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Case Report

Low-grade cribriform cystadenocarcinoma of the parotid gland: a case report and review of literature

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Abstract: Low-grade cribriform cystadenocarcinoma (LGCCC), also known as low-grade salivary duct carcinoma and low-grade intraductal carcinoma, is an exceedingly uncommon neoplasm of salivary glands. It is characterized by cystic, papillary, and cribriform proliferation that histologically resembles atypical ductal hyperplasia and low-grade ductal carcinoma in situ of the breast. The authors herein report an additional case of LGCCC of the parotid gland. A 42-year-old man presented with a slowly enlarging, painless mass on his right postauricular region that had been present for ten years. Computed tomography showed a relatively well-circumscribed, multicystic mass, measuring 2.5 × 2.7 × 3.5 cm in the right parotid gland. The patient underwent a subtotal parotidectomy with preservation of the facial nerve. Microscopically, the tumor had a typical feature of intraductal growth pattern composed of low-grade ductal epithelial cells with cribriform, micropapillary, or solid patterns. Immunohistochemically, the tumor cells showed diffuse expression of CK AE1/AE3, CK7, vimentin, S100, mammaglobin, and SOX10. Tumor cells were negative for DOG1, androgen receptor, p53, CD117 and Her-2. Immunostaining for myoepithelial markers (p63, p40, smooth muscle actin, HHF35 and calponin) displayed a continuous rim of myoepithelial cells around all tumor cysts and ducts. There were no signs of local recurrence or metastasis at his 14-month follow-up.

Keywords: Low-grade cribriform cystadenocarcinoma, low-grade salivary duct carcinoma, low-grade intraductal carcinoma, parotid gland

Introduction

Low-grade cribriform cystadenocarcinoma (LGCCC) of the salivary gland is a relatively recently described neoplasm that histologically resembles atypical ductal hyperplasia and low-grade ductal carcinoma in situ of the breast [1]. It is characterized by predominant intraductal growth, luminal ductal phenotype, bland microscopic features, and favorable clinical behavior. This entity was originally designated as low-grade salivary duct carcinoma and considered to be a variant of salivary duct carcinoma by Delgado et al. in 1996 [2]. However, the 2005 World Health Organization Classification of Head and Neck Tumors adopted the term LGCCC and regarded it as a variant of cystadenocarcinoma [1]. These tumors have been also referred as low-grade intraductal carcinomas in the literature [3]. Their relationship to cystadenocarcinomas and conventional salivary duct carcinomas remains unclear, and controversy in terminology has yet to be resolved [3].

The incidence of LGCCC is difficult to ascertain, but it seems to be a very rare tumor. Few cases have been published so far, and most histopathologists are not familiar with this entity. The authors herein report an additional case of LGCCC of the parotid gland in a 42-year-old man. The clinicopathologic and immunohistochemical features of this neoplasm, together with its main differential diagnoses are discussed.

Case report

A 42-year-old man presented with a slowly enlarging, painless mass on his right postauricular region that had been present for ten

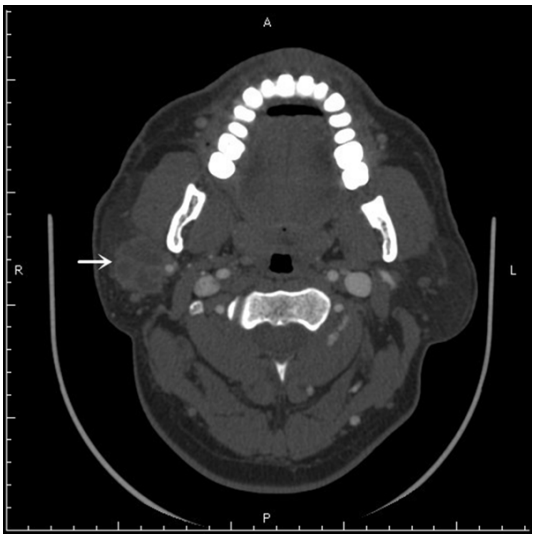

Figure 1. Axial computed tomography showing a relatively well-circumscribed, multicystic mass in the right parotid gland (arrow).

years. The patient reported a 10-year history of smoking (2 packs per day) with no alcohol consumption. The patient's past medical history included hypertension and hyperlipemia. His family history was unremarkable. The clinical examination showed movable firm nodule measuring 4 cm. No skin abnormalities were noted. There was no facial palsy or palpable lymphadenopathy. Routine hematologic and biochemical examination, chest radiograph, and abdomen ultrasound appeared normal. Computed tomography (CT) showed a relatively well-circumscribed, multicystic mass, measuring 2.5 × 2.7 × 3.5 cm in the right parotid gland (**Figure 1**). The lesion had a smooth and uniform enhancing wall and thin internal septation. A subtotal parotidectomy with preservation of the facial nerve was performed following a clinical diagnosis of benign parotid gland lesion.

