Giant inflammatory myofibroblastic tumor of oral cavity: a case report and literature review

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ABSTRACT

Background: Inflammatory myofibroblastic tumor is an infrequent lesion that is seen in the lungs, abdomen, skin, soft tissue, genital system, and mediastinum. It is rare in the oral cavity.

Case presentation: A 58-year-old woman presented with a mass in the left buccal mucosa. An extensive surgical intervention was performed. On gross examination, the mass was 9.5 x 8 x 3.5 cm in size. Microscopically, the tumor included spindle-shaped myofibroblast-like cells intermingling chronic inflammatory cells.

Differential diagnosis of inflammatory myofibroblastic tumor is extensive and includes benign and malignant spindle cell tumors, such as cranial fasciitis, solitary fibrous tumor, fibrosarcoma, and rhabdomyosarcoma.

Conclusion: Inflammatory myofibroblastic tumors are classified as tumors of intermediate biological potential due to a tendency of local recurrence and low risk of distance metastasis. We found it appropriate to submit this case because of its rarity and rapid growth; also, it is the largest size oral cavity location inflammatory myofibroblastic tumor that has been reported so far.

Keywords: Inflammatory myofibroblastic tumor, oral cavity, inflammatory pseudotumor, ALK-1, case report

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Background

Inflammatory myofibroblastic tumor (IMT) is an infrequent lesion that is seen in the lungs, abdomen, skin, soft tissue, genital system, and mediastinum. Presentation in oral cavity is rare [1,2]. Even though the cause of the IMT in the oral cavity is unknown, it is most likely reported to be associated with traumatic, inflammatory, or infectious conditions [3].

The main presentation is usually a mass in the site of origin. Radiologically, the lesion is nonspecific and an infiltrative growth pattern often suggests aggressive malignant tumors or granulomatous diseases [4].

The identification is pathological and spindle cell lesions are essential in differential diagnosis [5].

Here we present a case of IMT in the oral cavity that puzzled us with its size, growth rate, and intensive destruction.

Case Presentation

A 58-year-old woman presented with a mass in the left buccal mucosa which had been rapidly growing throughout 8 months. The patient had a history of having undergone an attempted excision of swelling in the same region at another center three times 3 years ago. Repeated biopsies were indicative of a chronic inflammatory process with no signs of malignancy or tumor. Laboratory tests were negative: HIV ag/ab, HbsAg, and Anti-hepatitis C virus antibody (anti-HCV) viral serology; there were no distinctive features in biochemistry. There was no evidence of any immunodeficiency as well.

Clinical intraoral examination in our center was carried out for the first time, and the lesion was 4 cm located in the left buccal mucosa and so an incisional biopsy was performed. The lesion had reached 10 cm in 5 months after the biopsy. The patient had respiratory distress and eating difficulties because of the large mass (Figure 1).

The imaging methods of the tumor showed that it was originating from the intramolar region on the left buccal mucosal area, an intense homogeneous contrast involvement and non-necrotic component. The mass also reached the floor of the mouth on the middle line and left side, causing pressure deformation on the tongue on computed tomography. The massive lesion was seen infiltrative to maxillary sinus, premaxillary area, posterior retromaxillary region, and midline nasal cavity by destructing the left alveolar arch in the magnetic resonance imaging (Figure 2).

