

Epithelial myoepithelial carcinoma of parotid gland-a case report

Akhilanand Chaurasia^{1*}, Gaurav Katheriyay²

¹Assistant Professor, ²Resident, Dept. of Oral Medicine & Radiology, Faculty of Dental Sciences, King George's Medical University, Lucknow

***Corresponding Author:**

Email: chaurasiaakhilanand49@gmail.com

Abstract

Epithelial-Myoepithelial Carcinoma is a rare malignant salivary gland neoplasm. It is also known as adenomyoepithelioma. It accounts for less than 1% of all salivary gland neoplasms. This unusual salivary gland tumors is first described by Donath et al in 1972. This tumor occurs in sixth decade and beyond having a female predominance. Parotid gland is the most commonly involved followed by submandibular gland and palate. Herein we are presenting a rare case of Epithelial-myoepithelial carcinoma of parotid gland.

Keywords: Epithelial–myoepithelial carcinoma, Adenomyoepithelioma, Parotid gland tumors

Access this article online

Website:

www.innovativepublication.com

DOI:

10.5958/2395-6194.2016.00035.7

Introduction

Epithelial-myoepithelial carcinoma (EMEC) of the salivary glands was described by Donath et al in 1972¹. It is a rare tumor, accounting for less than 1% of all salivary gland neoplasms that arises most commonly in the parotid gland but has also been described in the submandibular gland and in the minor salivary glands^{2,3}. There is a female predominance with a peak occurrence in the seventh decade⁴. Epithelial-myoepithelial carcinoma also known as adenomyoepithelioma is low grade malignant salivary gland neoplasm composed of clear myoepithelial cells that surround epithelial lined ducts resembling intercalated ducts. In 1991, the WHO recognized Epithelial-myoepithelial carcinoma as a distinct entity and subtype of salivary gland adenocarcinoma and it became part of the new classification system⁵. Epithelial-myoepithelial carcinoma tends to grow in a bulky lobulated fashion with necrosis and hyalinization of large tumor nodules. The tumor has a distinctive histopathologic pattern with a proliferation of ductular structures. The inner cells of these ductules constitute the epithelial component of Epithelial-myoepithelial carcinoma. These mildly to moderately pleomorphic cells have irregular ovoid shapes may overlap and have prominent nucleoli and fine chromatin. Local spread to lymph nodes has been reported⁴. The usual treatment is wide surgical resection including adjacent lymph nodes however there is a high reported rate of local recurrence approaching 50%^{6,7,8}. Therefore adequate resection with negative soft-tissue margins is the minimum

recommended and necessary therapy. It chiefly occurs in the parotid gland representing about 1% of all salivary gland tumors^{9,10,11}. In addition, the major sites of involvement are the maxillary sinus, trachea, larynx, hypopharynx, and minor salivary glands. Patients are mostly women in their fifth to eighth decades^{12,13}. Epithelial-myoepithelial carcinoma is a malignant biphasic salivary-type tumor and the diagnosis is based on conventional light microscopy confirmed by immunohistochemical and ultrastructural investigation. Histologically the tumor is characterized by well-defined tubules with two cell types: an outer layer of myoepithelial cells with clear cytoplasm surrounding an inner lining of eosinophilic cuboidal epithelial cells¹⁴ resembling intercalated ducts. It has been suggested that it derives from the intercalated ducts of the salivary glands because the tubular growth pattern of this tumor epitomizes this phenotype^{15,16}. It has been observed that some morphologically low-grade myoepithelial carcinomas behave aggressively¹⁶. Thus in the absence of frankly malignant cytomorphology, an invasive growth pattern is the single most useful criterion for establishing malignancy in salivary Epithelial-myoepithelial carcinoma. It was first described by Donath et al. in 1972 and recognized as a distinct entity by the World Health Organization (WHO) in 1991^{17,18,19}. Soft palate seems to be the site of predilection of minor salivary gland Epithelial-myoepithelial carcinoma^{18,19}. Histologically, the tumor is characterized by a biphasic cytomorphology comprised of an inner layer of duct lining cells and an outer layer of clear myoepithelial cells^{20,21,22}. It can also show a multinodular growth pattern with tumor islands separated by a basement membrane and dense fibrous connective tissue bands. In many cases, the clear myoepithelial cell components are more predominant than the typical biphasic character²³. Based on the primary histological characteristics, the Epithelial-myoepithelial carcinoma can be classified in four