Grossly, the surgical specimen measured 5.5 cm in the greatest diameter. On cut surface, it showed a well-circumscribed tumor with cystic spaces of varying size filled by gelatinous content or hemorrhagic fluid. The tumor was grayish-yellow in color. Microscopically, a well-circumscribed but nonencapsulated tumor was found within the atrophic parotid tissue with extensive fibrosis. The tumor was composed of large cystic ducts of variable diameter admixed with smaller proliferating ducts (**Figure 2A**). The larger cystic structures were lined mainly by a thick layer of proliferating, bland ductal cells forming a cribriform pattern or anastomosing, intracystic micropapillae with alternating areas of single layer or multilayered flat, low-cuboidal cells. The separate smaller ductal structures were variably filled with papillary ductal epithelium creating a solid to cribriform pattern occasionally characterized by "Roman Bridge" formations (**Figure 2B**). The tumor cells are small to medium sized with pale to eosinophilic cytoplasm. The nuclei were oval or round with finely dispersed to vesicular chromatin and inconspicuous or small nucleoli (**Figure 2C**). No mitoses were seen. Apocrine differentiation with apical snouts and cytoplasmic microvacuoles were present in some ductal cells. Some tumor cells contained intracytoplasmic mucus or lipofuscin-like, yellow to brown pigments. Necrosis was absent. A layer of flat, thin, or elongated myoepithelial cells beneath neoplastic ductal cells was visible at the periphery of some ducts and cysts (**Figure 2D**). No evidence of invasion was seen. Hemorrhage, abundant foam cells, cholesterol clefts, and hemosiderin were present within the dense hyalinized stroma. Immunohistochemically, the tumor cells showed diffuse expression of cytokeratin (CK) AE1/AE3, CK7 (**Figure 3A**), vimentin (**Figure 3B**), S100 (**Figure 3C**), mammaglobin (**Figure 3D**), and SOX10 (**Figure 4A**). Tumor cells were negative for DOG1, androgen receptor, p53, CD117/c-kit and Her-2. Ki67 index was less than 1% (**Figure 4B**). In addition, immunostaining for myoepithelial markers, such as p63, p40 (**Figure 4C**), smooth muscle actin, HHF35 and calponin (**Figure 4D**), displayed a continuous rim of myoepithelial cells around all tumor cysts and ducts.

On the basis of these histological and immunohistochemical features, the final diagnosis of LGCCC was established. The patient's postoperative course was uneventful. There were no signs of local recurrence or metastasis at his 14-month follow-up.

Discussion

LGCCC is an exceedingly rare neoplasm. To date, only 51 cases, including the present case, have been reported in the English literature (**Table 1**) [2, 4-24]. 28 tumors occurred in women, 22 tumors occurred in men, and, in 1 tumor, the sex of the patient was not stated [8]. The reported mean age at presentation was

