Review Article

Oral Focal Mucinosis: A Case Report and Literature Review

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Abstract

Introduction: Oral focal mucinosis (OFM) is the soft tissue counterpart of cutaneous focal mucinosis (CFM) and is often misdiagnosed as an oral myxoma. OFM occurs during the fourth and fifth decades of life, predominantly in women (two females per male).

Case Report: A 22-year-old lactating female presented with a growing painless, sessile tumor with pale pink color and a lobulated surface with ulcers at the depths of interlobular fissures in the premolar-molar area of the left mandibular alveolar ridge, dating back one year. The tumor was completely excised. No recurrence was observed during the follow-ups over the next three years.

Conclusion: The current case appears to be the only one with an OFM reported during the breastfeeding period; therefore, the role of hormonal factors in the pathogenesis of the lesion should be taken into consideration.

Key Words: Oral Focal Mucinosis, Mucous Membrane, Mucinoses, Gingival Overgrowth, Hyaluronic Acid

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Introduction

Oral focal mucinosis (OFM) is the soft tissue counterpart of cutaneous focal mucinosis (CFM) and is often misdiagnosed as an oral myxoma [1]. This etiologically unknown lesion was first named and described by Tomich in 1974 [2] and may be caused by the excessive production of hyaluronic acid by fibroblasts. According to Tomich [3], focal trauma does not seem to play any role in the development of oral or cutaneous mucinoses; however, some reports have suggested trauma and local swelling as the etiology of this lesion [4,5].

Clinically, this lesion appears as an asymptomatic, exophytic, sessile or pedunculated lesion containing a mucoid myxomatous substance surrounded by a relatively dense collagenous connective tissue [1,2]. The lesion is often similar to the normal oral mucosa in color [2] and is typically 1 cm or less in diameter [6].

The lesion appears to develop more frequently in the mucosa covering bony areas [4,7]. The gingiva and alveolar mucosa, followed by the hard palate, are the most common sites for OFM [2]. Other involved oral sites are the buccal mucosa, tongue, and lips (both cutaneous and mucosal areas) [8,9].

OFM occurs during the fourth and fifth decades of life, predominantly in women (two females per male) [6,10]; it has been reported rarely in younger people [8,11].

Diagnosis should be made after the rejection of a

number of benign lesions, including gingival hyperplasia, myxoma, fibroma, mucocele, pyogenic granuloma, peripheral giant cell granuloma (PGCG), peripheral ossifying fibroma, and epulis [5,12].

In this article, we report a case of OFM in the mandibular alveolar ridge of a breastfeeding woman and review all the reported cases of the incidence of this lesion since 1974.

All English articles published in Google Scholar, ScienceDirect, MEDLINE, PubMed, and Ovid databases during 1974-2017 were reviewed (Table 1).

The searched keywords included "oral focal mucinosis", "myxomatous lesion", "gingival overgrowth", and "hyaluronic acid".

Table 1. Comparative review of oral focal mucinosis (OFM) cases from 1974 to presen

Duration	Location	Age (years) and gender	Number of cases	Year	Author(s)
5-10 years	Palate	40/F	8	1974	Tomich [3]
1 year	Gingiva	31/F			
NA	Gingiva	16/M			
1 year	Buccal mucosa	NA/F			
2 months	Tip of the tongue	45/M			
NA	Mandibular alveolar mucosa	28/M			
4 months	Palate	22/F			
4 months	Palate	19/F			
3 months	Mandibular gingiva	35/M	2	1985	Saito et al [17]
	Mandibular gingiva	50/F			
9 months	Gingiva	18/F	15	1990	Buchner et al [22]
5 years	Gingiva	30/M			
1 month	Maxillary gingiva	32/F			
1 year	Maxillary gingiva	22/F			
NA	Mandibular gingiva	53/F			
NA	Maxillary gingiva	16/F			
NA	Mandibular gingiva	43/M			
NA	Mandibular alveolar mucosa	61/F			
NA	Maxillary alveolar mucosa	37/F			
NA	Mandibular gingiva	41/F			
3 years	Mandibular gingiva	37/F			
1 year	Mandibular gingiva	46/M			
1 year	Hard palate	38/F			
3 years	Mandibular retromolar area	46/M			
2 months	Ventral tongue	50/M			
NA	Larynx	3/M	2	1990	Gnepp et al [24]
NA	Hard palate	4/F			
3 years	Ventral Tongue	68/M	1	1998	Soda et al [20]
8 months	Gingiva	48/M	1	2001	Iezzi et al [19]

