Salivary Gland Tumor “Wishes” to Add to the Next WHO Tumor Classification: Sclerosing Polycystic Adenosis, Mammary Analogue Secretory Carcinoma, Cribriform Adenocarcinoma of the Tongue and Other Sites, and Mucinous Variant of Myoepithelioma

Douglas R. Gnepp

Received: 6 January 2014 / Accepted: 21 January 2014 / Published online: 5 March 2014
© Springer Science+Business Media New York 2014

Abstract This review is a continuation of suggested tumor additions to the next WHO Tumor Classification. The author will focus on four salivary gland entities that have recently become accepted in the literature as new neoplastic entities: sclerosing polycystic adenosis, mammary analogue secretory carcinoma, cribriform adenocarcinoma of the tongue and other sites, and mucinous variant of myoepithelioma.

Keywords Myoepithelioma · Mucin · Salivary gland neoplasms · Polycystic adenosis · Secretory carcinoma · Cribriform adenocarcinoma

Introduction

The last World Health Organization (WHO) Head and Neck Tumor Classification was published in 2005. Since this time there have been several new entities described in the literature worthy of including in the next edition. This review will briefly describe four of these: sclerosing polycystic adenosis (SPA), mammary analogue secretory carcinoma, cribriform adenocarcinoma of the tongue and other sites, and the mucinous variant of myoepithelioma.

Sclerosing Polycystic Adenosis

Sclerosing polycystic adenosis (SPA) is a recently described, rare, reactive/neoplastic, inflammatory process of the major or minor salivary glands that is similar to fibrocystic changes, sclerosing adenosis and adenosis tumors of the breast. Both have cystic components with a prominent lobular or multilobular arrangement often with small, proliferating, closely packed ductal structures, surrounded by a peripheral myoepithelial layer. Similar to breast, the salivary gland tumors may be associated with ductal epithelial hyperplasia and atypia, ranging from mild dysplasia to severe dysplasia/carcinoma-in situ.

Smith et al. [1] first reported SPA in 1996, describing nine patients from the files of the Armed Forces Institute of Pathology. Since this report, there have been several smaller series and case reports with the largest series of 16 cases published by Gnepp et al. [2].

To date, there are 63 cases reported [1–13]. Patients range in age from 9 to 84 years with a male to female ratio of 27:36. Forty-six tumors involve the parotid gland, five the submandibular gland, nine various sites of the oral cavity, two the nasal cavity and one the lacrimal gland. Patients typically present with a slow growing mass with occasional tenderness, mild pain or a “tingling” sensation. On gross exam, tumors are firm, rubbery, well circumscribed and frequently are embedded in normal salivary gland. Occasional tumors are multinodular; one patient presented with two separate masses [6]. Tumors range from a few millimeters to 7 cm in greatest dimension at initial presentation.

Microscopically tumors are well circumscribed, with multiple, densely sclerotic, irregularly defined lobules composed of abundant hyalinized collagen surrounding variably sized collections of ducts with cystic change.

D. R. Gnepp
Department of Pathology, Warren Alpert School of Medicine of Brown University, Providence, RI, USA

D. R. Gnepp (✉)
Department of Pathology, Rhode Island Hospital, APC 12, 593 Eddy St., Providence, RI 02903, USA
e-mail: DGnepp@lifespan.org

Fig. 1 Sclerosing polycystic adenos: **a** focally encapsulated tumor with a prominent variably sized microcystic pattern. **b** Detail of “a”. Note variable sized dilated ducts in a fibrous stroma lined by thin attenuated ductal epithelium (*inset*). **c** An area of pseudoinfiltration with slightly irregular elongated ducts (sclerosing adenos-like) surrounding several variably sized, slightly dilated ducts. *Inset* demonstrates peripheral staining of myoepithelial cells (calponin stain). **d** Central duct filled with hyperplastic acinar type cells with an early microcystic pattern; adjacent ducts are lined and focally filled by cells with abundant clear to foamy cytoplasm. **e** Focal area with apocrine-type secretory changes with several smaller adjacent acini lined by cells containing eosinophilic zymogen-type granules. **f** Area with acinar cell dysplasia with cribriform-type growth and rigid bridging consistent with ductal carcinoma in situ. **g** Calponin stain demonstrating a myoepithelial layer around all ducts and solid nests. *Inset* higher power detail of an area with atypical solid growth, demonstrating a complete myoepithelial layer