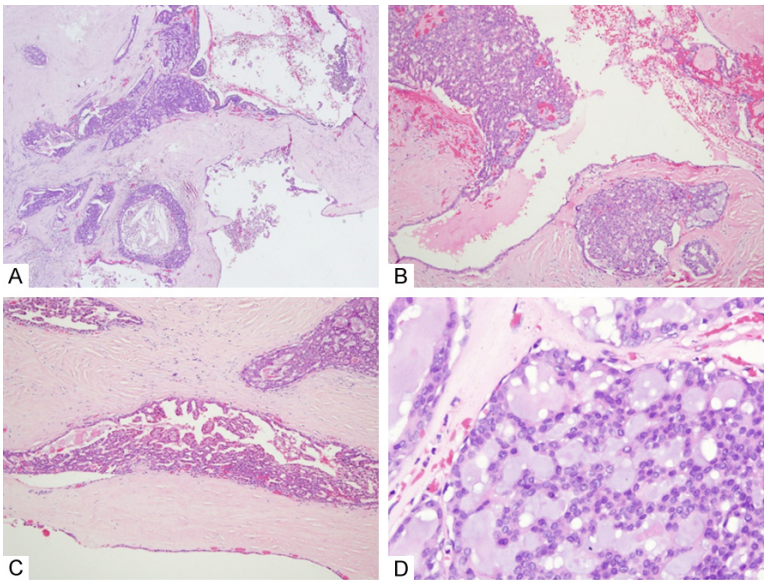

Figure 2. Histopathological findings. A. Low magnification shows multiple cysts of variable size and smaller ducts with intraductal proliferations (hematoxylin-eosin, × 40); B. The large cyst is lined by a thick layer of proliferating ductal cells forming anastomosing, cribriform pattern with alternating areas of single layer flat, low-cuboidal cells (hematoxylin-eosin, × 100); C. The tumor cells exhibit a cribriform architecture with intracystic micropapillae (hematoxylin-eosin, × 100); D. High magnification shows tumor cells with low-grade round to oval nuclei and eosinophilic cytoplasm. An attenuated layer of myoepithelial cells could be clearly identified around some of the tumor nests (hematoxylin-eosin, × 400).

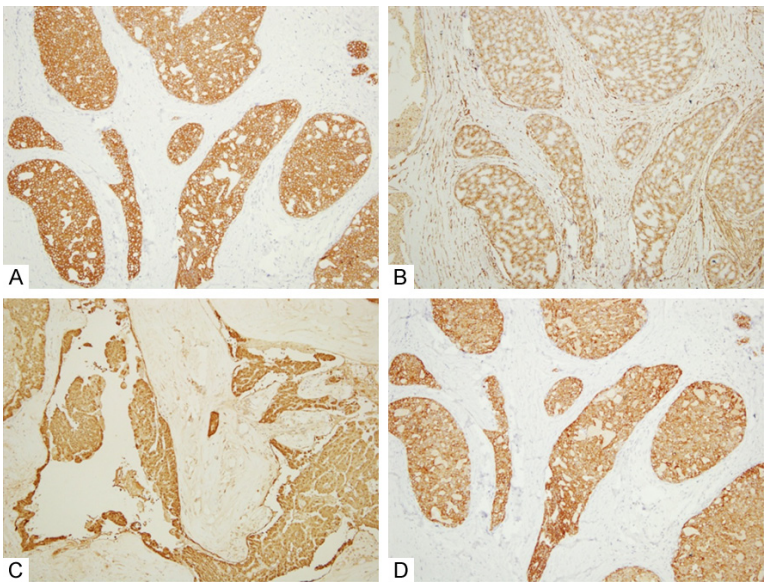

Figure 3. Tumor cells showed strong and diffuse immunoreactivity for CK7 (A), vimentin (B), S100 (C), and mammaglobin (D) (× 100).

60.3 years (range, 27-93 years). The primary location was the parotid in 44 (86.3%) tumors with 2 arising in intraparotid lymph nodes, accessory parotid gland in 1 tumor (2%), submandibular gland in 2 tumors (3.9%), and the minor salivary glands of the oral cavity in 4 (7.8%) tumors. The initial symptom at presentation was usually an asymptomatic and slow growing mass. No facial nerve paralysis has been recorded in any patient although one patient complained of paresthesia along the upper neck and ear [9]. The duration of the symptoms before presentation ranged from 2 weeks to 38 years. The tumor size varied from 0.7 to 5.3 cm. Most of the cases were treated with local excision without radiotherapy. All but one case have neither tumor recurrences nor evidence of regional or distant metastases after 3 months to 19 years. The exception transformed to a higher grade neoplasm and developed cervical nodal metastases [9]. This patient remains well with no recurrent disease 91 months after surgery. Thus, conservative resection of the involved gland, without neck dissection or adjuvant radiotherapy is adequate treatment, unless there is histological evidence of higher grade change.

Histologically, LGCCC is a well-circumscribed unencapsulated mass composed of single or multiple cysts with an intraductal proliferation. The cysts are lined by small, multilayered, proliferating, bland ductal cells. Within the cystic areas, they typically are arranged in a cribriform pattern and frequently have anastomosing, intracystic micropapillae lining the cavity, which may contain fibrovascular cores. Separate, smaller ductal structures are variably filled by proliferating ductal epithe-