categories: solid, tubular, papillary and cribriform²¹. In some cases, the local rate of recurrence is high, ranging from 31.3% to 43%, and most recurrences manifest within 5 years^{24,25}. This may be partly because Epithelial-myoeplithelial carcinoma often appears histologically benign and this can result in its incomplete excision²⁶. Metastasis to regional cervical lymph nodes has been reported in about 19.6% of patients²⁷ and distant metastasis to the kidney, lung and brain have been reported in 9.8%²⁸. The diagnosis of Epithelial-myoeplithelial carcinoma is difficult, partly because of the rarity of the tumor, partly because of the complicated histopathological characteristics and it has been speculated that most reported cases are not correctly diagnosed. Some authors divide Epithelial-myoeplithelial carcinoma into 2 subtypes: 1) a tubular cribriform type characterized by a double-layered tubule ductal structure and 2) a solid type dominated by clear cells²⁹. The solid variant of Epithelial-myoeplithelial carcinoma is found to be associated with a more aggressive behavior compared with the other histological types³⁰. Other microscopic features of Epithelial-myoeplithelial carcinoma include periodic acid-Schiff (PAS) positivity of the clear cells, with corresponding negativity on diastase digestion; markedly PAS-positive basement membrane, with minimal cellular atypia; infrequent mitoses and a tendency to exhibit ductal differentiation¹⁷. The differential diagnosis of Epithelial-myoeplithelial carcinoma includes clear cell dominated tumors such as myoeplitheliomas, acinic cell carcinomas, mucoepidermoid carcinomas, and metastatic clear cell tumors^{31,32,33}. Because adenoid cystic carcinoma (ACC) can also show a double-layered, duct-like structure, it can be mistaken for Epithelial-myoeplithelial carcinoma¹⁷ but different immunostaining characteristics are useful for distinguishing between Epithelial-myoeplithelial carcinoma and ACC. The identification of S-100 protein can help in this differentiation. The inner ductal cell layer in ACC will stain positive whereas only the outer ductal cell layer in EMC is positive for this protein¹⁹. For Yamada et al¹⁹ the value of image examination such as computed tomography, magnetic resonance imaging and positron emission tomography for the pathologic diagnosis of EMC has yet to be established. Epithelial-myoeplithelial carcinoma is a rare biphasic tumor of the salivary gland. It is generally composed of variable proportions of two cell types: An inner layer of duct lining cells and an outer layer of clear cells, which typically form double-layered duct-like structures. Clear cells, which are of myoeplithelial origin, often predominate in number³⁴. EMC is a rare, low-grade malignant neoplasm characterized by a dual cell population of luminal ductal cells surrounded by large, polygonal clear myoeplithelial cells. The criteria proposed to identify more aggressive lesions are a solid growth pattern, nuclear atypia, DNA aneuploidy, necrosis,

positive surgical margins and high proliferative activity; such cases generally have a more aggressive behavior and a higher frequency of local recurrences and metastases. Adenoid cystic carcinoma, as EMC, is a tumor comprising a dual cell population of epithelial and myoeplithelial cells and it can have a morphology similar to that of EMC in terms of its trabecular pattern, where the prominent hyalinised stroma surrounds and squeezes the tumor cells into thin strands. In contrast to EMC, these cells are smaller and usually have more hyperchromatic, irregular and angulated nuclei. The feature that distinguishes myoeplithelioma and myoeplithelial carcinoma from EMC is the lack of a ductal cell component. Because EMC is considered to be a low-grade malignant tumor, adequate resection with negative soft-tissue margins is the minimum recommended and necessary therapy. Neck node dissection should be considered in cases of lymph node positivity along with chemotherapy and radiotherapy in patients with highly advanced disease, positive surgical margins, or surgically unresectable disease. Other synonyms of epithelial-myoeplithelial carcinoma include epithelial carcinoma, myoeplithelial carcinoma and clear cell carcinoma of salivary gland origin³⁵. The tumor is usually encapsulated, and may exhibit areas of necrosis and cystic degeneration. It may show one or more of spindle cells, epithelioid cells, plasmacytoid hyaline cells and clear cells. Nuclear atypia ranges from mild to marked. Solid, fascicular, trabecular and lace-like growth patterns are common. There can be various amounts of myxoid, collagenous or hyaline stroma³⁶. Di Palma and Guzzo considered epithelial-myoeplithelial carcinoma to be low grade when it arose in a pleomorphic adenoma and high grade when it arose de novo³⁷. These tumor cells secrete extracellular matrix, proteinases and proteinase inhibitors and also inhibit angiogenesis, and modification of these attributes could affect their biological behavior³⁸. Donath et al. postulated that the cell of origin was from intercalated ducts¹. The occurrence of intercalated duct hyperplasia has been observed in association with EMC in the case described by Di Palma³⁷ and in three of the cases described by Chetty³⁹. The integration of the two elements probably means that the EMC started from preceding intercalated duct hyperplasia^{39,40}. CT and MR appearances of EMC are nonspecific, and that EMC cannot be differentiated from other parotid neoplasms⁴¹. The usual treatment is wide surgical resection, including adjacent lymph nodes; adequate resection with negative soft-tissue margins is the minimum recommended therapy⁴².