Occasional tumors are composed of one large lobule with numerous ducts surrounded by prominent sclerosis. The density of ductal elements and degree of cystic change varies within and between cases with some cases having abundant fibrous stroma separating each of the ducts; other cases demonstrate more closely packed ductal elements,

including foci of closely packed small ductular elements similar to sclerosing adenos of the breast (Fig. 1). Rarely, the lobular architecture is somewhat effaced by the epithelial proliferation and marked fibrosis. Ducts may be lined by flattened to cuboidal epithelium. Hyperplasia of ductal and acinar elements and areas of apocrine-like

metaplasia are common (Fig. 1e). Mucin containing, squamous, sebaceous-like and ballooned cells occasionally line ducts and cystic spaces. Atrophic and normal salivary gland acini are frequently found between and inside of the lobules. Brightly eosinophilic, intracytoplasmic modified zymogen granules are found in some tubuloacinar structures (Fig. 1e). The intraluminal epithelial proliferation infrequently form a cribriform pattern, some of which is associated with nesting basement membrane-like material. Occasional cases demonstrate prominent areas of central intraductal necrosis and regions with prominent, atypical acinar cell proliferation with foci of a microcystic or solid pattern to a degree that mimics acinic cell carcinoma. These atypical foci contain dysplastic ductal epithelium ranging to severe dysplasia/carcinoma in situ (Fig. 1f). Although these areas are atypical, lobular architecture is always maintained and invasive growth is not found. Rarely, however, ductal distortion and atypia mimics an infiltrative pattern.

Immunohistochemistry demonstrates preservation of the lobular architecture with staining of the myoepithelial markers in the peripheral myoepithelial cells surrounding almost every ductal and acinar structure, whether or not they contain normal appearing, atypical or dysplastic cells (Fig. 1g). The staining is frequently continuous with occasional ducts having a discontinuous staining pattern, confirming the in situ nature of this process.

Follow-up information of ≥ 1 year is available in 52 cases. Five of these cases recurred (10 %), however, many of these patients have not been followed sufficiently to be able to establish long term chance of recurrence. To date, none of the patients reported have developed metastases or died secondary to disease. However, there was a recent poster presentation at the European Society of Pathology meeting in Lisbon [14] that documented a case of SPA with a long history of multiple recurrences with the last being an aggressive carcinoma and Michael Michael has seen one case of SPA with an associated malignancy (personal communication).

The etiology of SPA is still unknown. Recently Swelam [10] reported three cases of SPA that are associated with Epstein Barr virus and Skálová et al. [3] demonstrated that this is a clonal process. Therefore, SPA appears to be a neoplastic process that has histologic similarity to fibrocystic changes, sclerosing adenosis and adenosis tumors of the breast. Fifty-six percent of cases in this authors' original series had dysplastic changes consistent with a diagnosis of moderate to high-grade dysplasia/carcinoma-in situ [2]. Therefore, SPA should be considered a neoplasm with a low recurrence rate (approximately 10 %) and an even smaller chance of developing an associated carcinoma (approximately 2–3 %). If there is any diagnostic doubt about the correct diagnosis, careful histologic

examination looking for a lobular growth pattern and lack of invasion together with immunohistochemical staining, to confirm the presence of a peripheral myoepithelial cell layer, will avoid an erroneous diagnosis of malignancy.

