DOI:10.5125/jkaoms.2010.36.6.533

Sialadenoma papilliferum: a case report and immunohistochemical study review

June-Ho Byun[1]*, Dong-Chul Kim[2]*, Gyung-Hyuck Go[2], Bong-Wook Park[1]

[1]*Department of Oral and Maxillofacial Surgery, School of Medicine, Institute of Health Sciences,*
[2]*Department of Pathology, School of Medicine, Gyeongsang National University, Jinju, Korea*

Abstract (J Korean Assoc Oral Maxillofac Surg 2010;36:533-7)

Sialadenoma papilliferum (SP) is a rare benign neoplasm that normally arises from the minor salivary glands, particularly in the palate. SP is normally encountered in older men with an exophytic papillary surface growth. In the present study, an SP of the hard palate of a 69-year-old woman was examined immunohistochemically. Myoepithelial cell markers, such as S-100, smooth muscle actin and vimentin, were observed in the basal or luminal layer of tumor cells, indicating that myoepithelial cells participate in the pathogenesis of SP. In addition, cytokeratin 7 was also strongly detected in the tumor cells, suggesting that excretory ductal epithelial cells have a role in its histogenesis. A review of the literature of immunohistochemical studies on SP showed that the expression and co-expression of cytokeratins and myoepithelial cell markers have been reported in tumor cells. These results suggested that excretory duct cells and myoepithelial cells participate in the pathogenesis of SP.

Key words: Sialadenoma papilliferum, Hard palate, Immunohistochemistry.

[paper submitted 2010. 8. 27 / revised 2010. 11. 30 / accepted 2010. 12. 17]

Ⅰ. Introduction

Sialadenoma papilliferum (SP) is a rare, benign exophytic tumor of salivary gland origin. According to recent studies[1,2], approximately 50 cases have been reported since the lesion was first described by Abrams and Finck[3] in 1969, who proposed the term "sialadenoma papilliferum" because of the histological similarity between this type of salivary gland tumor and syringocystadenoma papilliferum of cutaneous adnexal origin. Clinically, it usually occur in men older than 50, as a painless papillary growth at the junction of the hard and soft palate[1,4,5]. Histologically, it is characterized by both exophytic and endophytic proliferation of ductal epithelium composed of a double layer of cells[2,5,6].

The histogenesis of SP remains unclear. Some authors have suggested that it has an excretory duct[7,8] or pluripotential myoepithelial[6,9] cellular origin, while others have proposed that it originates from intercalated salivary ducts, because of the presence of squamous differentiation[10,11]. Recently, a number of investigators have presented immunohistochemical results concerning the pathogenesis of SP[1,2,6,9,10,12,13], but these results vary in the point of view. In the present study, we describe immunohistochemical studies for the antibodies of cytokeratins (CK) and myoepithelial cell (MEC) markers in a new SP case. In addition, in order to further understand the pathogenesis of this tumor, we reviewed recent literature for immunohistochemical studies on SP.

Ⅱ. Case presentation

A 69-year-old woman presented with an exophytic mucosal growth on the palate, which the patient noted had grown slowly over about 2 years. A clinical examination revealed an exophytic dome-shaped mass, measuring approximately 1.5×1 cm, at the posterior hard palate lateral to midline. No discoloration or ulceration was observed on the mass.(Fig. 1. A) A tissue sample of the lesion was incised under local anesthesia for histopathological examination, which resulted in a pathological finding of a benign salivary gland duct tumor, resembling sialadenoma papilliferum. In magnetic resonance imaging (MRI), the underlying palatine bone was intact and healthy. Accordingly, the lesion was completely excised with an adequate safety margin under general anesthesia.(Figs. 1. B, C).

박 봉 욱
660-702 경남 진주시 칠암동 90
경상대학교 의학전문대학원 치과학교실 구강악안면외과
Bong-Wook Park
Department of Oral and Maxillofacial Surgery, School of Medicine,
Institute of Health Science, Gyeongsang National University
Chilam-dong 90, Jinju, Gyeongnam, 660-702, Korea.
TEL: +82-55-750-8264 FAX: +82-55-761-7024
E-mail: parkbw@gnu.ac.kr

*These two authors contributed equally to this work.