Case Report

A 28-year-old male patient (**Fig. 1**) reported to us with chief complaint of swelling involving right side of face since 3 years. The swelling was progressively increasing in size. There was no associated pain or bleeding. The swelling was causing disfigurement in

right side. There was no significant past medical/ dental history. He has normal gait and posture. He has normal intelligence and well oriented to surroundings. He had normal vitals. On extra-oral examination a firm, non-tender swelling of 4x4 cm is noted in right tragus area extending from right tragus to middle of canthus- tragus line antero-posteriorly. Superio-inferiorly the swelling was extending from lower hairline to middle of ramus of mandible(**Fig. 2**). The right ear lobe was elevated. The skin overlying the swelling was of normal texture and colors however it was erythematous at its apex. There was no associated dysfunction with swelling. Intra-orally no significant finding in noted. The mouth opening was normal (**Fig. 3**). On the basis of clinical and radiological findings a provisional diagnosis of parotid gland neoplasm is reached. The patient was advised for radiographic investigations and FNAC of right parotid swelling. The panoramic radiograph shows a well-defined radiolucency of 3x3 cm extending from medial side of condyle to lateral side of coronoid process antero-posteriorly and till middle of right ramus inferiorly(**Fig. 4**). All the other structures were within normal limit. The contrast enhanced CT shows ill-defined heterogeneously enhancing soft tissue attenuation lesion measuring (4.5x4.8x5.0cm) in size is noted in right infratemporal fossa. The lesion is seen thinning and remodeling of ramus of mandible with deepening and widening of mandibular fossa. Anterolaterally the lesion is causing thinning and buckling of posterior wall of right maxillary sinus. The lesion is also seen abutting and displacing the masseter and temporalis muscle with focal loss of fat plane. Medially the lesion seen abutting left lateral and medial pterygoid with loss of fat plane. The lesion is also causing thickening and remodeling of right lateral pterygoid plate(**Fig. 5a, 5b, 5c**). All other structures were normal. The FNAC from right parotid region shows benign epithelial and myoepithelial cells with bland nucleoli arranged in clusters as well as dispersed singly in a chondromyxoid matrix. The individual myoepithelial cells are predominantly spindle shaped. There is no evidence of granuloma and atypia(**Fig. 6**). The radiological features and FNAC were suggestive of malignant tumor of parotid gland. The patient was advised for right parotidectomy with radical neck dissection under GA in ENT department (**Fig. 7**). The histopathology of resected section shows.

Gross:

Vial 1- Labelled as right level 1B and level II lymph node, received as two grayish brown soft tissue pieces larger measuring 1x0.5x0.2 cm. Larger soft tissue piece- outer surface smooth cuts firm. Cut surface shows grayish white areas. Whole sanctioned maller soft tissue piece-- outer surface smooth cuts firm. Cut surface shows grayish white areas.

Vial 2- Labeled as infratemporal fossa tissue, received as multiple grayish white soft tissues measuring 3x2x1cm.

Microscopic features- (Fig. 8a & 8b)

Vial 1- The section shows malignant biphasic tumor of salivary gland comprising of epithelial and myoepithelial component. The individual myoepithelial component is disposed in glandular and acinar pattern having round to ovoid nuclei, hyperchromatic chromatin, have high nucleocytoplasmic ratio, inconspicuous nucleoli and scanty cytoplasm. The individual myoepithelial / stromal components are comprising of ovoid or spindle cells having high nucleocytoplasmic ratio, coarse chromatin, inconspicuous nucleoli and moderate eosinophilic cytoplasm.

Vial 2. Section shows three lymph nodes showing reactive lymphoid hyperplasia and are free from tumor invasion.

The histopathology was suggestive of Epithelial-Myoepithelial carcinoma of right parotid gland.

So on the basis of radiological and histopathological investigations a final diagnosis of Epithelial-Myoepithelial carcinoma of right parotid gland has reached. The patient is referred to radiotherapy department for further management by radiation. The patient is treated in radiotherapy department for 1 year. The patient is followed for 2 years but no active lesion has been detected.