NA	Lip	38/F			
1 month	Gingiva	30/F			
4 months	Gingiva	16/F			
NA	Buccal mucosa	56/F			
<1 year	Gingiva	60/F			
10 years	Gingiva	49/M			
6 months	Gingiva	31/F			
1 year	Lip	52/M	15	2003	Aldred et al [28]
NA	Gingiva	74/M			
4 months	Tongue	40/F			
3 months	Gingiva	55/M			
3 months	Gingiva	37/F			
1 year	Gingiva	35/F			
1 year	Gingiva	33/F			
1 year		68/M			
NA	Buccal mucosa	63/F	1	2004	Talacko et al [9]
NA	Maxillary gingiva	35/M	1	2008	Germano et al[10]
4 months	Gingiva	36/F	1	2008	Soares de Lima et al [11]
NA	Gingiva	37/F			
NA	Gingiva	54/F			
NA	Hard palate	49/M			
NA	Gingiva	27/F	7	2008	Narayana and Casey [32]
NA	Gingiva	26/M			
NA	Gingiva	32/F			
NA	Gingiva	48/F			
2 months	Gingiva	50/M	1	2010	Madhusudhan et al [12]
NA	Mandibular gingiva	44/F	1	2010	Gabay et al [25]
2 months	Gingiva	NA/F	1	2012	Garcia et al [5]
NA	Gingival papilla	17/F	1	2012	Lee et al [8]
4-5 months	Posterior palatal mucosa	32/F	1	2012	Bharti and Singh [2]
2 months	Tongue	62/F	1	2012	Pacifici et al [30]
1 year	Maxillary gingiva	26/M	2	2013	Ena et al [1]
NA	Maxillary gingiva	36/F			
NA	Hard palate	30/F	1	2013	Pauna et al [7]

NA	Palate	19/M	1	2013	Tekkesin et al [29]
8 months	Gingiva	20/F	1	2014	Neto et al [4]
6 years	Maxillary gingiva	42/M	1	2014	Bosco et al [27]
NA	Gingiva	23/F	1	2014	Silva et al [6]
3 months	Palate	2/F	1	2015	Woo and Cheung [18]
NA	Mandibular gingiva	54/M	1	2015	Sowmya et al [31]
5 weeks	Maxillary gingiva	29/F	1	2016	Tiwana et al [15]
6 months	Buccal mucosa	60/F	1	2016	Rambhia and Khopkar [26]
4 months 4 years	Gingiva Alveolar ridge	35/F 35/M	2	2016	Narana Ribeiro El Achkar et al [13]
7-8 months	Gingiva	53/F	1	2017	Joshi et al [16]
NA	Tongue	88/F	1	2017	Mattsson and Lindberg [14]

NA=Not Available, M=Male, F=Female

Case Report

Clinical View:

A 22-year-old female visited the Department of Oral and Maxillofacial Medicine at the School of Dentistry of Tehran University of Medical Sciences, complaining of a growing painless tumor in the premolar-molar area of the left mandibular alveolar ridge, dating back one year.

Clinical examinations showed a sessile exophytic tumor with a lobular surface and ulcerated areas at the depth of interlobar fissures on the left side of the molar alveolar ridge. The color of the lesion was pale pink. There was no pain, paresthesia, or anesthesia. The lesion was 1.5×2.5×3 cm in dimension. The tumor was firm and painless to the examining hand (Figure 1).