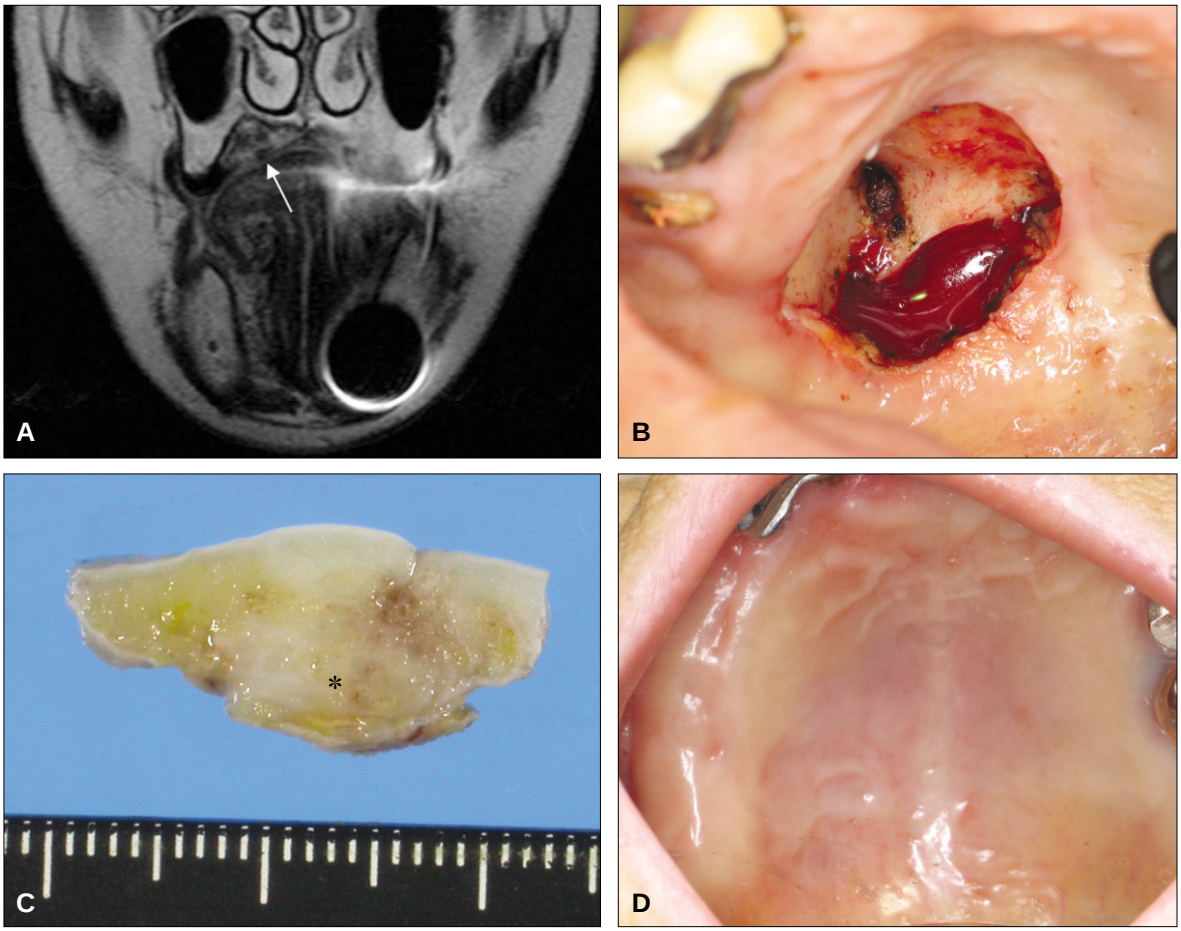

Fig. 1. Perioperative radiologic and clinical features. A. In preoperative MRI view, well demarcated firm mass was observed under the palatal mucosa (white arrow). B. After removal of tumor, intact hard palatal bone was detected. C. Main mass (*), approximately 1.5x1 cm size, was resected with peripheral normal tissues. D. After 6 months of operation, completely healed palatal mucosa was observed.
(MRI: magnetic resonance imaging)

Histologically, the tumor was an irregular shaped, non-capsulated nodular mass in oral mucosa, although it was well demarcated. The superficial portion had a large ductal structure, lined by squamous epithelium with acanthosis and parakeratosis. The deeper portion disclosed irregular ductal structure proliferation, which was composed of multiple papillary projections, cleft formation, ductal dilation, and microcystic lesions.(Figs. 2A, B) The lining epithelium was composed of two cellular components, namely, luminal columnar cells and short cuboidal or basaloid cells.(Fig. 2. C) The luminal cells had a single round to oval nucleus with minute nucleoli and no atypism. Some mucin cells were occasionally interspersed among lining cells.(Fig. 2. D) No invasion of surrounding stromal tissue was evident. The tumor was finally diagnosed as a benign sialadenoma papilliferum based on these pathologic findings.