Fig. 1: Profile photo of patient



Fig. 2: Showing swelling of 4x4 cm is noted in right tragus area extending from right tragus to middle of canthus- tragus line antero-posteriorly. Superior-inferiorly the swelling was extending from lower hairline to middle of ramus of mandible

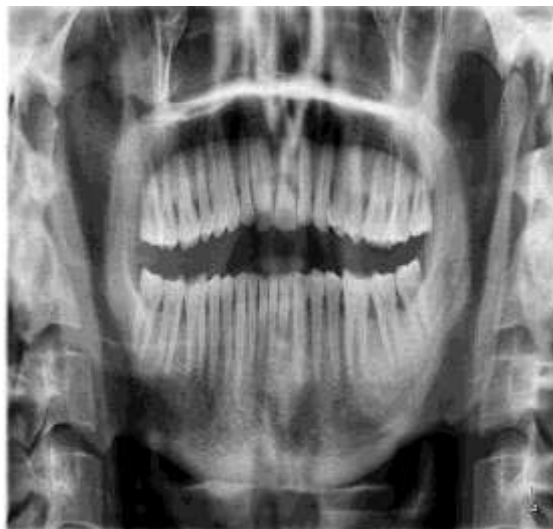


Fig. 4: Panoramic radiograph showing a well-defined radiolucency of 3x3 cm extending from medial side of condyle to lateral side of coronoid process antero-posteriorly and till middle of right ramus inferiorly



Fig. 3: Intra-oral view showing no significant findings



Fig. 5a: CECT (Axial) showing ill-defined heterogeneously enhancing soft tissue attenuation lesion measuring (4.5x4.8x5.0cm) in size is noted in right infratemporal fossa

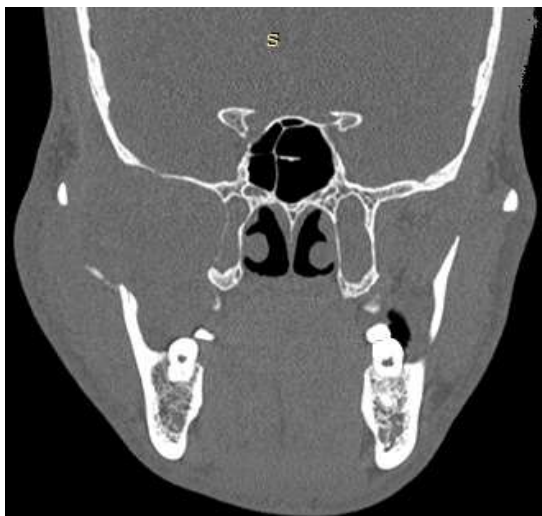


Fig. 5b: CECT (Coronal section) showing thinning and remodeling of ramus of mandible with deepening and widening of mandibular fossa. Anterolaterally the lesion is causing thinning and buckling of posterior wall of right maxillary sinus

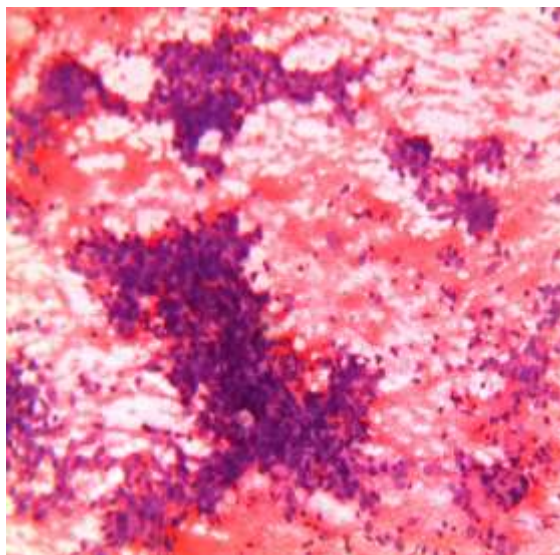


Fig. 6: FNAC shows benign epithelial and myoepithelial cells with bland nucleoli arranged in clusters as well as dispersed singly in a chondromyxoid matrix. The individual myoepithelial cells are predominantly spindle shaped



Fig. 5c: CECT (sagittal section) The lesion is also seen abutting and displacing the masseter and temporalis muscle with focal loss of fat plane



Fig. 7: Profile view of patient showing the surgical scar of total parotidectomy with radical neck dissection