The patient's calcium, phosphorous, and alkaline phosphatase levels were within the normal range.

Radiographic Findings:

Panoramic radiography showed a unilocular radiolucent lesion with well-defined irregular borders on the molar alveolar ridge of the left mandible. All the teeth had already been extracted, except for the remaining roots of the lower left first and second molars located at the lower posterior region of the tumor (Figure 2).

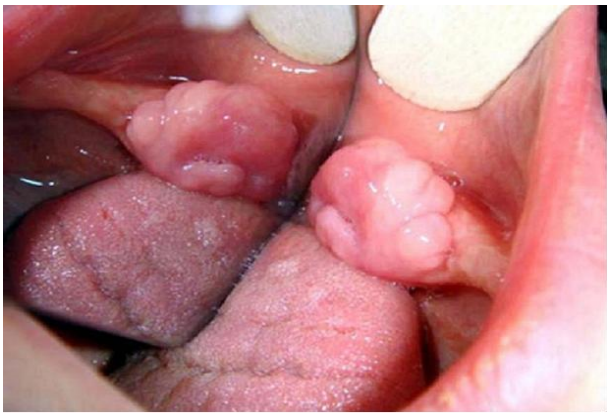

Figure 1. Oral focal mucinosis (OFM): a sessile, exophytic, lobulated mass on the alveolar ridge of the left mandibular molar area during the clinical examination

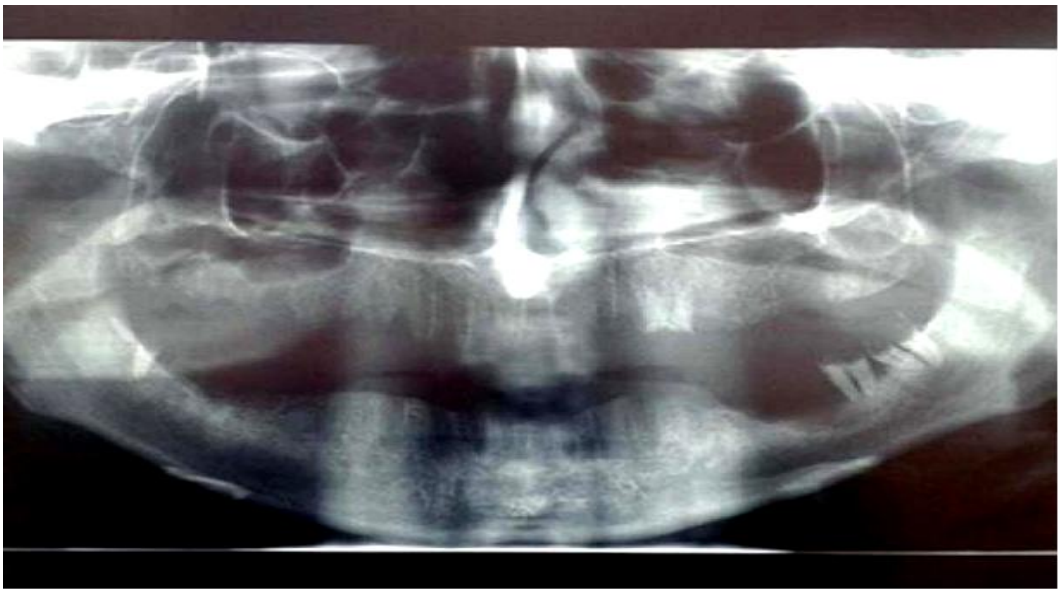

Figure 2. Panoramic view of oral focal mucinosis (OFM) showing a unilocular radiolucent lesion with well-defined, irregular margins, involving the left mandibular alveolar ridge

Considering the age and gender of the patient as well as the affected site (anterior to the first molar) and bone destruction, the best diagnosis was central giant cell granuloma (CGCG).