Cribriform Adenocarcinoma of the Tongue and Other Minor Salivary Glands

Cribriform adenocarcinoma of the tongue and other minor salivary glands (CATS), also referred to as cribriform adenocarcinoma of minor salivary gland origin, is a rare, recently recognized entity. It was first described in 1999 as a unique tumor [15], although there are two earlier case reports of “tubular adenocarcinoma” of the tongue [16] and of “papillary adenocarcinoma” of the tongue [17] that are likely this entity. Since this initial report there has been one additional case report [18] and the largest series of these lesions to date (23 cases), was recently published [19]. The most common site of presentation is the tongue (74 %) with 9 % each involving the palate and tonsil area; 8 % arise in other intraoral sites. The mean age at presentation is 53.4 with a range of 5–85 years. These low-grade malignant tumors initially were thought to occur exclusively in the tongue, usually on the posterior one-third. However, the series by Skálová et al. indicates that they arise in other minor salivary gland sites, including the palate, retromolar triangle area, tonsils and upper lip. Initially they were thought to arise from a thyroglossal duct anlage [15], but currently are believed to arise from the minor salivary glands. Clinically, CATS is an infiltrative, poorly circumscribed tumor generally presenting as a submucosal mass, which infiltrates skeletal muscles and adjacent tissues, although a pedunculated lesion at the tongue base has been described [18]. A consistent clinical finding of CATS is early metastases into the cervical lymph nodes. 71 % of the 34 patients presented with cervical lymph node metastases at or very close to initial presentation and one developed late cervical lymph node metastases. No patients have developed distant metastasis to date and all patients with follow-up are alive and well without disease except for one patient who has a recurrent palatal tumor.

Treatment should be directed toward complete surgical excision with good margins; the neck should be surgically treated if there is evidence of metastatic spread/lymphadenopathy. The majority of patients have also received adjuvant radiation therapy. Chemotherapy has not been used.

Tumors are unencapsulated and may range up to 8 cm in greatest dimension. This carcinoma is arranged in lobules separated by fibrous septae with infiltration into the surrounding tissues. Both solid and microcystic growth

Fig. 2 Cribriform adenocarcinoma of the tongue and other sites: **a** multinodular submucosal infiltrating carcinoma composed of sheets of tumor with a microcystic growth pattern, focal solid areas and areas with intraluminal mucinous secretions. **b** Detail of “a”. There is mild nuclear pleomorphism and irregular ductal spaces, some of

which contain mucinous secretions. **c** Cribriform and solid areas surrounded by eosinophilic, prominent basement membrane-type material. **d** Solid area with mild nuclear pleomorphism and prominent nuclear clearing. *Inset* higher power detail of nuclei

patterns are present. The solid component often exhibits a hyperchromatic, palisaded peripheral layer, which frequently detaches from the tumor nest creating a papillary appearance. Rarely, spindling of the cells in the solid pattern has been described. The microcystic growth pattern of CATS exhibits both tubular and cribriform patterns that can be admixed (Fig. 2). Within the lumina of the tubules, mucin can be noted, which is positive when stained with alcian blue, pH 2.5, but negative for PAS and mucicarmine. Hyalinization of the stroma may occur, and in these areas the tumor cells are arranged in cords and single tubules. Although different growth patterns are appreciated in CATS, cytologically the tumor is composed of one cell type. The cytoplasm ranges from clear to oxyphilic, containing a pale, vesicular nuclei with a ground glass quality. The nuclei often overlap similar to papillary carcinoma of the thyroid. Necrosis and hemorrhage are not usual features of CATS, and mitotic figures are rare. Lymph node metastases are histologically identical to the primary tumor. CATS is strongly immunoreactive to cytokeratin markers AE1/AE3, CAM 5.2, CK7, CK8, and CK18. S100 protein immunoreactivity is usually strong but may be patchy. C-kit (CD117) stained all tumors but is more variable; basal and myoepithelial markers are also positive but

to a lesser extent and with greater variability. The proliferative activity of these tumors is low, averaging <4 %. Thyroglobulin and TTF antibody staining is negative.