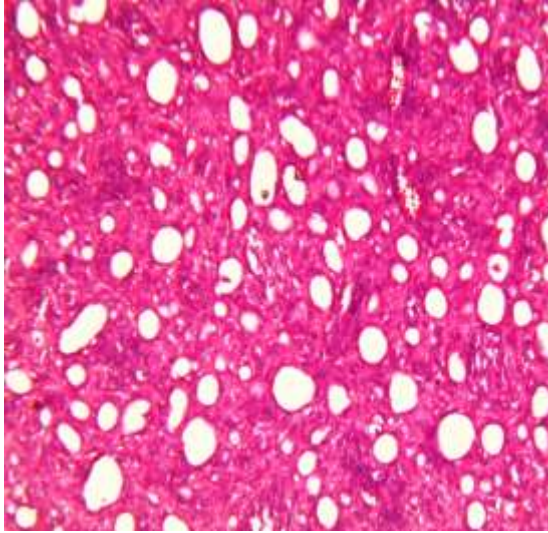


Fig. 8a

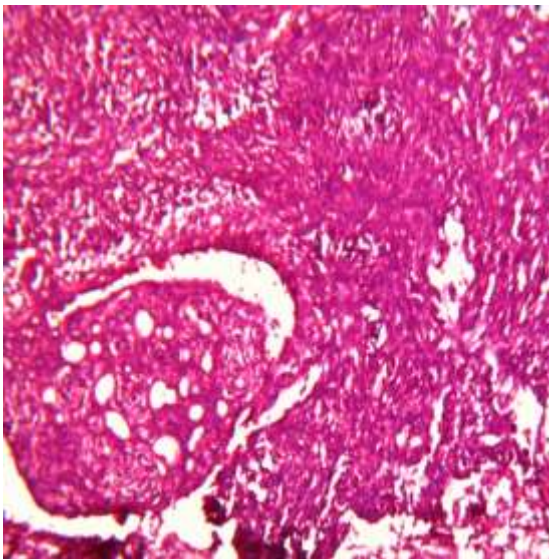


Fig. 8b

Fig. 8a & 8b: The section shows malignant biphasic tumor of salivary gland comprising of epithelial and myoepithelial component. The individual myoepithelial component is disposed in glandular and acinar pattern having round to ovoid nuclei, hyperchromatic chromatin, have high nucleocytoplasmic ratio, inconspicuous nucleoli and scanty cytoplasm

Discussion

Pleomorphic adenoma is the most common neoplasm of both the major and minor salivary glands. It is composed of an array of tissue types of both epithelial and mesenchymal origins and is regarded as benign in clinical behavior but has the potential to undergo malignant transformation. Epithelial-myoeplithelial carcinoma (EMC) is a rare biphasic tumor of the salivary glands typically arising in the parotid⁴³. Epithelial-myoeplithelial carcinoma (EMC) is

a rare type of malignant tumor accounting for about 1% of all salivary gland tumors^{44,45} and recognizes a typical biphasic pattern: a central ductular structure often containing eosinophilic material surrounded by clear cells of myoeplithelial origin. It was firstly described as a glycogen rich or clear cell adenoma because of the clear cell component. Epithelial-myoeplithelial carcinoma (EMC) is a rare biphasic tumor of the salivary gland. It is generally composed of variable proportions of two cell types: An inner layer of duct lining cells and an outer layer of clear cells which typically form double-layered duct like structures. Clear cells which are of myoeplithelial origin often predominate in number⁴⁶. The first description of this tumor with the terminology of EMC was introduced by Donath in 1972⁴⁷. EMC is primarily a tumor of older adults with a peak incidence in the sixth and seventh decades of life. Our case is one of the rarest described arising in a younger patient 28 years old⁴⁸. Clinical presentation is not specific and is usually that of a long-standing and progressively enlarging painless mass. Facial nerve palsy occurs only rarely⁴⁹. The clinical behavior and histologic findings of EMC originally prompted its previous classification as an adenoma (so called glycogen-rich, clear cell adenoma) or adenomyoeplithelioma⁵⁰. Most tumors arise in the major salivary glands, especially the parotid, but cases have been described in the minor glands of the mouth and even in the maxillary sinus. The history is typically that of a mass enlarging over several months or even years⁵¹. Perineural and vascular invasion are frequent and recurrence occurs in around 40% of cases and metastasis in 14%⁵². The association of EMC with other salivary gland tumors may also be a reflection of a common differentiation pathways as suggested by multidirectional differentiation that may be mediated through intercalated duct hyperplasia⁵³. Analogous to its breast and skin counterparts, this neoplasm comprises two populations of cells: myoeplithelial and epithelial as adenomyoeplithelioma and clear cell hydradenoma respectively. Microscopically on histological examination the tumor is biphasic and characterized as in this case by tubules lined by an inner layer of cytokeratin-positive bland cuboidal epithelial cells surrounded by an outer layer of S100 positive myoeplithelial cells⁴³. Fine needle aspiration cytology is widely used in the initial investigation of salivary gland swellings and whilst the cytological features of this tumor have been described they are not well recognized. It has been suggested that there is bidirectional differentiation from a stem cell to form myoeplithelial and intercalated ductal epithelial cells⁵⁴. CT and MR appearances of EMC are nonspecific, and that EMC cannot be differentiated from other parotid neoplasms⁵⁵. The morphological features of epithelialmyoeplithelial carcinoma are generally quite distinct from other salivary tumours. Monomorphic or pleomorphic adenomas do not invade locally and the