The surgical specimen was sectioned at 4 μm for immunohistochemical studies. Immunostaining was conducted using an automated immunostainer (Lab Vision Autostainer, Lab Vision, CA, USA). CK 7 was strongly expressed, but CK 20 was absent in tumor cells.(Figs. 3. A, B) S-100 protein was moderately expressed in all epithelial layers of luminally and basally located cells.(Fig. 3. C) Staining for smooth muscle actin (SMA) was strong in the basal layer, but negative in the luminal columnar cells.(Fig. 3. D) Vimentin was weakly expressed in the basal layer of some tumor cells (Fig. 3. E), but carcinoembryonic antigen (CEA) staining was negative in all tumor cell layers.(Fig. 3. F)

The primary antibodies used and our immunohistochemical staining results are summarized in Table 1. Positive immunostaining intensities were graded as +++, ++, + and - for strong, moderate, weak and negative staining, respectively.

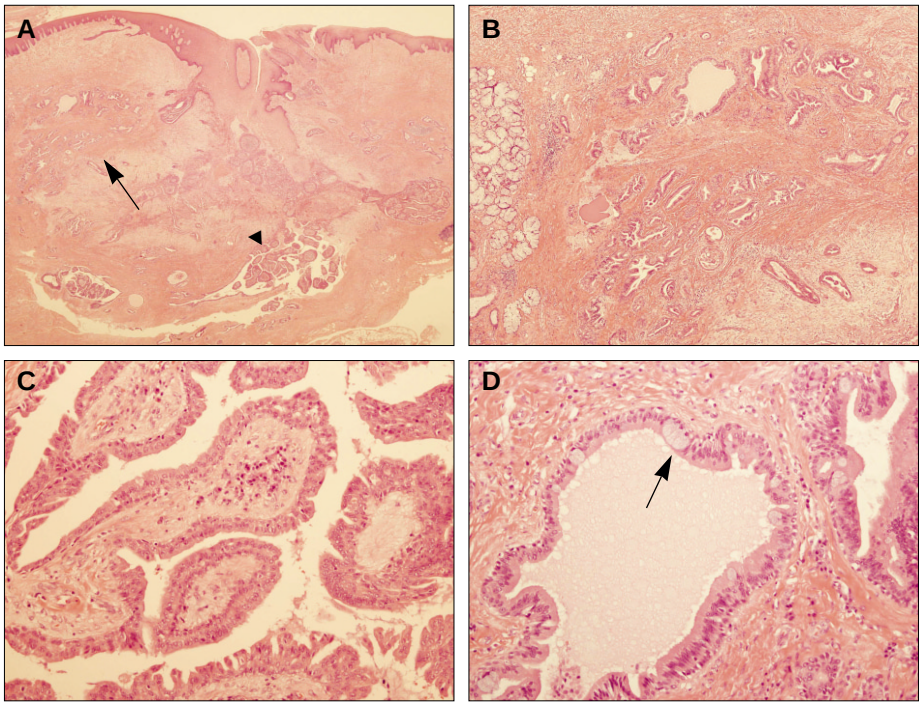

Fig. 2. Photomicrograph of the lesion.(H&E staining) A. The central portion of the tumor was contained hyperplastic squamous epithelium connected to surface mucosa, whereas the remaining tumor showed glandular (arrow) and projecting papillary portion (arrowhead).(original magnification x12) B. Ductal proliferation and dilation with papillary folds were observed in the glandular portion under moderate magnification. (original magnification x40) C. High magnification image of a region showing papillary projection. Papillary fronds were lined by a double row of cells composed of luminal columnar cells and short cuboidal or basaloid cells.(original magnification x200) D. High magnification glandular portion. Some mucin-secreting cells (arrow) were occasionally observed among lining columnar cells of the dilated duct .(original magnification x200)