Because of the prominent microscopic feature of overlapping nuclei with ground glass appearance, the differential diagnosis of CATS would include papillary thyroid carcinoma, either metastatic or from lingual thyroid. Clinically, papillary thyroid carcinoma also exhibits early metastatic spread to the cervical lymph nodes similar to CATS. However, CATS is always thyroglobulin negative and lacks colloid. Ultrastructural studies have also demonstrated myoepithelial differentiation in CATS. Polymorphous low-grade adenocarcinoma (PLGA) and the solid variant of adenoid cystic carcinoma would also be considered in the differential diagnosis of CATS. The nuclear morphology of CATS is very different from the hyperchromatic angulated nuclei seen in adenoid cystic carcinoma. Generally the solid variant of adenoid cystic carcinoma will also have more frequent mitoses. PLGA does share some histologic similarities with CATS, however, PLGA has a more diverse histology than CATS, and lacks the ground glass nuclei. Finally, early metastases to cervical lymph nodes are not a common feature of PLGA.

Mammary Analogue Secretory Carcinoma of the Salivary Glands

Secretory carcinoma of the breast, which is also referred to as juvenile carcinoma, is a rare breast tumor predominantly arising in children or young adults; occasional cases have also been reported in adults. Four years ago, a series of 16 histologically similar carcinomas was reported in the salivary glands by Skalova et al. [20]. Both of these tumors have the same chromosomal translocation, $t(12;15)(p13;q25)$, which leads to a fusion gene between the ETV6 gene on chromosome 12 and the NTRK3 gene on chromosome 15, which has not been found in other salivary gland tumors [20, 27]. These tumors were termed mammary analogue secretory carcinomas (MASC). Since this initial report, there have been approximately 100 additional cases published [21–40]. These have been previously diagnosed as unusual variants of acinic cell carcinoma, adenoid cystic carcinoma, cystadenocarcinoma, mucoepidermoid carcinoma or adenocarcinoma, NOS.

The mean age at presentation is 47 years (range 13–78); there is a slight male predominance. Approximately 60 % arose in the parotid gland, 30 % in the oral cavity, 9 % in the submandibular gland and 1 tumor arose in an accessory parotid gland. The majority of patients describe slow growing tumors over a several year period; however, a

significant percentage describe recent rapid growth. Mean tumor size is 1.7–2.1 cm with a range from 0.2 to 5.5 cm. Grossly tumors are circumscribed but not encapsulated and frequently infiltrated adjacent tissues. Histologically tumors are made up of solid, microcystic, tubular and, focally, micropapillary structures containing cells with vesicular nuclei, finely granular chromatin, centrally located nucleoli and pale, eosinophilic, granular or vacuolated cytoplasm (Fig. 3). Cellular atypia is mild and mitotic figures are usually infrequent; perineural invasion is noted in a few tumors. Tumor necrosis and vascular invasion are not found. Bubbly secretory material, that was PAS-Diastase and mucicarmine positive, is present within microcystic and tubular spaces (Fig. 3c). Strong diffuse S100 and staining with Vimentin, CK7, CK8, CK18, CK19, Mammaglobin, Stat 5a and EMA are usually found; MUC1 and MUC4 are frequently positive. Calponin, p63, CK14, CK5/6, EGFR, c-erbB-2, ER/PR, AR are typically negative. The proliferative rate ranges from 5 to 28 % [20]. Several recent studies demonstrated that the combination of S100, mammaglobin and especially large vacuole adipophilin staining is very helpful to eliminate almost all of the other differential diagnostic mimics of mammary analogue secretory carcinoma [24, 27, 30, 39]. This latter stain is important, as occasionally mammaglobin, similar to acinic cell carcinoma, is only focally positive in MASC.