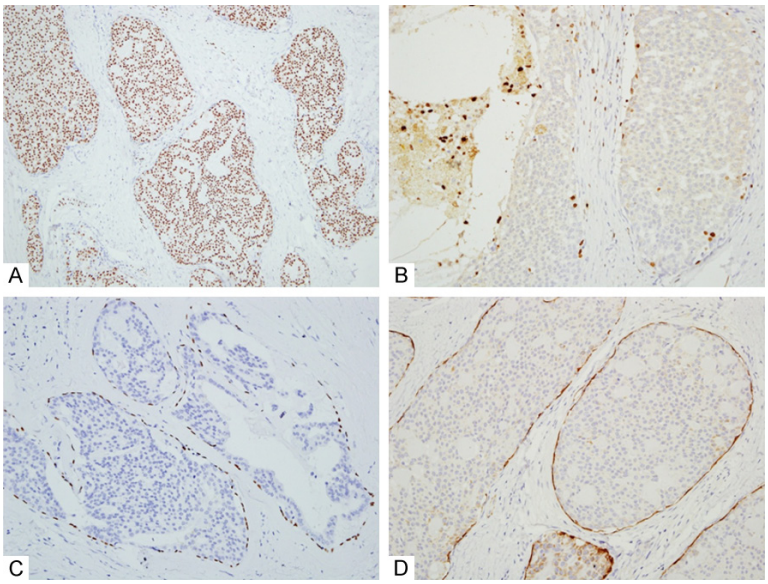

Figure 4. A. Tumor cells were diffusely positive for SOX10 (× 100); B. Ki67 index was less than 1% (× 100); C. P40 was positive only in myoepithelial cells along the periphery of tumor nests (× 200); D. Calponin highlighted the continuous rim of myoepithelial cells surrounding the tumor nests (× 200).

lium with cribriform, micropapillary and solid areas. The tumor cells are small to medium sized with indistinct cell borders, pale to eosinophilic cytoplasm, and round to oval nuclei, which may contain finely dispersed or dark condensed chromatin. Prominent nucleoli are absent in the majority of the cells but small eosinophilic nucleoli can be seen. Mitotic rate is low. Very few neoplastic cells contain lipofuscin pigment in the cytoplasm. Apocrine differentiation with apical snouts and cytoplasmic microvacuoles is occasionally present. The stroma is often sclerotic and exhibits secondary changes such as haemorrhage, chronic inflammatory infiltrate and dystrophic calcification. Perineural and/or angiolymphatic invasion and necrosis are absent. Five reported cases of LGCCC demonstrated limited areas of transition to higher cytologic grade including necrosis [2, 4, 8, 9]. Most neoplastic islands are surrounded by intact rim of flattened myoepithelial cells, which may not be evident on light microscopy. Invasive or micro-invasive carcinoma may be better appreciated after immunohistochemical staining for myoepithelial markers; this has been reported in 9 cases (17.6%) of LGCCC [6-9, 11, 15]. In 6 of these 9 cases, the invasion was described as limited or focal [6, 7, 11], in 2 cases the invasive component was called "adenocarcinoma NOS" [8, 15], and in one case was an adenosquamous carcinoma [9].

Immunohistochemically, the tumor cells of LGCCC are positive for AE1/AE3, CAM5.2, CK7, and CK19 [2, 4-24]. High-molecular keratin (HMWK, CK-34βE12) is reported as positive in both ductal and non-neoplastic myoepithelial neoplastic cells. CK20 is negative in all 6 reported cases. Epithelial membrane antigen expression was present in all 3 tumors that were examined, carcinoembryonic antigen was present in 6 of 9 tumors, and vimentin expression was present in 3 of 4 tumors. 34 of 37 tumors showed positivty for S100, usually with diffuse and strong nuclear and cytoplasmic immunoreactivity. 9 of 17 tumors showed positivty for GCDFP-15, especially in areas with apocrine metaplasia. Expression of androgen receptor was present in 5 of 12 tumors [9, 11, 14]. Estrogen receptor and progesterone receptor were usually absent, with only 1 of 9 tumors showing partial immunopositivity [11]. All 4 tumors reportedly showed positivty for mammaglobin, including the present case [21-23]. The expression Her-2, p53, and DOG1 in 20 tumors, 6 tumors, and 3 tumors, respectively, were all negative. Smooth muscle actin, calponin, p63, p40 and CK14 have clearly demonstrated a continuous layer of myoepithelial cells rimming the ducts and cyst spaces. No myoepithelial cells are admixed within the proliferative cellular component. In tumors with areas of invasion, this myoepithelial layer appeared discontinuous. The Ki-67 index is usually low.

The main differential diagnosis of LGCCC includes salivary duct carcinoma in situ/high-grade intraductal carcinoma (HG-IDC), conventional salivary duct carcinoma, cystadenocarcinoma, papillary-cystic variant of acinic cell carcinoma, and mammary analog secretory carcinoma. Without identifying the myoepithelial layer, the diagnosis of LGCCC can be easily missed.

