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 Mucinosi, Mucous Membrane, Mucinoses, Gingival Overgrowth, Hyaluronic Acid

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 present

| 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                   | 1               | 1974 | Tomich [3]              |
| NA         | Gingiva                           | 16/M                   | 8               | 1974 | Tomich [3]              |
| 1 year     | Buccal mucosa                     | NA/F                   | 1               | 1974 | Tomich [3]              |
| 2 months   | Tip of the tongue                 | 45/M                   | 8               | 1974 | Tomich [3]              |
| NA         | Mandibular alveolar mucosa        | 28/M                   | 2               | 1985 | Saito et al [17]        |
| 4 months   | Palate                            | 22/F                   | 2               | 1985 | Saito et al [17]        |
| 4 months   | Palate                            | 19/F                   | 2               | 1985 | Saito et al [17]        |
| 3 months   | Mandibular gingiva                | 35/M                   | 2               | 1985 | Saito et al [17]        |
|            | Mandibular gingiva                | 50/F                   | 2               | 1985 | Saito et al [17]        |
| 9 months   | Gingiva                           | 18/F                   | 2               | 1985 | Saito et al [17]        |
| 5 years    | Gingiva                           | 30/M                   | 2               | 1985 | Saito et al [17]        |
| 1 month    | Maxillary gingiva                 | 32/F                   | 2               | 1985 | Saito et al [17]        |
| 1 year     | Maxillary gingiva                 | 22/F                   | 2               | 1985 | Saito et al [17]        |
| NA         | Mandibular gingiva                | 53/F                   | 2               | 1985 | Saito et al [17]        |
| NA         | Maxillary gingiva                 | 16/F                   | 2               | 1985 | Saito et al [17]        |
| NA         | Mandibular gingiva                | 43/M                   | 2               | 1985 | Saito et al [17]        |
| NA         | Mandibular alveolar mucosa        | 61/F                   | 15              | 1990 | Buchner et al [22]      |
| NA         | Maxillary alveolar mucosa         | 37/F                   | 2               | 1990 | Buchner et al [22]      |
| NA         | Mandibular gingiva                | 41/F                   | 2               | 1990 | Buchner et al [22]      |
| 3 years    | Mandibular gingiva                | 37/F                   | 2               | 1990 | Buchner et al [22]      |
| 1 year     | Mandibular gingiva                | 46/M                   | 2               | 1990 | Buchner et al [22]      |
| 1 year     | Hard palate                       | 38/F                   | 2               | 1990 | Buchner et al [22]      |
| 3 years    | Mandibular retromolar area        | 46/M                   | 2               | 1990 | Buchner et al [22]      |
| 2 months   | Ventral tongue                    | 50/M                   | 2               | 1990 | Buchner et al [22]      |
| NA         | Larynx                            | 3/M                    | 2               | 1990 | Iezzi et al [19]        |
| NA         | Hard palate                       | 4/F                    | 2               | 1990 | Iezzi et al [19]        |
| 3 years    | Ventral Tongue                    | 68/M                   | 1               | 1998 | Soda et al [20]         |
| 8 months   | Gingiva                           | 48/M                   | 1               | 2001 | Iezzi et al [19]        |

83

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| Time   | Location                           | Children Count | Year | Reference                                |
|--------|------------------------------------|----------------|------|------------------------------------------|
| 1 month| Lip                                | 38/F           |      | Aldred et al [28]                        |
| 4 months|Gingiva                             | 30/F           |      |                                          |
| NA     | Gingiva                            | 16/F           |      |                                          |
| NA     | Gingiva                            | 56/F           |      |                                          |
| <1 year| Buccal mucosa                      | 60/F           |      |                                          |
| 10 years|Gingiva                             | 49/M           |      |                                          |
| 6 months|Gingiva                             | 31/F           |      |                                          |
| 1 year | Lip                                | 52/M 15 2003  |      |                                          |
| NA     | Gingiva                            | 74/M           |      |                                          |
| 4 months|Gingiva                             | 40/F           |      |                                          |
| 3 months|Tongue                              | 55/M           |      |                                          |
| 3 months|Gingiva                             | 37/F           |      |                                          |
| 1 year | Gingiva                            | 35/F           |      |                                          |
| 1 year | Gingiva                            | 33/F           |      |                                          |
| 1 year | Gingiva                            | 68/M           |      |                                          |
| NA     | Buccal mucosa                      | 63/F 1 2004    |      | Talakco et al [9]                        |
| NA     | Maxillary gingiva                  | 35/M 1 2008    |      | Germano et al[10]                        |
| NA     | 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 2 2013    |      |                                          |
| NA     | Hard palate                        | 30/F 1 2013    |      | Pauna et al [7]                          |
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.

**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.
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 Yasumatsu [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.

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