filaments PAC stains positive for CK7 and vimentin. CK8 and CK18 in solid tumors [24]. Integrin β1, β2, β3 detected in the pseudo cribriform areas [25]. S-100 is almost always present strong and diffuse [20,26]. 80% cells stain positive for WT1. P63 positivity is also noted. 70% cases exhibit PRKD1 mutation [27].

Differential Diagnosis

PAC is commonly mistaken for Adenoid cystic carcinoma and this is addressed by Ellis & Auclair & Dardick [8,22]. They are mainly differentiated by contour of tumor cells and contour/ nature of luminal spaces and cytology [21]. IHC plays a central role mainly S100 protein, WT1 & SMA like S 100 protein and WT1 are regularly expressed in PAC as opposed to AdCC where SMA is frequently positive.

MYP overexpression is hallmark of AdCC [26] but is absent in PAC [28] High grade transformation has been reported but rare [29].

Management

Surgical excision provides best locoregional control [12]. SEER database 5-years to 10-years disease specific survival of 98.6% and 96.4% respectively [12] prevention of recurrence is important because recurrent lesion behave far more aggressively. Palatal PAC require extended maxillectomy with rehabilitation [30]. Since metastasis is

rare, no need of neck dissection [31]. Radiotherapy and chemotherapy are restricted to palliative cases [4].

Follow-up of 15 years - 20 years is necessary and chest X-ray for pulmonary metastasis. Prognosis is good in cases with low Ki67 but cases of death are noted.

CONCLUSION

Palatal salivary gland malignancies pose a diagnostic dilemma for the pathologists. Although being the second most common salivary gland malignancy, reported cases of PAC are only handful. Sometimes underdiagnosis can also occur due to its bland cytology. Hence any general practitioner should be skeptical about the palatal swelling and refer the patient to a specialist.

DECLARATIONS

Conflicts of Interest

None.

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Availability of Data and Material

Not applicable

Code Availability

Not applicable

Authors' Contribution

Dr. Riya Jain and Dr Suchitra Gosavi formulated the manuscript, and data collection. Dr. Deepak Sethia and Dr. Akshay Trimukhe assisted in writing the manuscript and the proof reading.

Ethical Approval

Since it is a case report, ethical approval was not required

Consent to Participate

The authors declare that they have no conflict of interest.

Consent to Publish

A written consent was taken from the patient in his vernacular language.

REFERENCES

1. Young A, Okuyemi OT (2022) Malignant tumors of the palate. In: StatPearls. Treasure Island: StatPearls Publishing.
2. Batsakis JG, Pinkston GR, Luna MA, et al. (2007) Adenocarcinomas of the oral cavity: A clinicopathologic study of terminal duct carcinomas. Journal of Laryngology and Otology 97(9): 825-835.
3. Freedman PD, Lumerman H (1983) Lobular carcinoma of intraoral minor salivary gland origin: Report of twelve cases. Oral Surgery, Oral Medicine and Oral Pathology 56: 157-66.
4. Vander Poorten V, Triantafyllou A, Skalova A, et al. (2018) Polymorphous adenocarcinoma of the salivary glands: Reappraisal and update. European Archives of Otorhinolaryngology 275: 1681-1695.
5. Luna MA, Wenig BM (2005) Polymorphous low-grade adenocarcinoma. In: Barnes L, Eveson JW, Reichart P, Sidransky D, editors. Pathology & Genetics Head and Neck Tumours. Lyon: IARC Press 118.
6. Tomar R, Garg N, Agarwal S (2015) Polymorphous low-grade adenocarcinoma of lip clinically mimicking squamous cell carcinoma: An unusual presentation. Journal of Cytology 32(1): 59-61.
7. Mills ES, Carter CD (2010) In: Sternberg's diagnostic surgical pathology. Philadelphia: Lippincott Williams & Wilkins; 2010. Salivary glands 841-842.