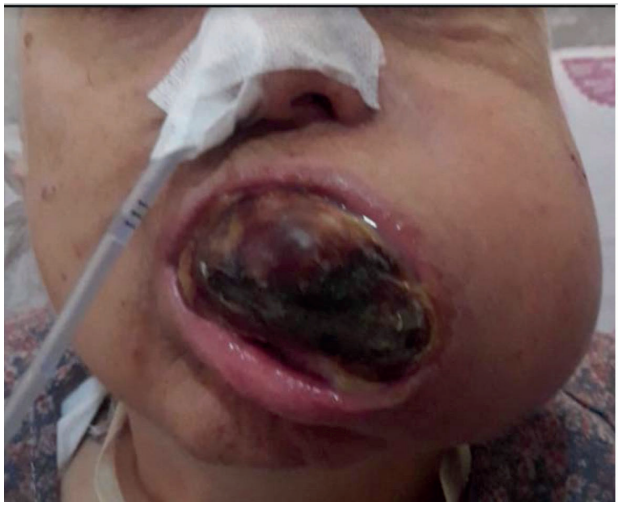

Figure 1. *The giant tumoral mass protruding from the patient's mouth.*

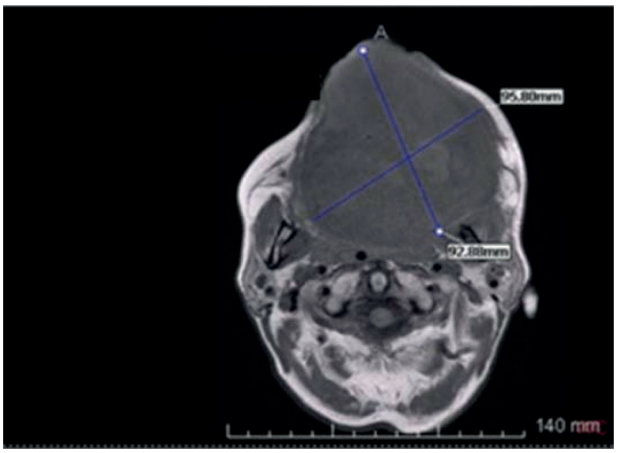

Figure 2. *Magnetic resonance imaging of the tumor.*

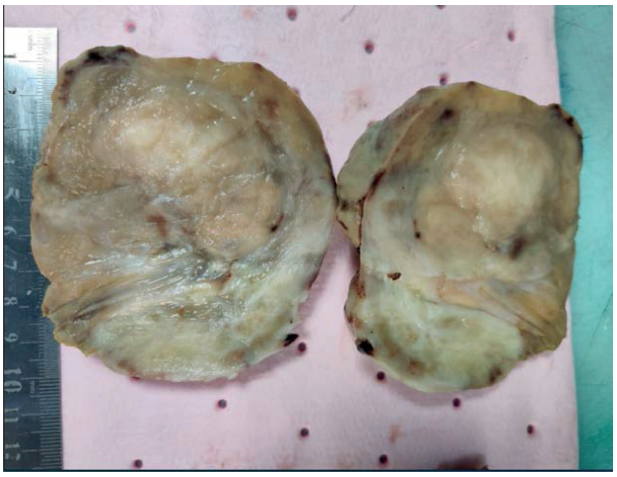

Figure 3. *Macroscopic appearance of the tumor.*

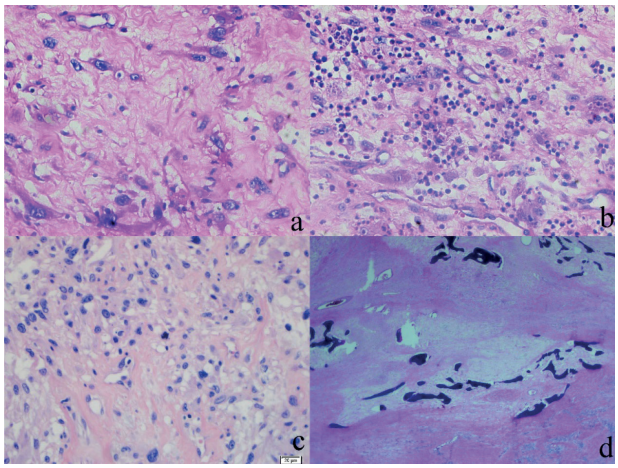

Figure 4. *(a) Atypical myofibroblastic cells in loose stroma (H&E ×400). (b) Myofibroblastic lesion with inflammatory cells (H&E ×400). (c) Occasional mitotic figures (H&E ×400). (d) Bone destruction (H&E ×200).*

A tumor excision with intraoral and external sinus surgery and mucosal reconstruction was performed and intraoperative frozen examination was made for surgical margins. The surgical margins were reported benign, and the specimen was sent to the pathology laboratory. On gross examination, the mass was 9.5 × 8 × 3.5 cm in size, with no capsule forming and the cut surface of the lesion was homogenous, rubbery, solid, white in color, and firm in consistency. There was no necrosis macroscopically (Figure 3).