The tumor was completely excised, and the remaining roots were removed. The affected bone was also removed unless there was no bleeding. A healthy bone margin was confirmed by the pathologist. No recurrence was observed during the follow-ups over the next three years.

Histological Findings:

In the histological view, a stratified squamous epithelium with some ulcerated areas was observed. The underlying connective tissue was a hypocellular neoplastic tissue containing numerous star-like elongated cells with hyperchromatic nuclei located in a myxoid matrix.

The initial histopathological diagnosis was a spindle cell tumor with a myxoid stroma. For further examination, an immunohistochemistry (IHC) test was necessary.

The IHC markers were positive for S100 (a family of proteins found in the neural cells derived from the neural cleft, such as Schwann cells and melanocytes) and Ki-67 (an indicator of cell proliferation, 1%), and negative for h-caldesmon (found in smooth muscle cells), Desmin (found in cells with a myogenic origin), smooth muscle actin (SMA), and CDX2 (detectable in mucinous adenocarcinomas; Figure 3). These markers were assessed by IHC to determine the nature of the cells in the lesion. These results indicated the non-tumoral nature of the lesion (1% positive Ki-67) and some degrees of possible neural or melanocyte differentiation (positive S100) in the tumor, which have not been previously reported.

Discussion

OFM is a pseudotumoral lesion with an unknown etiology, which is often misdiagnosed due to the absence of a specific clinical feature [13-15]. It is worth mentioning that the clinical diagnosis was not OFM in any of the reported cases. Therefore, histopathological examination is essential to distinguish this lesion from other lesions and to reach a final accurate diagnosis [16-18].

In general, intraoral myxomatous lesions are rare. These lesions include OFM, nerve sheath myxoma, odontogenic myxomas, and soft tissue myxoma [19-21].

An extensive search was carried out in Google Scholar, Science Direct, MEDLINE, PubMed, and Ovid databases between November 1974 and March 2017.