8. Ellis G, Auclair P (1996) Salivary gland tumors: Malignant epithelial tumors. In: Ellis, G, Auclair P. Atlas of tumor pathology. Tumors of the salivary glands. Third series, seventienth fascicle. Armed Forces Institute of Pathology, Washington DC: 155-228.
9. Castle JT, Thompson LDR, Frommelt RA, et al. (1999) Poly morphous low-grade adenocarcinoma: a clinicopathologic study of 164 cases. Cancer 86(2): 207-219.
10. Skalova A, Sima R, Vanecek T, et al. (2009) Acinic cell carcinoma with high-grade transformation: A report of 9 cases with immunohistochemical study and analysis of TP53 and HER-2/neu genes. The American Journal of Surgical Pathology 33(8): 1137-1145.
11. Seethala RR, Johnson JT, Barnes L, et al. (2010) Polymorphous low-grade adenocarcinoma: The University of Pittsburgh experience. Archives of Otolaryngology, Head and Neck Surgery 136(4): 385-392.
12. Patel TD, Vazquez A, Marchiano E, et al. (2015) Polymorphous low-grade adenocarcinoma of the head and neck: A population based study of 460 cases. Laryngoscope 125: 1644-1649.
13. Tian Z, Li L, Wang L, et al. (2010) Salivary gland neoplasms in oral and maxillofacial regions: A 23-year retrospective study of 6982 cases in an eastern Chinese population. International Journal of Oral and Maxillofacial Surgery 39: 235-242.
14. Bradley PJ, McGurk M (2013) Incidence of salivary gland neoplasms in a defined UK population. Brazilian Journal of Oral and Maxillofacial Surgery 51(5): 399-403.
15. Kato H, Kanematsu M, Makita H, et al. (2014) CT and MR imaging findings of palatal tumors. European Journal of Radiology 83(3): e137-e146.
16. Hannen EJM, Bulten J, Festen J, et al. (2000) Polymorphous low-grade adenocarcinoma with distant metastases and deletions on chromosome 6q23-qter and 11q23-qter: A case report. Journal of Clinical Pathology 53(12): 942-945.
17. Tanaka F, Wada H, Inui K, et al. (1995) Pulmonary metastasis of polymorphous low-grade adenocarcinoma of the minor salivary gland. The Thoracic and Cardiovascular Surgery 43(3): 178-180.
18. Pfeiffer J, Ridder GJ (2012) Diagnostic value of ultrasound guided core needle biopsy in patients with salivary gland masses. International Journal of Oral and Maxillofacial Surgery 41: 437-443.
19. Gibbons D, Hossein Saboorian M, Vuitch F, et al. (1999) Fine needle aspiration findings in patients with polymorphous low-grade adenocarcinoma of the salivary glands. Cancer Cytopathology 87(1): 31-36.
20. Regezi JA, Zarbo RJ, Stewart JCB, et al. (1991) Polymorphous low-grade adenocarcinoma of minor salivary gland. A comparative histologic and immunohistochemical study. Oral Surgery, Oral Medicine and Oral Pathology 71(4): 469-475.
21. Woolgar J, Triantafyllou A (2011) Contemporary salivary clinical pathology - facts and dilemmas. In: Bradley P, Guntinas Lichius O Salivary gland disorders and diseases: Diagnosis and management (1st Edn.) Thieme, Stuttgart: 27-41.
22. Dardick I (1996) Color atlas/text of salivary gland tumor pathology. Jgaku-Shoin, New York
23. Triantafyllou A, Hunt JL, Devaney KO, et al. (2014) A perspective of comparative salivary and breast pathology. Part I: Microstructural aspects, adaptations and cellular events. European Archives of Oto-rhino Laryngology 271: 647–663.
24. Marotta Reis de Vasconcellos L, Avila Sarmento Silveira V, Eduardo Blumer Rosa L, et al. (2006) Immunohistochemistry as a fundamental tool for the differential diagnosis of polymorphous low-grade adenocarcinoma. Quintessence International 37: 565-573.
25. Araujo V, Sousa S, Jaeger M, et al. (1999) Characterization of the cellular component of polymorphous low-grade adenocarcinoma by immunohistochemistry and electron microscopy. Oral Oncology 35(2): 164–172.

26. Leader R, Deol-Poonia RK, Sheard J, et al. (2014) Immunohistochemical localization of WT1 in epithelial salivary tumors. Pathology and Research Practice 210(11): 726-732.
27. Weinreb I, Piscuoglio S, Martelotto LG, et al. (2014) Hotspot activating PRKD1 somatic mutations in polymorphous low-grade adenocarcinomas of the salivary glands. Nature Genetics 46: 11661169.
28. Persson F, Fehr A, Sundelin K, et al. (2012) Studies of genomic imbalances and the MYB-NFIB gene fusion in polymorphous low-grade adenocarcinoma of the head and neck. International Journal of Oncology 40(1): 80-84.
29. Nagao T (2013) "Dedifferentiation" and high-grade transformation in salivary gland carcinomas. Head and Neck Pathology 7: 37-47.
30. El-Naaj IA, Leiser Y, Wolff A (2011) Peled M Polymorphous low-grade adenocarcinoma: Case series and review of surgical management. Journal of Oral and Maxillofacial Surgery 69(7): 1967-1972.
31. Pogodzinski MS, Sabri AN, Lewis JE, et al. (2006) Retrospective study and review of polymorphous low-grade adenocarcinoma. The Laryngoscope 116(12): 2145-2149.