HG-IDC shares with LGCCC many features including partly cystic appearance, cribriform, solid, and micropapillary patterns, and neo-

Table 1. Previously reported cases of LGCCC in the English literature

Case No.	Author and year	Age	Sex	Location	Size (cm)	Treatment	Follow-up, months
1	Delgado et al. [2] 1996	58	M	Parotid	1	Superficial parotidectomy	NA
2	Delgado et al. [2] 1996	62	F	Parotid	0.7	Parotidectomy	NA
3	Delgado et al. [2] 1996	32	F	Parotid	1.1	Parotidectomy, radiotherapy	NED 144
4	Delgado et al. [2] 1996	63	M	Parotid	1.3	Parotidectomy	NED 133
5	Delgado et al. [2] 1996	74	M	Parotid	1.8	Parotidectomy	NED 72
6	Delgado et al. [2] 1996	56	F	Parotid	1	Parotidectomy	NED 24
7	Delgado et al. [2] 1996	42	M	Parotid	1.2	Parotidectomy	NED 24
8	Delgado et al. [2] 1996	69	F	Parotid	4	Parotidectomy	NED 24
9	Delgado et al. [2] 1996	69	M	Parotid	0.9	Parotidectomy	NA
10	Delgado et al. [2] 1996	52	F	Parotid	0.8	Parotidectomy, radiotherapy	NED 9
11	Tatemoto et al. [4] 1996	58	F	Hard palate	1.0	NA	NED 30
12	Khurana et al. [5] 1997	75	F	Parotid gland	NA	NA	NA
13	Chen et al. [6] 2000	83	F	Parotid gland	2	Superficial parotidectomy	NED 36
14	Brandwein-Gensler et al. [7] 2004*	62	F	NA	NA	NA	NED 12
15	Brandwein-Gensler et al. [7] 2004	82	M	NA	NA	NA	NED 44
16	Brandwein-Gensler et al. [7] 2004	78	F	NA	NA	NA	NED 17
17	Brandwein-Gensler et al. [7] 2004	72	F	NA	NA	NA	NED 108
18	Brandwein-Gensler et al. [7] 2004	93	F	NA	NA	NA	NED 24
19	Brandwein-Gensler et al. [7] 2004	NA	F	NA	NA	NA	NED 30
20	Brandwein-Gensler et al. [7] 2004	NA	NA	NA	NA	NA	NED 62
21	Brandwein-Gensler et al. [7] 2004	64	F	NA	NA	NA	NED 33
22	Brandwein-Gensler et al. [7] 2004	66	M	NA	NA	NA	NA
23	Brandwein-Gensler et al. [7] 2004	57	F	NA	NA	NA	NED 30
24	Brandwein-Gensler et al. [7] 2004	63	F	NA	NA	NA	NA
25	Brandwein-Gensler et al. [7] 2004	64	M	NA	NA	NA	NED 6
26	Brandwein-Gensler et al. [7] 2004	62	M	NA	NA	NA	NED 132
27	Brandwein-Gensler et al. [7] 2004	72	M	NA	NA	NA	NED 40
28	Brandwein-Gensler et al. [7] 2004	76	M	NA	NA	NA	NED 24
29	Brandwein-Gensler et al. [7] 2004	54	M	NA	NA	NA	NA
30	Ide et al. [8] 2004	58	M	Palate	3	Simple excision	NED 228
31	Weinreb et al. [9] 2006	50	F	Parotid	2	Superficial parotidectomy	NED 5
32	Weinreb et al. [9] 2006	73	M	Parotid	1.5	Superficial parotidectomy and supraomohyoid neck dissection	NED 60
33	Weinreb et al. [9] 2006	67	F	Parotid	2.5	Total parotidectomy, chemotherapy, radiation therapy	NA
34	Arai et al. [10] 2009	32	F	Parotid	2.8	Total parotidectomy	NED 24
35	Kusafuka et al. [11] 2010	38	F	Parotid	3.5	Superficial parotidectomy	NED 8
36	Laco et al. [12] 2010	50	F	Parotid	1.4	Enucleation	NED 24
37	Nakazawa et al. [13] 2011	56	F	Parotid	3	Parotidectomy	NED 12
38	Weinreb et al. [14] 2011	59	F	Parotid (intraparotid lymph node)	3.5	NA	NA
39	Nakatsuka et al. [15] 2011	27	M	Accessory parotid gland	1.5	Local excision	NED 3
40	Wang et al. [16] 2013	48	M	Parotid gland	2	Parotidectomy	NED 16
41	Wang et al. [16] 2013	59	F	Parotid gland	3	Parotidectomy	NED 7
42	Obokata et al. [17] 2013	65	M	Submandibular gland	4	Resection of the tumor/regional lymph node dissection	NA
43	Ko et al. [18] 2013	57	M	Parotid	0.7	Resection of the tumor	NED 2
44	Jeong et al. [19] 2013	90	M	Parotid	5.3	Parotidectomy	NA
45	Kokabu et al. [20] 2015	56	F	Hard palate	2	Resection of tumor	NED 12
46	Urano et al. [21] 2015	46	F	Parotid	1.5	NA	NED
47	Urano et al. [21] 2015	50	F	Parotid	1	NA	NED
48	Projetti et al. [22] 2015	57	M	Parotid	2.7	NA	NA
49	Kimura et al. [23] 2016	72	M	Buccal mucosa	0.8	Resection of tumor	NED 12
50	Ohta et al. [24] 2016	44	F	Parotid	0.8	Superficial parotidectomy	NA
51	Yang et al.	42	M	Parotid	3.5	Parotidectomy	NED 14