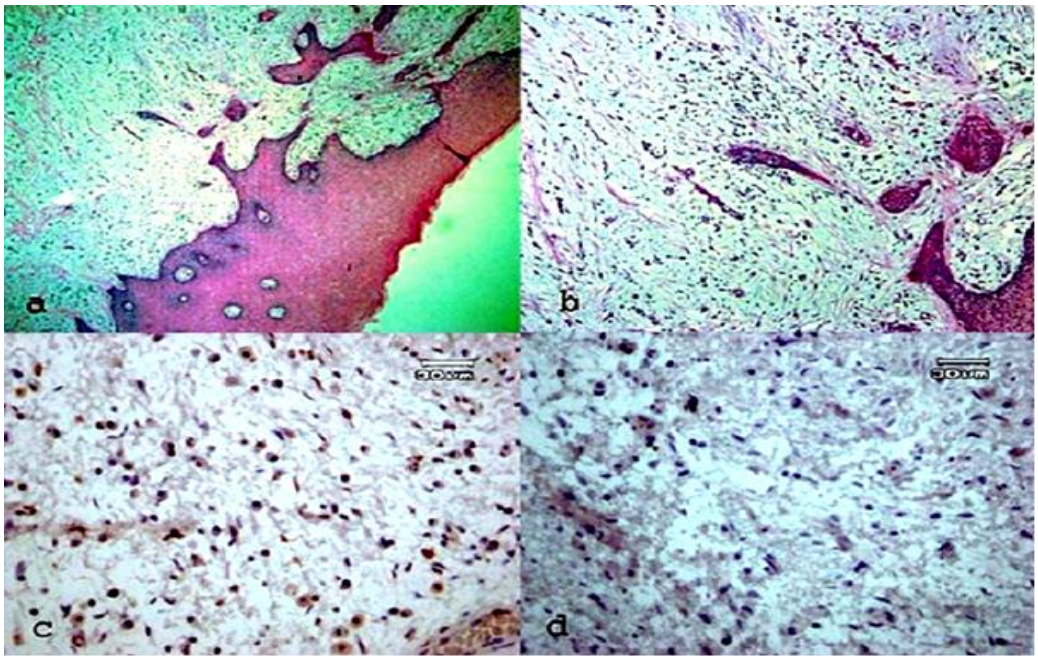

Figure 3. Histopathologic view of oral focal mucinosis (OFM): (a) Hematoxylin and eosin (H&E)-stained photomicrograph showing the surface epithelium with the underlying myxoid stroma (HE×4). (b) H&E-stained photomicrograph showing a myxomatous stroma with plump fibroblasts (HE×10). (c) Immunohistochemical staining (IHC) of OFM showing positive S100 staining, and (d) 1% positive ki-67 staining

The searched keywords were "oral focal mucinosis", "myxomatous lesion", "hyaluronic acid", and" gingival overgrowth". In total, 29 English articles reporting 77 cases of OFM were reviewed. Female patients accounted for 49 cases (63.64%). The affected sites were the gingiva (49; 63.64%), palate (11; 14.29%), tongue (6; 7.79%), buccal mucosa (4; 5.19%), lips (2; 2.60%), alveolar mucosa (3; 3.90%), mandibular retromolar area (1; 1.30%), alveolar ridge (1; 1.30%), and larynx (1; 1.30%).

Local trauma has been reported in a number of articles as the etiology of OFM. In a case report by Joshi et al [22], local trauma was introduced as the aggravating cause of OFM. Kempf et al [23] reported two cases of CFM with a history of trauma (laser epilation and piercing). Gnepp et al [24] reported two cases in the larynx and hard palate with a history of local trauma during intubation and surgery, respectively. Gabay et al [25] observed cervical resorption of the dental root adjacent to the lesion, and the mechanical pressure was suggested as the probable etiological factor. Rambhia and Khopkar [26] observed the lesion in a tobacco chewer, adjacent to the chewing site. Bosco et al [27] observed a porcelain veneer with a poor marginal seal at the lesion site. In general, it seems that local trauma has a greater role in the formation of OFM than previously thought.

OFM develops following an excessive secretion of hyaluronic acid and mucoid accumulation between collagen fibers. Ultimately, hyaluronic acid replaces collagen fibers [28-31].

OFM occurs predominantly in adults during the fourth and fifth decades of life [8]. It is a rare problem among younger people such as the present case who was one decade younger than the common age of incidence. The first-line treatment for OFM is surgery with no reported recurrence, except for the one reported by Narayana and Casey [32].

The present case was a 22-year-old breastfeeding female. Given the increased prolactin level during the breastfeeding period, the lesion may have developed due to the stimulating effects of

prolactin on fibroblasts, resulting in an excessive production of hyaluronic acid which is extensively present in OFM. In an animal study, Yoshizato and Yasumasu [33] reported the stimulating effects of bovine prolactin on the synthesis of hyaluronic acid by fibroblasts in the tadpole tail fin. Another study showed that prolactin can bond with proteoglycan in the synovial fluid and can suppress the expression of decorin, resulting in a reduced collagen fiber production [34]. The extensive bone resorption in the present case cannot be solely due to previous periodontal diseases or chronic pressure that sometimes results from a benign lesion, and it is logical to assume that it has been caused by the combined effect of prolactin and local factors.

During the literature review, we found that such bone resorption has not been previously reported. In the reviewed articles, no changes in bony tissues had been reported, except for a bone displacement case [6] and a case of cervical resorption of the dental root adjacent to the lesion [18].

Excessive production of hyaluronic acid and reduced production of collagen are two important etiologies of OFM. Since the incidence of the lesion coincided with breastfeeding, an increased prolactin level, which occurs during this period, seems to be the cause of the lesion in this case.