Fig. 3 Mammary analogue secretory carcinoma: **a** infiltrating multinodular tumor separated by fibrous bands. **b** Area with a microcystic pattern and prominent intraluminal secretory material. **c** Detail of

“**b**”; note mild nuclear pleomorphism and atypia with prominent intraluminal secretory material. **d** Area with a micropapillary pattern, mild nuclear pleomorphism and atypia

Fig. 4 Mucinous variant of myoepithelioma: **a, b** encapsulated myoepithelioma composed of sheets of mildly pleomorphic cells with epithelioid/polygonal and plasmacytoid growth patterns. Note scattered cells with abundant intracytoplasmic mucin (**b**, lower right).

c A mucicarmine stain demonstrates abundant intracellular mucin material. **d, e** Keratin cocktail and S100 immunohistochemical stains, respectively. The tumor also stained for SMA and GFAP; dendritic cell markers were negative (not shown)

Up to 20 % of patients develop local recurrences, which rarely may extend to the temporal bone. Approximately 20 % of MASC metastasize to the cervical lymph nodes and 5 % spread to distant sites, including pleura, lung and pericardium [21]. The overall mortality is approximately 5 %; tumors that present with a higher stage are usually more aggressive and have a worse prognosis. Four cases have been associated with high-grade transformation [21, 29]. These latter tumors are larger than typical MASC, reported up to 8 cm in greatest dimension. MASC without high-grade transformation appears to be a low to intermediate grade neoplasm capable of aggressive local growth and metastatic spread. The treatment should be wide local excision with radiation added for larger/higher stage tumors. Tumors with high-grade transformation are associated with an accelerated clinical course and a poor outcome [21].

Mucinous Myoepithelioma: A New Myoepithelioma Variant

Myoepithelial neoplasms are tumors composed almost exclusively of cells with myoepithelial differentiation.

They frequently contain spindle, plasmacytoid or epithelioid shaped cells and may have oncocytic or clear cytoplasmic features. They are uncommon, accounting for 1.5 % of all salivary gland tumors and for 2.2–5.7 % of major and minor salivary gland tumors, respectively [41]. Recently this author, together with several colleagues, described three unusual myoepithelial tumors, two benign parotid tumors and one malignant palatal tumor that contained abundant intracellular mucin material, which was termed the mucinous variant of myoepithelioma [42]. Tumor cells have abundant eosinophilic to foamy grayish-blue cytoplasm, often containing intracellular mucin, mild nuclear pleomorphism, fine peppery chromatin and inconspicuous nucleoli (Fig. 4). One benign tumor stains for cytokeratin, smooth muscle actin (SMA), S-100 and glial fibrillary acidic protein (GFAP) (Fig. 4c, d), while the second is positive for calponin, smooth muscle myosin heavy chain, p63, S-100 and CAM 5.2. The malignant tumor is positive for calponin, cytokeratin cocktail, S-100, CK7, polyclonal carcinoembryonic antigen (focal) and GFAP.

A careful literature review found 12 similar tumors, all published as signet ring carcinomas [43–46]; all of these,

except for one tumor, have myoepithelial differentiation. In addition to these 12 cases, there are two previously published similar appearing benign tumors arising on the lip with abundant intracellular mucin and areas of plasmacytoid differentiation, but without documented myoepithelial characteristics [47, 48]. As plasmacytoid myoepitheliomas are known to occasionally not stain with myoepithelial markers [49; personal experience], it is likely that these two tumors also are mucinous myoepitheliomas.