The histological examination of the excised sample revealed an ill-defined circumscribed tumor mass covered by stratified squamous epithelium showing surface erosion. In the histopathological examination, the tumor mass included spindle-shaped myofibroblast-like cells intermingling with inflammatory cells. There were bone fragments destructed by the tumor. The myofibroblast-like tumoral cells were spindle-shaped with pleomorphism showing mild to moderate atypia in some areas. Although cells were showing epithelioid morphology, these areas were not dominant. Myxomatous degeneration areas were also visible in the stroma (Figure 4). The inflammatory cells comprised lymphocytes, plasma cells, and eosinophils. Some cells had coarse chromatin with clumping. Necrosis was not noted; mitotic figures were 1 in 10 High power field (HPF). Immunohistochemically, the tumor cells were positive for vimentin and CD 68 cytoplasmic. Rare, isolated cells were positive for anaplastic lymphoma kinase 1 (ALK-1) (Figure 5). Ki-67 proliferation index was 15% in hot-point areas. All immunohistochemical markers that were performed are summarized in Table 1.

The final diagnosis in the comment was "inflammatory myofibroblastic tumor." The patient's last review was about 3 months post-surgery; there has been no recurrence of the lesion.

Discussion

IMT is a tumor that was described first in 1939 in the lung [6] and has many names historically, such as benign myofibroblastoma, histiocytoma, xanthomatous granuloma, and spindle cell pseudotumor. The tumor was

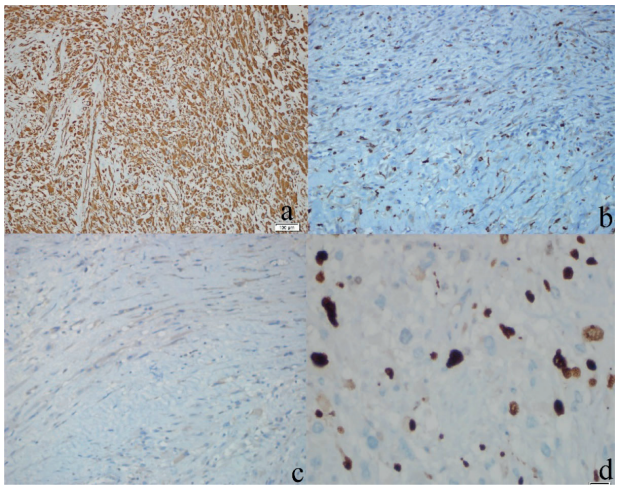

Figure 5. *(a) Vimentin positivity (×200). (b) CD68 staining (×200). (c) Weak ALK expression in spindle cells (×400). (d) Ki-67 proliferation (×400).*

Table 1. *Immunohistochemical panel results.*

POSITIVE[A]	NEGATIVE
CD 68 (C)	CD 31, CD34
Vimentin (C)	Smooth Muscle Actin (SMA)
Fascin (C)	Pancytokeratins
Myogenin (C)	CK 5/6
Caldesmon (C)	CK 7, CK 20
CD 163 (C)	P63
ALK[a] (C)	Desmin
MYO D1[a] (N)	HMB-45
P53 20% (N)	S-100
Ki-67 15% (Hot spot) (N)	Melan-A
Androgen 1-2%nuclear (N)	EMA

[a]Focal, Nuclear: N, Cytoplasmic: C.

classified as an "intermediate soft tissue tumor that is composed of myofibroblasts-differentiated spindle cells accompanied by numerous inflammatory cells, plasma cells and/or lymphocytes" in 1994, by the World Health Organization (WHO) 2nd edition [7].