latter often contain abundant alcian blue positive stromal mucin. Salivary duct adenocarcinoma is aggressive and resembles ductal carcinoma of the breast. Terminal duct carcinoma⁵¹ or polymorphous low grade adenocarcinoma is a locally invasive tumour arising almost always in minor salivary glands and is characterised by cytological uniformity and histological diversity single lined ducts often with intraluminal papillae are typical, but a biphasic ductal lining is not a feature⁵⁶. The pathologic differential diagnosis includes other clear cell salivary tumors as clear cell carcinoma, acinar cell carcinoma, mucoepidermoid carcinoma, metastatic renal cell carcinoma, clear cell oncocytoma and pleomorphic adenoma^{57,58}. The usual treatment is wide surgical resection, including adjacent lymph nodes; adequate resection with negative soft-tissue margins is the minimum recommended therapy⁵⁹. EMC is considered to be a low-grade malignant tumor that may commonly recur locally after resection in 23-50% of cases. This is often because the capsule which normally delimits this neof ormation may be incomplete. Less frequent is the finding of lymph node and hematogenous metastasis⁶⁰. Distant metastases to kidney, lung, and brain have also been reported.

References

1. Donath K, Seifert G, Schmitz R. Zur Diagnose und Ultrastruktur des Tubularen Speichelgangkarzinoms. Epithelial-myoe pithelial Schaltstuckkarzinom. Virchows Arch [A] 1972;356:16–31.
2. Batsakis JG, El-Naggar AK, Luna MA. Epithelial-myoe pithelial carcinoma of salivary glands. Ann Otol Rhinol Laryngol 1992;101:540–542.
3. Morrow TA, Chun T, Mirani N. Epithelial myoe pithelial carcinoma of the parotid gland. Ear Nose Throat J 1990;69:646–648.
4. Noel S, Brozna JP. Epithelial-myoe pithelial carcinoma of salivary gland with metastasis to lung: report of a case and review of the literature. Head Neck 1992;14:401–406.
5. G. Seifert and L. H. Sobin, “Epithelial-Myoe pithelial Carcinoma, in World Health Organization International Histo-logical Classification of Tumours,” Histological Typing of Salivary Gland Tumours, 2nd Edition, Springer-Verlag Berlin, 1991, pp. 23-24.
6. Luna MA, Ordenez NG, Mackay B, et al. Salivary epithelial-myoe pithelial carcinoma of intercalated ducts: a clinical, electron microscopic, and immunocytochemical study. Oral Surg Oral Med Oral Path 1985;59:482–490.
7. Seifert G, Brocheriou C, Cardesa A, Eveson JW. WHO International histological classification of tumours: tentative histological classification of salivary gland tumours. Pathol Res Pract 1990;186:555–581.
8. Micco AG, Shattuck MC, Wolff AP. Pathologic quiz case 2. Arch Otolaryngol Head Neck Surg 1991;117:926–929.
9. Ellis GI and Auclair PL: In: Malignant epithelial tumors. Tumors of the Salivary Glands. Rosai J (ed). Washington, DC: Armed Forces Institute of Pathology; pp. 268-289,1996.
10. Lau D P, Goddard M J, Bottrill I D and Moffat D A: Epithelialmyoe pithelial carcinoma of the parotid gland: an unusual cause of ear canal stenosis. J Laryngol Otol 110:493-495,1996.
11. Maurer MH, Gartenslager S and Dietrich C: Giant epithelialmyoe pithelial carcinoma of the parotid gland. Clin Imaging 33:237-239,2009.
12. Teppo H and Paronen I: Epithelial-myoe pithelial carcinoma in minor salivary gland of the hard palate. J Craniofac Surg 19:1689-1691,2008
13. Daley TD, Wysocki GP, Smout MS et al: Epithelialmyoe pithelial carcinoma of salivary glands. Oral Surg Oral Med Oral Pathol 57:512-519,1984.
14. Mills SE, Andrew GH and Augusto FGP: Salivary Glands In: Sternberg’s Diagnostic Surgical Pathology. Sternberg SS (ed.). Philadelphia: Lippincott Williams and Wilkins, pp. 950-951, 2004.
15. Corio RL, Sciubba JJ, Brannon RB et al: Epithelialmyoe pithelial carcinoma of intercalated duct origin. A clinicopathologic and ultrastructural assessment of sixteen cases, Oral Surg Oral Med Oral Pathol 53:280-287,1982.
16. Fonseca I, Felix A and Soares J: Dedifferentiation in salivary gland carcinomas. Am J Surg Pathol 24:469-471,2000.
17. Teppo H, Paronen I. Epithelial-myoe pithelial carcinoma in minor salivary gland of the hard palate. J Craniofac Surg 2008;19:1689-91.
18. Matos FR, Miranda JL, Mesquita AT, Santos CR, Freitas R de A. Epithelial-myoe pithelial carcinoma in the ventral surface of the tongue. Braz J Otorhinolaryngol 2010;76:540.
19. Yamada H, Kawaguchi K, Yagi M, Morita Y, Mishima K, Uno K et al. Epithelial-myoe pithelial carcinoma of the submandibular gland with a high uptake of 18F-FDG: a case report and image diagnosis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;104:243-8.
20. Kainuma K, Oshima A, Suzuki H, Fukushima M, Shimojo H, Usami S. Hybrid carcinoma of the parotid gland: report of a case (epithelial-myoe pithelial carcinoma and salivary duct carcinoma) and review of the literature. Acta Otolaryngol 2010;130:185-9.
21. Seethala RR, Barnes EL, Hunt JL. Epithelial-myoe pithelial carcinoma. A review of the clinicopathologic spectrum and immunopheno-typic characteristics in 61 tumors of the salivary glands and upper aerodigestive tract. Am J Surg Pathol 2007;31:44-57.
22. Yang S, Chen X. Epithelial-myoe pithelial carcinoma with high grade transformation. Int J Oral Maxillofac Surg 2012;41:810-3.
23. De Araújo VC, Altemani A, Furuse C, Martins MT, de Araújo NS. Immunoprofile of reactive salivary myoe pithelial cells in intraductal areas of carcinoma ex-pleomorphic adenoma. Oral Oncol 2006;42:1011-16.
24. Yang S, Chen X. Epithelial-myoe pithelial carcinoma with high grade transformation. Int J Oral Maxillofac Surg 2012;41:810-3.
25. Singh G, Sharma MC, Agarwal S, Prasad GL, Mishra S, Singh MM et al. Epithelial-myoe pithelial carcinoma of the lacrimal gland: a rare case. Ann Diagn Pathol 2012;16:292-7.
26. Peters P, Repanos C, Earnshaw J, Stark P, Burmeister B, McGuire L et al. Epithelial-myoe pithelial carcinoma of the tongue base: a case for the case-report and review of the literature. Head Neck Oncol 2010;2:2-4.
27. Teppo H, Paronen I. Epithelial-myoe pithelial carcinoma in minor salivary gland of the hard palate. J Craniofac Surg 2008;19:1689-91.
28. Yamada H, Kawaguchi K, Yagi M, Morita Y, Mishima K, Uno K et al. Epithelial-myoe pithelial carcinoma of the submandibular gland with a high uptake of 18F-FDG: a