To date, there are 17 mucinous myoepitheliomas reported; 13 arose in minor salivary glands, most frequently the palate and four in the parotid gland; the male to female ratio is approximately equal. Four are classified as benign tumors and 13 as malignant. One patient presented with a lymph node metastasis. Tumors ranged in size from 1 to 5 cm and all were treated by surgical excision. Follow-up information is available on only five patients, ranging from 5 months to 8 years; all are alive and well. To date, this appears to be a benign to low-grade malignancy. However, more experience with this unusual tumor is necessary to better understand its biologic behavior. One should use the same histologic criteria for this tumor to evaluate for malignancy as any other myoepithelioma, i.e. encapsulation, circumscription, destructive peripheral growth, mitotic and proliferative rates, neural invasion, tumor necrosis, and degree of pleomorphism, to decide whether or not it is benign or malignant.

References

- Smith BC, Ellis GL, Slater LJ, Foss RD. Sclerosing polycystic adenosis of major salivary glands: a clinicopathologic analysis of nine cases. *Am J Surg Pathol*. 1996;20:161–70.
- Gnepp DR, Wang LJ, Brandwein-Gensler M, et al. Sclerosing polycystic adenosis of the salivary gland. *Am J Surg Pathol*. 2006;30:154–64.
- Skálová A, Gnepp DR, Simpson RH, et al. Clonal nature of sclerosing polycystic adenosis of salivary glands demonstrated by using the polymorphism of the human androgen receptor (HUMARA) locus as a marker. *Am J Surg Pathol*. 2006;30:939–44.
- Eliot CA, Smith AB, Foss RD. Sclerosing polycystic adenosis. *Head Neck Pathol*. 2012;6:247–9.
- Park IH, Hong SM, Choi H, et al. Sclerosing polycystic adenosis of the nasal septum: the risk of misdiagnosis. *Clin Exp Otorhinolaryngol*. 2013;6:107–9.
- Petersson F, Tan PH, Hwang JS. Sclerosing polycystic adenosis of the parotid gland: report of a bifocal, paucicystic variant with ductal carcinoma in situ and pronounced stromal distortion mimicking invasive carcinoma. *Head Neck Pathol*. 2011;5:188–92.
- Kim BC, Yang DH, Kim J, et al. Sclerosing polycystic adenosis of the parotid gland. *J Craniofac Surg*. 2012;23:e451–2.
- Tokyo C, Aktepe F, Hastürk GS, et al. Sclerosing polycystic adenosis of the parotid gland presenting with a Warthin tumor. *Kulak Burun Bogaz Ihtis Derg*. 2012;22:288–92.
- Su A, Bhuta SM, Berke GS, Lai CK. A unique case of sclerosing polycystic adenosis of the sinonasal tract. *Hum Pathol*. 2013;44:1937–40.
- Swelam W. The pathogenic role of Epstein–Barr virus (EBV) in sclerosing polycystic adenosis. *Pathol Res Pract*. 2010;206:565–71.
- Beato Martínez A, Moreno Juara A, Candia Fernández A. Sclerosing polycystic adenosis of the submandibular gland. *Acta Otorrinolaringol Esp*. 2013;64:78–80.
- Pfeiffer ML, Yin VT, Bell D, et al. Sclerosing polycystic adenosis of the lacrimal gland. *Ophthalmology*. 2013;120:873–873.e1.
- Petersson F. Sclerosing polycystic adenosis of salivary glands: a review with some emphasis on intraductal epithelial proliferations. *Head Neck Pathol*. 2013;7(Suppl 1):S97–106.