M, male; F, female; NED, no evidence of disease; NA, not available. *Of the 16 cases reported by Brandwein-Gensler et al. [7], 15 tumors arose from the parotid, including one that arose from an intraparotid lymph node, and one arose in the submandibular gland. These cases were treated with parotidectomy or submandibular excision.

plastic cells with ductal phenotype surrounded by an attenuated layer of myoepithelial cells [25, 26]. The differences between LGCCC and HG-IDC are nuclear grade and the presence of necrosis. HG-IDC is composed of neoplastic ductal cells showing high nucleocytoplasmic ratio, large pleomorphic nuclei with prominent nucleoli, occasional to frequent mitoses, and foci of necrosis. The expression of S100 protein may help to separate these two lesions. LGCCC is usually strongly positive for S100, while HG-IDCs have been either negative or only partially positive for S100 [25, 26].

In contrast with LGCCC, conventional salivary duct carcinoma exhibits a high-grade histology similar to invasive ductal carcinoma of the breast, with both intraductal and widely invasive components [1]. Comedonecrosis, perineural invasion and lymph-vascular tumor emboli are very common. Salivary duct carcinoma usually expresses androgen receptor, and overexpresses HER2 [27]. In addition, salivary duct carcinoma usually exhibits a high Ki-67 labeling index. Myoepithelial markers, such as smooth muscle actin, calponin, HHF35, p63 and S100, are negative in salivary duct carcinoma. Androgen receptors may be expressed in up to 42% of LGCCC. However, HER2 is not overexpressed in LGCCC, and the Ki-67 index is usually low. Recently, Hsieh et al. [28] found strong SOX10 expression in 2/2 LGCCC, while salivary duct carcinoma was SOX10 negative, suggesting SOX10 is useful in the differential diagnosis. The present case also showed strong positivity to SOX10.

Although both LGCCC and cystadenocarcinoma share a cystic appearance, cystadenocarcinoma is a clearly infiltrative neoplasm, often with complex papillary architecture, and usually lacks the solid and cribriform architecture of LGCCC [1]. It is generally S100 negative and lacks the periphery myoepithelial layer.

Papillary cystic variant of acinic cell carcinoma contains serous acinar cells with cytoplasmic PAS positive zymogen-like granules. Compared with LGCCC, acinic cell carcinoma is usually negative for S100 and mammaglobin, and also lacks non-neoplastic myoepithelial cells when stained with myoepithelial markers. DOG1 expression was limited or absent in LGCCC, whilst acinic cell carcinoma expresses DOG1 diffusely in a canalicular pattern [21, 27]. Mammary analogue secretory carcinoma is a recently recognized salivary gland tumor harboring an ETV6-NTRK3 translocation similar to secretory carcinoma of the breast [29]. Histologically, mammary analogue secretory carcinoma shows a lobulated growth pattern and is composed of microcystic, tubular, and solid structures with abundant eosinophilic homogeneous or bubbly secretory material. The tumor cells have pink or vacuolated cytoplasm, vesicular nuclei and distinct nucleoli. Distinguishing LGCCC from mammary analogue secretory carcinoma may be challenging, and the histological features of the 2 tumors overlap. Moreover, immunohistochemical profile of LGCCC and mammary analogue secretory carcinoma seems very similar. Both tumors are positive for pancytokeratin, CK7, CK19, epithelial membrane antigen, vimentin, GCDFP15, S100, mammaglobin and SOX-10 [21, 22, 27-31]. However, mammary analogue secretory carcinoma is predominantly infiltrating, while LGCCC is typically an intraductal multicystic proliferation. Mammary analogue secretory carcinoma is typically negative for high-molecular weight keratin and basal cell/myoepithelial markers, such as smooth muscle actin, calponin, CK14, CK5/6, and p63. Myoepithelial stains may in some cases reveal a peripheral rim of positive cells, suggesting an intraductal component [31]. However, the presence of a complete myoepithelial layer around tumor nests seen in LGCCC is not a feature of mammary analogue secretory carcinoma. Fluorescent in situ hybridization (FISH) for the ETV-NTRK3 fusion remains the gold standard in establishing the diagnosis of mammary analogue secretory carcinoma. To our knowledge, 14 LGCCCs have been tested for the ETV6 gene rearrangement, and all have been negative [21, 27, 29-32].