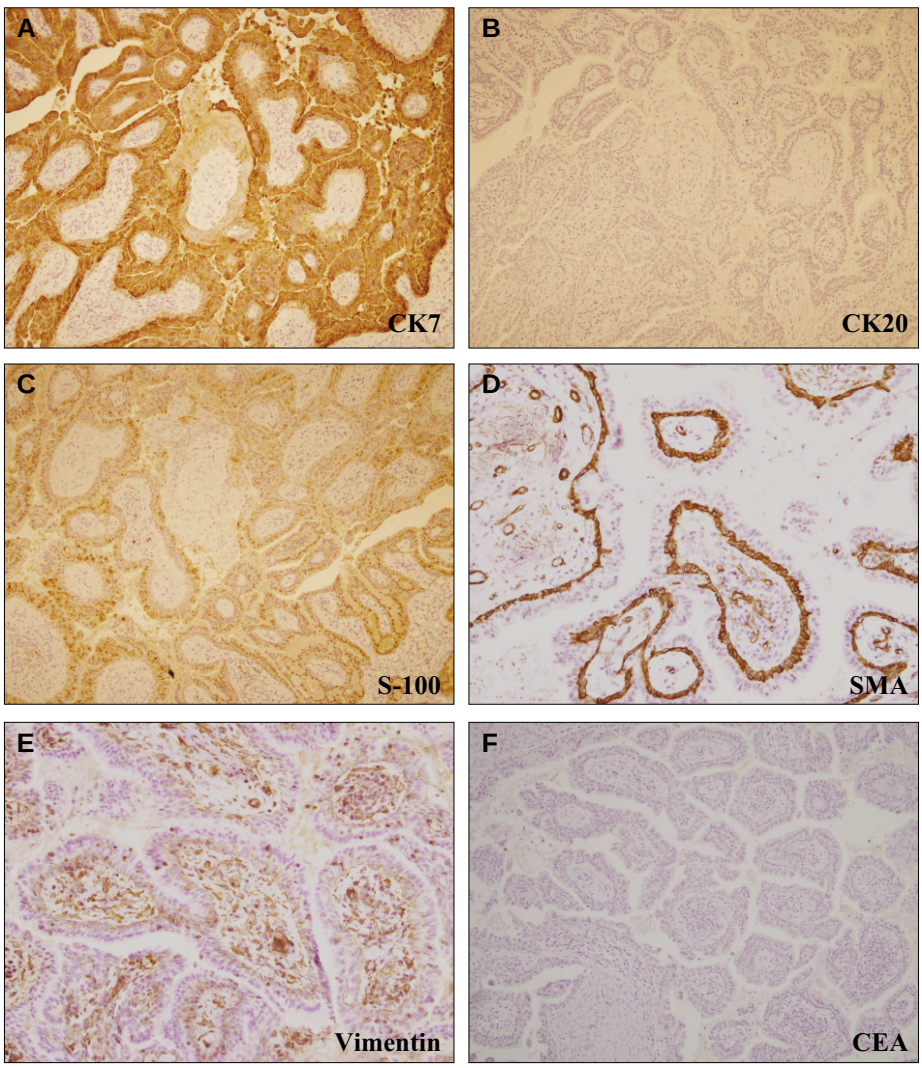

Fig. 3. Immunohistochemical findings of the lesion. A, B. CK 7 was strongly expressed, but CK20 was absent in tumor cells.(original magnification x100) C. S-100 protein was moderately expressed in tumor cell luminal and basal layers.(original magnification x100) D. SMA was strongly expressed in the basal layer of tumor cells (arrow), but was not observed in the luminal columnar cells.(original magnification x200) E. Vimentin was weakly expressed in the basal layer of tumor cells.(original magnification x200) F. CEA expression was not observed in any tumor cell layer. (original magnification x100)
(CK7: cytokeratin 7, CK20: cytokeratin 20, S-100: S-100 protein, SMA: smooth muscle actin, CEA: carcinoembryonic antigen)

Ⅲ. Discussion

Abrams and Finck[3] first described SP as having two distinct histological components: the superficial squamous epithelium composing the exophytic papillomatous portion of the lesion and the tortuous, widely dilated duct-like structures with the typical double layering. The junction of hard and soft palate is most frequently affected, other intraoral sites are the buccal mucosa, retromolar pad, lip, and parotid gland1, although rarely SP has been reported in broncheal[12] and esophageal[14] mucosa. This tumor is best treated by conservative surgical excision. Recurrence and malignant transformation are rare. In the English literature, two cases of recurrence[15,16] have been described, and one malignant SP case2 has been reported. Various theories have been proposed regarding the cellular origin of SP, and hyperplastic and neoplastic origins have been considered. Many researchers believed it to have a neoplastic origin, but its precise pathogenesis is not understood.

In one study, immunohistochemical and electron microscopic examinations were unhelpful in terms of arriving at a correct histological diagnosis[17], which indicates that a proper diagnosis can be made by conventional histopathological examination. However, immunohistochemical studies are required to probe its pathogenesis. In addition to the present case, our literature review revealed seven other immunohistochemical studies on SP (Table 2), and that various types of CK have been used to detect tumors of excretory duct cell origin, and that MEC markers have been used to detect those of MEC origin.