- Canas Marques A, Felix A. Invasive carcinoma arising in sclerosing polycystic adenosis of the salivary gland. *European Society of Pathology Meeting Lisbon, Portugal, Poster number PS-03-015*, 31 Aug to 4 Sept 2013.
- Michal M, Skálová A, Simpson RHW, et al. Cribriform adenocarcinoma of the tongue: a hitherto unrecognized type of adenocarcinoma characteristically occurring in the tongue. *Histopathology*. 1999;35:495–501.
- Yajima M, Yamazaki T, Minemura T, Kotani A. Tubular adenocarcinoma of the apex of the tongue. *J Oral Maxillofac Surg*. 1989;47:86–8.
- Crocker TP, Kreutner A, Otherson HB, Garvin J. Papillary adenocarcinoma of minor salivary gland origin in a child. *Arch Otolaryngol*. 1983;109:827–31.
- Prasad KC, Kaniyur V, Pai RR, Nesari SS. Pedunculated cribriform adenocarcinoma of the base of the tongue. *ENT-Ear Nose Throat J*. 2004;83:62–4.
- Skalova A, Sima R, Kaspirkova-Nemcova J, et al. Cribriform adenocarcinoma of minor salivary gland origin principally affecting the tongue: characterization of new entity. *Am J Surg Pathol*. 2011;35:1168–76.
- Skalova A, Vanecek T, Sima R, et al. Mammary analogue secretory carcinoma of salivary glands, containing the *ETV6-NTRK3* fusion gene: A hitherto undescribed salivary gland tumor entity. *Am J Surg Pathol*. 2010;34:599–608.
- Skálová A, Vanecek T, Majewska H, et al. Mammary analogue secretory carcinoma of salivary glands with high-grade transformation: report of 3 cases with the *ETV6-NTRK3* gene fusion and analysis of TP53, β -catenin, EGFR, and CCND1 genes. *Am J Surg Pathol*. 2014;38:23–33.
- Patel KR, Solomon IH, El-Mofty SK, Lewis JS Jr, Chernock RD. Mammaglobin and S-100 immunoreactivity in salivary gland carcinomas other than mammary analogue secretory carcinoma. *Hum Pathol*. 2013;44:2501–8.
- Hwang MJ, Wu PR, Chen CM, Chen CY, Chen CJ. A rare malignancy of the parotid gland in a 13-year-old Taiwanese boy: case report of a mammary analogue secretory carcinoma of the salivary gland with molecular study. *Med Mol Morphol*. 18 Aug 2013. (Epub ahead of print).
- Mariano FV, Dos Santos HT, Azañero WD, et al. Mammary analogue secretory carcinoma of salivary glands is a lipid-rich tumour, and adipophilin can be valuable in its identification. *Histopathology*. 17 May 2013. doi:10.1111/his.12192. (Epub ahead of print).
- Woo J, Seethala RR, Sirintrapun SJ. Mammary analogue secretory carcinoma of the parotid gland as a secondary malignancy in a childhood survivor of atypical teratoid rhabdoid tumor. *Head Neck Pathol*. 7 Aug 2013. (Epub ahead of print).
- Skalova A. Mammary analogue secretory carcinoma of salivary gland origin: an update and expanded morphologic and immunohistochemical spectrum of recently described entity. *Head Neck Pathol*. 2013;7(Suppl 1):S30–6.
- Bishop JA, Yonescu R, Batista D, et al. Utility of mammaglobin immunohistochemistry as a proxy marker for the *ETV6-NTRK3* translocation in the diagnosis of salivary mammary analogue secretory carcinoma. *Hum Pathol*. 2013;44:1982–8.