- case report and image diagnosis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007;104:243-8.
29. Kainuma K, Oshima A, Suzuki H, Fukushima M, Shimojo H, Usami S. Hybrid carcinoma of the parotid gland: report of a case (epithelial-myoepithelial carcinoma and salivary duct carcinoma) and review of the literature. *Acta Otolaryngol* 2010;130:185-9.
 30. Seethala RR, Barnes EL, Hunt JL. Epithelial-myoepithelial carcinoma. A review of the clinicopathologic spectrum and immunophenotypic characteristics in 61 tumors of the salivary glands and upper aerodigestive tract. *Am J Surg Pathol* 2007;31:44-57.
 31. Cherian S, Kulkarni R, Bhat N. Epithelial-myoepithelial carcinoma in the hard palate: a case report. *Acta Cytol* 2010;54:835-9.
 32. De Araújo VC, Altemani A, Furuse C, Martins MT, de Araújo NS. Immunoprofile of reactive salivary myoepithelial cells in intraductal areas of carcinoma ex-pleomorphic adenoma. *Oral Oncol* 2006;42:1011-16.
 33. Voss PJ, Leow AM, Schulze D, Metzger MC, Liebehenschel N, Schmelzeisen R. Navigation-guided resection with immediate functional reconstruction for high-grade malignant parotid tumour at skull base. *Int J Oral Maxillofac Surg* 2009;38:886-90.
 34. Seifert G, Sobin LH. Epithelial-myoepithelial carcinoma. In: World Health Organization International Histological Classification of Tumours. *Histological Typing of Salivary Gland Tumours*. 2nd ed. Berlin: Springer-Verlag; 1991. p. 23-4.
 35. Rosai J. Major and minor salivary glands. In: Rosai J, editor. *Rosai and Ackerman's Surgical Pathology* (vol 1). 9th Ed. New Delhi: Mosby 2004. p. 873-916.
 36. Cheuk W, Chan JKC. Salivary gland tumors. In: Fletcher CDM, editor. *Diagnostic histopathology of tumors* (vol 1). 2nd Ed. London: Churchill Livingstone 2000. p. 231-311.
 37. Di Palma S, Guzzo M. Malignant myoepithelioma of salivary glands: Clinicopathological features of ten cases. *Virchows Arch A Pathol Anat Histopathol* 1993;423:389-96.
 38. Batsakis JG, El-Naggar AK. Myoepithelium in salivary and mammary neoplasms is host-friendly. *Adv Anat Pathol* 1999;6:218-26.
 39. R Chetty. Intercalated duct hyperplasia: possible relationship to epithelial-myoepithelial carcinoma and hybrid tumours of salivary gland *Histopathology*, 37 (2000), pp. 260–263.
 40. R.T Grenko, C.S Abendroth, A.T Davis, R.J Levin, I Dardick. Hybrid tumors or salivary gland tumors sharing common differentiation pathways? Reexamining adenoid cystic and epithelialmyoepithelial carcinomas *Oral. Surg. Oral. Med. Oral. Pathol.* 86 (1998), pp. 188–195.
 41. A King, A.T Ahuja, E To, C.K Chan, P.W Allen, I.J Witterick, et al. Carcinosarcoma of the parotid gland: ultrasound and computed tomography findings *Australasian Radiol.*, 43 (1999), pp. 520–522.
 42. A Silvers, P Som, M Brandwein. Epithelial-myoepithelial carcinoma of the parotid gland *AJNR*, 17 (1996), pp. 560–562.