Conclusion

A review of the literature showed that the current case appears to be the only one with an OFM reported during the breastfeeding period; therefore, the role of hormonal factors in the pathogenesis of the lesion is suggested. Additionally, excessive bone destruction and neural differentiation (positive S100) have not been mentioned in previous articles. The lesion was completely excised and no recurrence was observed during the three-year follow-up. In conclusion, accurate examination, diagnosis, treatment, and follow-up of oral lesions are essential for maintaining the oral health.

References

1. Ena S, Nadellamanjari, Chatterjeeanirban, Ramesh A. Oral focal mucinosis: A rare case report of two cases. Ethiop J Health Sci. 2013 Jul; 23(2):178-82.

2. Bharti V, Singh J. Oral focal mucinosis of palatal mucosa: A rare case report. Contemp Clin Dent. 2012 Sep;3(Suppl 2):S214-S218.

3. Tomich CE. Oral focal mucinosis. A clinicopathologic and histochemical study of eight cases. Oral Surg Oral Med Oral Pathol. 1974 Nov; 38(5):714-24.

4. Neto JR, Sendyk M, Uchida LM, Nunes FD, de Paiva JB. Oral focal mucinosis associated with surgically assisted rapid maxillary expansion. Am J Orthod Dentofacial Orthop. 2014 Apr; 145(4): 534-8.

5. Garcia A, Bravo-Calderón D, Costa M, Oliveira D. Oral focal mucinosis arising on the gingiva of orthodontic patient. OJST. 2012 Dec;2(4):277-9.

6. Silva KR, Monterio BV, Norões TS, Goday GP, Miguel MC. Large oral focal mucinosis: a case report. J Bras Patol Med Lab. 2014 Feb;50(1):54-6.

7. Pauna HF, Bette P, Fernandes FL, Bellini BS, de Carvalho GM, Guimarães AC, et al. Oral Focal Mucinosis: A Painful Lesion of the Palate. J Rhinol Otol. 2013 Jun;1(1):2-5.

8. Lee JG, Allen G, Moore L, Gue S. Oral focal mucinosis in an adolescent: a case report. Aust Dent J. 2012 Mar;57(1):90-2.

9. Talacko AA, Lacy MF, Besly WJ, Aldred MJ. Oral focal mucinosis: report of two cases with ulceration. Pathology. 2004 Dec;36(6):582-3.

10. Germano F, Abate R, Santini F, Dri M, Arcuri C. Oral focal mucinosis: case report. Oral Implantol (Rome). 2008 Jul;1(2):91-3.

11. Soares de Lima AA, Naval Machado MA, Martins WD, Trindade Gregio AM, Dirschnabel AJ, Folador Mattioli TM, et al. Oral focal mucinosis. Quintessence Int. 2008 Jul-Aug; 39(7): 611-5.

12. Madhusudhan AS, Nagarajappa Das, Manjunatha BS, Swati Saawarn, Charan Babu HS. Oral focal mucinosis: report of two cases. Rev Odonto Ciênc. 2010 Aug;25(3):310-3.

13. Narana Ribeiro El Achkar V, Posch Machado AC, Dias de Almeida J, Rodarte Carvalho Y, Anbinder AL. Oral focal mucinosis: review of the literature and two case reports. Dermatol Online J. 2016 Sep 15;22(9).

14. Mattsson U, Lindberg P. Oral focal mucinosis of the tongue: A rare clinical entity? Oral Maxillofac Surg Cases. 2017 Mar;3(1):1-4.