Many attempts have been made to identify a suitable

Table 1. Primary antibodies, staining methods, and results of immunohistochemical staining

Antibody	Dilution	Source	Immunostaining intensity	
			Basal layer	Luminal layer
CK 7	1:1,500	Zymed (CA, USA)	+++	+++
CK 20	1:1,500	Neomarker (CA, USA)	-	-
S-100	1:10	DAKO (Denmark)	++	++
SMA	1:1,500	Neomarker (CA, USA)	+++	-
Vimentin	1:20	DAKO (Denmark)	+	-
CEA	1:20	DAKO (Denmark)	-	-

(CK: cytokeratin, SMA: smooth muscle actin, CEA: carcinoembryonic antigen)

Table 2. Summary of immunohistochmical studies conducted on sialadenoma papilliferum

Authors	Number of case/Location	Result of immunohistochemistry
Nakahata *et al*[10], 1990	1 / No description	CK (+++)[1], Vimentin (++)[2], Desmin (+)[3]: co-expression
		CK 19, S-100: Pos in luminal cells
Maiorano *et al*[9], 1996	4/ Hard palates and	1st subset of basal cells
	1/ Cheek	CK 14, SMA, S-100, Vimentin, GFAP: Pos
		2nd subset of basal cells
		SMA, Vimentin, S-100, GFAP: Neg
		CK 7, CEA, EMA, Vimentin, S-100: Pos
Ubaidat *et al*[6], 2001	2/ Hard palates	GFAP, Desmin, CK 20, MSA: Neg
		CK 19, 14, 13, 7, 8: Pos
Gomes *et al*[13], 2004	2/ Hard palates	Vimentin, SMA: Neg
		CK 7, 17, 19: Pos: CK 20: Neg
Bobos *et al*[12], 2003	1/ Bronchus	S-100, EMA: Pos in epithelium
		SMA, S-100: Pos in myoepithelium
		CKs, EMA, CEA: Pos in luminal cells
Shimoda *et al*[2], 2004	1 Malignant case/	SMA, S-100, Vimentin: Pos in basal cells
	Hard palate	P53, CKs, EMA, S-100, CEA: Pos in cancer cells
		CKs: Pos
Mahajan *et al*[1], 2007	1/ Cheek	Vimentin, SMA: Neg
		Basal layer: CK 7 (+++), S-100 (++), SMA (+++),
Current case	1/ Hard palate	Vimentin (+)
		Luminal layer: CK 7 (+++), S-100 (++), SMA (-)[4]
		CK 20, CEA: Neg in all tumor cells

(+++[1]: strong, ++[2]: moderate, +[3]: weak, -[4]: negative, Pos: positive expression, Neg: negative expression, CK: cytokeratin, SMA: smooth muscle actin, GFAP: glial fibrillary acidic protein, EMA: epithelial membrane antigen, MSA: muscle-specific actin, CEA: carcinoembryonic antigen)

immunohistochemical marker for MEC in salivary gland neoplasms. Initially, S-100 protein was the most popular marker for MEC, but subsequent studies found it unreliable, because it can also be expressed in ductal cells[18]. Accordingly, SMA was adopted as a standard marker for normal and neoplastic MEC, but later study showed that neoplastic MEC may not express SMA[19]. Vimentin has also been used as a neoplastic MEC marker, and as an early marker of myoepithelial differentiation. More recently, novel markers of smooth muscle differentiation, such as, calponin and H-caldesmon, have been described in MEC of normal and modified neoplastic types, and some authors have suggested that the best way to identifying MEC is by using vimentin plus SMA or calponin, because in tumors MEC are hardly ever fully differentiated[20].

Nakahata *et al*[10] observed the co-expression of three different types of intermediate-sized filaments, including cytokeratin, vimentin and desmin, in SP, and suggested that a primitive precursor cell capable of multidirectional differentiation could account for the different components of SP. Maiorano *et al*[9] and Ubaidat *et al*[6] observed the positive expression of SMA, S-100, and vimentin in basal cells of SP, and suggested that MEC might participate in the pathogenesis of SP. However, Gomes *et al*[13] and Mahajan *et al*[1] did not observe vimentin or SMA expression in SP, but could detect CK expression in those tumor cells. These results indicate that SP probably has an excretory duct cell origin, and Gomes *et al*[13] refined this suggesting a more distal duct origin, because enhanced CK 7 and 8 expression.