In summary, LGCCC is a rare tumor that should be distinguished from other salivary carcinomas because of its indolent nature. The correct diagnosis is ascertained by combining morphologic and immunohistochemical evaluations. The presence of an intact myoepithelial layer around all tumor islands, ideally confirmed by immunohistochemistry, is crucial for the definite diagnosis and exclusion of an invasive component. More studies are required to better understand this entity.

Disclosure of conflict of interest

None.

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References

[1] Barnes L, Eveson JW, Reichart P. World Health Organization classification of tumors: pathology and genetics of the head and neck tumours. Lyon: IARC Press; 2005.

[2] Delgado R, Klimstra D and Albores-Saavedra J. Low grade salivary duct carcinoma. A distinctive variant with a low grade histology and a predominant intraductal growth pattern. Cancer 1996; 78: 958-967.

[3] Kuo YJ, Weinreb I and Perez-Ordonez B. Low-grade salivary duct carcinoma or low-grade intraductal carcinoma? Review of the literature. Head Neck Pathol 2013; 7 Suppl 1: S59-67.

[4] Tatemoto Y, Ohno A and Osaki T. Low malignant intraductal carcinoma on the hard palate: a variant of salivary duct carcinoma? Eur J Cancer B Oral Oncol 1996; 32B: 275-277.

[5] Khurana KK, Pitman MB, Powers CN, Korourian S, Bardales RH and Stanley MW. Diagnostic pitfalls of aspiration cytology of salivary duct carcinoma. Cancer 1997; 81: 373-378.

[6] Chen KT. Cytology of salivary duct carcinoma. Diagn Cytopathol 2000; 22: 132-135.

[7] Brandwein-Gensler M, Hille J, Wang BY, Urken M, Gordon R, Wang LJ, Simpson JR, Simpson RH and Gnepp DR. Low-grade salivary duct carcinoma: description of 16 cases. Am J Surg Pathol 2004; 28: 1040-1044.

[8] Ide F, Mishima K and Saito I. Circumscribed salivary duct carcinoma of the palate: a non-threatening variant. Histopathology 2004; 45: 89-91.

[9] Weinreb I, Tabanda-Lichauco R, Van der Kwast T and Perez-Ordonez B. Low-grade intraductal carcinoma of salivary gland: report of 3 cases with marked apocrine differentiation. Am J Surg Pathol 2006; 30: 1014-1021.

[10] Arai A, Taki M, Mimaki S, Ueda M and Hori S. Low-grade cribriform cystadenocarcinoma of the parotid gland: a case report. Auris Nasus Larynx 2009; 36: 725-728.

[11] Kusafuka K, Itoh H, Sugiyama C and Nakajima T. Low-grade salivary duct carcinoma of the parotid gland: report of a case with immunohistochemical analysis. Med Mol Morphol 2010; 43: 178-184.

[12] Laco J, Podhola M and Dolezalova H. Low-grade cribriform cystadenocarcinoma of the parotid gland: a neoplasm with favorable prognosis, distinct from salivary duct carcinoma. Int J Surg Pathol 2010; 18: 369-373.

[13] Nakazawa T, Kondo T, Yuminomochi T, Nakazawa K, Ishii Y, Mochizuki K, Kawasaki T, Yamane T, Miyata M, Motosugi U and Katoh R. Fine-needle aspiration biopsy of low-grade cribriform cystadenocarcinoma of the salivary gland. Diagn Cytopathol 2011; 39: 218-222.

[14] Weinreb I. Intraductal carcinoma of salivary gland (so-called low-grade cribriform cystadenocarcinoma) arising in an intraparotid lymph node. Head Neck Pathol 2011; 5: 321-325.

[15] Nakatsuka S, Harada H, Fujiyama H, Takeda K, Kitamura K, Kimura H, Nagano T, Ito M and Asada Y. An invasive adenocarcinoma of the accessory parotid gland: a rare example developing from a low-grade cribriform cystadenocarcinoma? Diagn Pathol 2011; 6: 122.