15. Tiwana F, Janic A, Wheater M, Kinaia BM. A

rare oral focal mucinosis presentation in the aesthetic zone: a case report. Dent Open J. 2016 Feb;2(5):132-6.
16. Joshi CP, Dani NH, Mahale SA, Patel NR. A case of oral focal mucinosis of gingiva: Lesion in disguise. J Indian Soc Periodontol. 2015 Sep-Oct; 19(5):586-8.
17. Saito I, Ide F, Enomoto T, Kudo I. Oral focal mucinosis. J Oral Maxillofac Surg. 1985 May; 43 (5):372-4.
18. Woo J, Cheung WS. Bilateral oral focal mucinosis on the palate of a 2-year-old child: a case report. Int J Paediatr Dent. 2015 Jan;25(1):70-2.
19. Iezzi G, Rubini C, Fioroni M, Piattelli A. Oral focal mucinosis of the gingiva: case report. J Periodontol. 2001 Aug;72(8):1100-2.
20. Soda G, Baiocchini A, Bosco D, Nardoni S, Melis M. Oral focal mucinosis of the tongue. Pathol Oncol Res. 1998 Dec;4(4):304-7.
21. Manor Y, Merdinger O, Katz J, Taicher S. Unusual peripheral odontogenic tumors in the differential diagnosis of gingival swellings. J Clin Periodontol. 1999 Dec;26(12):806-9.
22. Buchner A, Merrell PW, Leider AS, Hansen LS. Oral focal mucinosis. Int J Oral Maxillofac Surg. 1990 Dec;19(6):337-40.
23. Kempf W, von Stumberg B, Denisjuk N, Bode B, Rongioletti F. Trauma-Induced Cutaneous Focal Mucinosis of the Mammary Areola: An Unusual Presentation. Dermatopathology (Basel). 2014 Jan 29;1(1):24-8.
24. Gnepp DR, Vogler C, Sotelo-Avila C, Kielmovitch IH. Focal mucinosis of the upper aerodigestive tract in children. Hum Pathol. 1990 Aug;21(8):856-8.
25. Gabay E, Akrish S, Machtei EE. Oral focal mucinosis associated with cervical external root resorption: a case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010 Oct;110(4):e75-8.
26. Rambhia KD, Khopkar US. Verrucous oral focal mucinosis. Indian J Dermatol Venereol Leprol. 2016 May-Jun;82(3):330-2.
27. Bosco AF, Macarini VC, Milanezi de Almeida J, Theodoro LH, Novaes VC, Júnior EC, et al. Oral focal mucinosis: Clinical case presentation with a focus on esthetic and functional surgical resolution. Clin Adv Periodontics. 2014 Nov;(4): 251-5.
28. Aldred MJ, Talacko AA, Ruljancich K, Story RD, Newland S, Chen ST, et al. Oral focal mucinosis: report of 15 cases and review of the literature. Pathology. 2003 Oct;35(5):393-6.
29. Tekkeşın MS, Yilmaz M, Olgaç V. [Oral focal mucinosis: a case report and review of the literature]. [Article in Turkish]. Turk Patoloji Derg. 2013;29(3):235-7.
30. Pacifici L, Meleo D, Pompa G, Pacifici A, Gambarini G, Testarelli L. Oral focal mucinosis of the tongue: a rare clinical case. Eur J Inflamm. 2012 Apr;10(1):111-5.
31. Sowmya GV, Manjunatha BS, Nahar P, Aggarwal H. Oral focal mucinosis: a rare case with literature review. BMJ Case Rep. 2015 Mar 10; 2015.
32. Narayana N, Casey J. Oral focal mucinosis: review of the literature and seven additional cases. Gen Dent. 2009 Mar-Apr;57(2):e11-3.
33. Yoshizato K, Yasumasu I. Effect of prolactin on the tadpole tail fin. II. Stimulatory effect of prolactin on the synthesis of acid mucopolysaccharide of the tadpole tail fin. Dev Growth Differ. 1971 Feb;12(4):265-72.
34. Ogueta S, Muñoz J, Obregon E, Delgado-Baeza E, García-Ruiz JP. Prolactin is a component of the human synovial liquid and modulates the growth and chondrogenic differentiation of bone marrow-derived mesenchymal stem cells. Mol Cell Endocrinol. 2002 Apr 25;190(1-2);51-63.