28. Williams L, Chiosea SI. Mammary analogue secretory carcinoma mimicking salivary adenoma. *Head Neck Pathol.* 2013;7:316–9.
29. Jung MJ, Song JS, Kim SY, et al. Finding and characterizing mammary analogue secretory carcinoma of the salivary gland. *Korean J Pathol.* 2013;47:36–43.
30. Bishop JA. Unmasking MASC: bringing to light the unique morphologic, immunohistochemical and genetic features of the newly recognized mammary analogue secretory carcinoma of salivary glands. *Head Neck Pathol.* 2013;7:35–9.
31. Griffith CC, Stelow EB, Saqi A, et al. The cytological features of mammary analogue secretory carcinoma: a series of 6 molecularly confirmed cases. *Cancer Cytopathol.* 2013;121:234–41.
32. Bishop JA, Yonescu R, Batista DA, Westra WH, Ali SZ. Cytopathologic features of mammary analogue secretory carcinoma. *Cancer Cytopathol.* 2013;121:228–33.
33. Levine P, Fried K, Krevitt LD, Wang B, Wenig BM. Aspiration biopsy of mammary analogue secretory carcinoma of accessory parotid gland: another diagnostic dilemma in matrix-containing tumors of the salivary glands. *Diagn Cytopathol.* 2014;42:49–53.
34. Chiosea SI, Griffith C, Assaad A, Seethala RR. Clinicopathological characterization of mammary analogue secretory carcinoma of salivary glands. *Histopathology.* 2012;61:387–94.
35. Fehr A, Löning T, Stenman G. Mammary analogue secretory carcinoma of the salivary glands with ETV6-NTRK3 gene fusion. *Am J Surg Pathol.* 2011;35:1600–2.
36. Rastatter JC, Jatana KR, Jennings LJ, Melin-Aldana H. Mammary analogue secretory carcinoma of the parotid gland in a pediatric patient. *Otolaryngol Head Neck Surg.* 2012;146:514–5.
37. Petersson F, Lian D, Chau YP, Yan B. Mammary analogue secretory carcinoma: the first submandibular case reported including findings on fine needle aspiration cytology. *Head Neck Pathol.* 2012;6:135–9.
38. Griffith C, Seethala R, Chiosea SI. Mammary analogue secretory carcinoma: a new twist to the diagnostic dilemma of zymogen granule poor acinic cell carcinoma. *Virchows Arch.* 2011;459:117–8.
39. Connor A, Perez-Ordóñez B, Shago M, et al. Mammary analog secretory carcinoma of salivary gland origin with the ETV6 gene rearrangement by FISH: expanded morphologic and immunohistochemical spectrum of a recently described entity. *Am J Surg Pathol.* 2012;36:27–34.
40. Sethi R, Kozin E, Remenschneider A, et al. Mammary analogue secretory carcinoma: update on a new diagnosis of salivary gland malignancy. *Laryngoscope.* 2014;124:188–95.
41. Ellis GL, Auclair PL. Atlas of tumor pathology: tumors of the salivary glands. Benign epithelial neoplasms. Armed Forces Institute of Pathology, Washington, DC, p 57, 1996.
42. Esteva CJ, Slater LJ, Gnepp DR. Mucinous myoepithelioma, a previously unrecognized variant. *Mod Pathol.* 2012; 25(Suppl 2): 308A, 1297.
43. Ghannoun JE, PD Freedman PD. Signet-ring cell (mucin-producing) adenocarcinomas of minor salivary glands. *Am J Surg Pathol.* 2004;28:89–93.
44. Singh M, Khurana N, Wadhwa R, Gulati A. Signet ring carcinoma parotid gland: a case report. *Head Neck.* 2011;33:1656–9.
45. Bastaki J, Summersgill K. Signet-ring cell (mucin-producing) adenocarcinoma of minor salivary glands: report of a case. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2010;110:e33–6.
46. Bastaki JM, Purgina BM, Dacic S, Seethala RR. Primary signet-ring cell (mucin-producing) adenocarcinoma of minor salivary glands: a clinicopathologic, immunohistochemical and molecular survey. *Mod Pathol.* 2012; 25(Suppl 2):304A, 1279.
47. Zamecnik M, Gogora M. Signet-ring cells simulating carcinomas in minor salivary gland of the lip. *Pathol Res Pract.* 1999;195: 723–4.
48. Foschini MP, Baldovini C, Pennesi MG, Cocchi R, Simpson RH. Signet ring cell tumor of the minor salivary gland exhibiting benign behavior. *Hum Pathol.* 2012;43:303–6.
49. Franquemont DW, Mills SE. Plasmacytoid monomorphic adenoma of salivary glands. Absence of myogenous differentiation and comparison to spindle cell myoepithelioma. *Am J Surg Pathol.* 1993;17:146–53.