Immunohistochemical studies on SP have shown different expression pattern for CK and MEC markers. In some reports, the co-expression of CK and MEC markers were observed[2,6,9,10]. In the present study, we also observed the expression of S-100, vimentin, and SMA, suggesting MEC differentiation, and CK 7 expression, suggesting ductal cell differentiation. We consider that this dual immunohistochemical expression pattern suggests that excretory duct cells and MEC might co-participate in the pathogenesis of SP, which supports the suggestion made by Nakahata *et al*[10] that primitive precursor cells are probably involved in its pathogenesis.

References

1. Mahajan D, Khurana N, Setia N. Sialadenoma papilliferum in a young patient: a case report and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103:e51-4.
2. Shimoda M, Kameyama K, Morinaga S, Tanaka Y, Hashiguchi K, Shimada M, *et al*. Malignant transformation of sialadenoma papilliferum of the palate: a case report. Virchows Arch 2004; 445:641-6.
3. Abrams AM, Finck FM. Sialadenoma papilliferum. A previously unreported salivary gland tumor. Cancer 1969;24:1057-63.
4. Crocker DJ, Christ TF, Cavalaris CJ. Sialadenoma papilliferum: report of case. J Oral Surg 1972;30:520-1.
5. Markopoulos A, Kayavis I, Papanayotou P. Sialadenoma papilliferum of the oral cavity: report of a case and literature review. J Oral Maxillofac Surg 1997;55:1181-4.
6. Ubaidat MA, Robinson RA, Belding PJ, Merryman DJ. Sialadenoma papilliferum of the hard palate: report of 2 cases and immunohistochemical evaluation. Arch Pathol Lab Med 2001;125:1595-7.
7. Fantasia JE, Nocco CE, Lally ET. Ultrastructure of sialadenoma papilliferum. Arch Pathol Lab Med 1986;110:523-7.
8. Freedman PD, Lumerman H. Sialadenoma papilliferum. Oral Surg Oral Med Oral Pathol 1978;45:88-94.
9. Maiorano E, Favia G, Ricco R. Sialadenoma papilliferum: an immunohistochemical study of five cases. J Oral Pathol Med 1996; 25:336-42.
10. Nakahata A, Deguchi H, Yanagawa T, Yoshida H, Sato M, Hayashi Y. Coexpression of intermediate-sized filaments in sialadenoma papilliferum and other salivary gland neoplasms. J Oral Pathol Med 1990;19:313-8.
11. Shirasuna K, Watatani K, Miyazaki T. Ultrastructure of a sialadenoma papilliferum. Cancer 1984;53:468-74.
12. Bobos M, Hytiroglou P, Karkavelas G, Papakonstantinou C, Papadimitriou CS. Sialadenoma papilliferum of bronchus. Virchows Arch 2003;443:695-9.
13. Gomes AP, Sobral AP, Loducca SV, de Araújo VC. Sialadenoma papilliferum: immunohistochemical study. Int J Oral Maxillofac Surg 2004;33:621-4.
14. Rouse RV, Soetikno RM, Baker RJ, Barnard IC, Triadafilopoulos G, Longacre TA. Esophageal submucosal gland duct adenoma. Am J Surg Pathol 1995;19:1191-6.
15. Pimentel MT, López Amado M, García Sarandeses A. Recurrent sialadenoma papilliferum of the buccal mucosa. J Laryngol Otol 1995;109:787-90.
16. Rennie JS, MacDonald DG, Critchlow HA. Sialadenoma papilliferum. A case report and review of the literature. Int J Oral Surg 1984;13:452-4.
17. van der Wal JE, van der Waal I. The rare sialadenoma papilliferum. Report of a case and review of the literature. Int J Oral Maxillofac Surg 1992;21:104-6.
18. Hara K, Ito M, Takeuchi J, Iijima S, Endo T, Hidaka H. Distribution of S-100b protein in normal salivary glands and salivary gland tumors. Virchows Arch A Pathol Anat Histopathol 1983;401:237-49.
19. de Araujo VC, Carvalho YR, de Araujo NS. Actin versus vimentin in myoepithelial cells of salivary gland tumors. A comparative study. Oral Surg Oral Med Oral Pathol 1994;77:387-91.
20. Furuse C, Sousa SO, Nunes FD, Magalhaes MH, Araújo VC. Myoepithelial cell markers in salivary gland neoplasms. Int J Surg Pathol 2005;13:57-65.