[16] Wang L, Liu Y, Lin X, Zhang D, Li Q, Qiu X and Wang EH. Low-grade cribriform cystadenocarcinoma of salivary glands: report of two cases and review of the literature. Diagn Pathol 2013; 8: 28.

[17] Obokata A, Sakurai S, Hirato J, Sakamoto K, Takekoshi T and Aoki J. Cytologic features of low-grade cribriform cystadenocarcinoma of the submandibular gland: a case report. Acta Cytol 2013; 57: 207-212.

[18] Ko YS and Koo JS. Cytomorphological findings and histological correlation of low-grade cribriform cystadenocarcinoma of salivary gland in fine-needle aspiration: a case study. Korean J Pathol 2013; 47: 592-595.

[19] Jeong JY, Ahn D and Park JY. Fine-needle aspiration cytology of low-grade cribriform cystadenocarcinoma with many psammoma bodies of the salivary gland. Korean J Pathol 2013; 47: 481-485.

[20] Kokabu S, Nojima J, Kayano H and Yoda T. Low-grade cribriform cystadenocarcinoma of the palatal gland: a case report. Oncol Lett 2015; 10: 2453-2457.

[21] Urano M, Nagao T, Miyabe S, Ishibashi K, Higuchi K and Kuroda M. Characterization of mammary analogue secretory carcinoma of the salivary gland: discrimination from its mimics by the presence of the ETV6-NTRK3 translocation and novel surrogate markers. Hum Pathol 2015; 46: 94-103.

[22] Projetti F, Lacroix-Triki M, Serrano E, Vergez S, Barres BH, Meilleroux J, Delisle MB and Uro-Coste E. A comparative immunohistochemistry study of diagnostic tools in salivary gland tumors: usefulness of mammaglobin, gross cystic disease fluid protein 15, and p63 cytoplasmic staining for the diagnosis of mammary analog secretory carcinoma? J Oral Pathol Med 2015; 44: 244-251.

[23] Ohta Y, Hirota Y, Kohno Y, Kishimoto K, Norose T, Ohike N, Takimoto M, Shiokawa A and Ota H.

Cytology of low-grade cribriform cystadenocarcinoma in salivary glands: cytological and immunohistochemical distinctions from other salivary gland neoplasms. Diagn Cytopathol 2016; 44: 241-245.

[24] Kimura M, Mii S, Sugimoto S, Saida K, Morinaga S and Umemura M. Low-grade cribriform cystadenocarcinoma arising from a minor salivary gland: a case report. J Oral Sci 2016; 58: 145-149.

[25] Cheuk W, Miliauskas JR and Chan JK. Intraductal carcinoma of the oral cavity: a case report and a reappraisal of the concept of pure ductal carcinoma in situ in salivary duct carcinoma. Am J Surg Pathol 2004; 28: 266-270.

[26] Simpson RH, Desai S and Di Palma S. Salivary duct carcinoma in situ of the parotid gland. Histopathology 2008; 53: 416-425.

[27] Stevens TM, Kovalovsky AO, Velosa C, Shi Q, Dai Q, Owen RP, Bell WC, Wei S, Althof PA, Sanmann JN, Sweeny L, Carroll WR, Siegal GP, Bullock MJ and Brandwein-Gensler M. Mammary analog secretory carcinoma, low-grade salivary duct carcinoma, and mimickers: a comparative study. Mod Pathol 2015; 28: 1084-1100.

[28] Hsieh MS, Lee YH and Chang YL. SOX10-positive salivary gland tumors: a growing list, including mammary analogue secretory carcinoma of the salivary gland, sialoblastoma, low-grade salivary duct carcinoma, basal cell adenoma/adenocarcinoma, and a subgroup of mucoepidermoid carcinoma. Hum Pathol 2016; 56: 134-142.

[29] Skalova A, Vanecek T, Sima R, Laco J, Weinreb I, Perez-Ordonez B, Starek I, Geierova M, Simpson RH, Passador-Santos F, Ryska A, Leivo I, Kinkor Z and Michal M. 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.

[30] Bishop JA, Yonescu R, Batista D, Begum S, Eisele DW and Westra WH. 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: 1982-1988.

[31] Chiosea SI, Griffith C, Assaad A and Seethala RR. Clinicopathological characterization of mammary analogue secretory carcinoma of salivary glands. Histopathology 2012; 61: 387-394.

[32] Shah AA, Wenig BM, LeGallo RD, Mills SE and Stelow EB. Morphology in conjunction with immunohistochemistry is sufficient for the diagnosis of mammary analogue secretory carcinoma. Head Neck Pathol 2015; 9: 85-95.