 43. Bakshi J. Epithelial-Myoepithelial Carcinoma of Parotid Gland—A Surprising Clinical Entity. *Surg Sci*. 2012;03(05):274–8.
 44. Batsakis JG, el-Naggar AK, Luna MA. Epithelial-myoepithelial carcinoma of salivary glands. *Ann Otol Rhinol Laryngol*. 1992;101(6):540–2.
 45. T. A. Morrow TC and NM. Epithelial Myoepithelial Carcinoma of the Parotid Gland. *Ear, Nose Throat J*. 1990;69(9):646–8.
 46. Seifert G SL. Epithelial-myoepithelial carcinoma. In: World Health Organization International Histological Classification of Tumours. 2nd ed. Berlin: Springer-Verlag; 1991. 23-24 p.
 47. Donath K, Seifert G SR. Diagnosis and ultrastructure of the tubular carcinoma of salivary gland ducts. Epithelial-myoepithelial carcinoma of the intercalated ducts. *Virchows Arch A Pathol Anat* 1972;356:16–31. 1972;356:16–31.
 48. Morinaga S, Hashimoto S, Tezuka F. Epithelial-myoepithelial carcinoma of the parotid gland in a child. *Acta pathologica japonica*. 1992. p. 358–63.
 49. Goode RK, Corio RL. Oncocytic adenocarcinoma of salivary glands. *Oral Surg Oral Med Oral Pathol*. 1988;65(1):61–6.
 50. Friedrich RE DK. Epithelial-myoepithelial carcinoma of the parotid gland with multiple distant metastases: A case report. *J Oral Maxillofac Surg*. 2000;58:690–4.
 51. Luna MA, Batsakis JG, Ordóñez NG, Mackay B, Tortoledo ME. Salivary gland adenocarcinomas: a clinicopathologic analysis of three distinctive types. *Semin Diagn Pathol*. 1987;4(2):117–35.
 52. Barnes L, Eveson JW, Reichart P, Sidransky D. *Pathology and Genetics of Head and Neck Tumours* [Internet]. WHO Classification of Tumour. 2005. 163-175 p. Available from: Available from: <http://www.iarc.fr/en/publications/pdfs-online/pat-gen/bb9/index.php>.
 53. Di Palma S. Epithelial-myoepithelial carcinoma with coexisting multifocal intercalated duct hyperplasia of the parotid gland. *Histopathology*. 1994;25:494–6.
 54. Corio RL, Sciubba JJ, Brannon RB, Batsakis JG. Epithelial-myoepithelial carcinoma of intercalated duct origin. A clinicopathologic and ultrastructural assessment of sixteen cases. *Oral Surg Oral Med Oral Pathol*. 1982;53(3):280–7.
 55. King AD, Ahuja AT, To EWH, Chan ECK, Allen PW. Carcinosarcoma of the parotid gland: Ultrasound and computed tomography findings. *Australas Radiol*. 1999;43(4):520–2.
 56. Daley TD, Wysocki GP, Smout MS, Slinger RP. Epithelial-myoepithelial carcinoma of salivary glands. *Oral Surg Oral Med Oral Pathol*. 1984;57(5):512–9.
 57. Seifert G, Donath K. Multiple tumours of the salivary glands—terminology and nomenclature. *Eur J Cancer B Oral Oncol*. 1996;32B(1):3–7.
 58. V Tralongo ED. Epithelial-myoepithelial carcinoma of the salivary glands: a review of literature. *Anticancer Res.* 1998;18:603–8.
 59. A Silvers, P Som MB. Epithelial-myoepithelial carcinoma of the parotid gland. *AJNR Am J Neuroradiol*. 1996;17:560–2.
 60. Palmer RM. Epithelial-myoepithelial carcinoma: an immunocytochemical study. *Oral Surg Oral Med Oral Pathol*. 1985;59(5):511–5.