The pathogenesis and etiology of IMT are not enlightened. Various predisposing factors have been proposed, which include ALK gene rearrangements, viral infections like Ebstein-Barr Virus (EBV), HIV, or Human herpes virus-8 (HHV-8), Immunoglobulin G4 (IgG4)-related disease, trauma, chronic inflammation, and autoimmune diseases.

ALK gene rearrangement is responsible for the pathogenesis of IMT which can be demonstrable with ALK immunohistochemistry. Approximately 50% of IMTs are ALK-positive [8]. In our case, ALK immunostaining was focally positive. Most of the other myofibroblastic and fibroblastic tumors are ALK-negative.

IMTs in the pulmonary region are seen in children and young adults more commonly; however, extrapulmonary IMTs affect mostly after second decade and have a more aggressive clinical outcome [9]. The first case of IMT in the oral cavity has been reported by Liston et al. [10] in 1981. Including the current one, 31 cases of oral IMT have been reported to date (Table 2).

IMTs' differential diagnosis in a wide range of benign and malignant spindle cell tumors such as cranial fasciitis, solitary fibrous tumor, fibrosarcoma, and rhabdomyosarcoma.

Cranial fasciitis contains less inflammatory infiltrate than IMTs. Also, they have an appearance of a loose haphazard arrangement of plump spindled cells which fascicles and stromal mucin. In our case, these typical features of cranial fasciitis were not observed and chronic inflammatory cells and spindle-shaped myofibroblastic cells are more prominent.

Solitary fibrous tumor is important in differential diagnosis, but its classical features which are oval to spindle-shaped nuclei with narrow cytoplasm, patternless collagen bands, and "staghorn" blood vessels and immunoreactivity for CD34 and STAT-6. IMT did not show either of those histologic features or CD 34 immune expression; also, our tumor was negative in CD34 and CD31 [11].

Fibrosarcoma is extremely rare in the oral cavity, a distinctly malign spindled cell tumor with collagenous areas and a herringbone pattern. Also, it has a lower inflammatory infiltrate than IMT and was excluded with these features.

Rhabdomyosarcoma occurs mostly in children. However, pleomorphic rhabdomyosarcoma is mostly seen in patients above 45 years of age. These tumors have sheets of large, pleomorphic, and frequently multinucleated eosinophilic cells and lack alveolar or embryonal components. Desmin positivity could be helpful in the differential diagnosis, and they have additional malignant features, like marked mitosis and necrosis. Our case was negative for desmin antibody and lacked marked malignant features.

Ki-67 proliferation rate is between 0 and 10% generally in the literature, and it is slightly higher in our tumor [9].

On the authority of the WHO soft tissue 5th edition [12], IMTs are categorized as intermediate biological potential tumors due to a tendency of local recurrence and low risk of distance metastasis.

There are reports of malignant transformations and fatalities with IMTs in paranasal sinus area in the head and neck region [13,14]. However, there is no reported case of malignant transformation, metastasis, or death in oral IMTs.

Table 2. *Clinical features of inflammatory myofibroblastic tumor cases in the oral cavity in the English literature.*

AUTHOR	AGE (YEARS)	GENDER	LOCATION	SIZE (CM)	DURATION	FOLLOW-UP
Liston et al.	4	Female	Buccal mucosa	4×5	2 weeks	6 months; NED
Liston et al.	2	Female	Buccal mucosa	3×5	4 days	10 months; NED
Liston et al.	6	Male	Buccal mucosa	4×5	1 day	NA
Earl et al.	44	Male	Buccal mucosa	-	-	2 years; NED
Ramachandra et al.	77	Female	Buccal mucosa	1.5	5 months	28 years; NED
Sheket al.	20	Male	Right cheek	2x2	1 month	13 months; NED
Sheket al.	36	Female	Left maxilla	NA	1 year	13 months; NED
Ideet al.	68	Female	Buccal mucosa	0.5×0.6	Few years	NA
Ideet al.	43	Female	Retromolar area	1×2.3	1 month	1 year; NED
Cable et al.	29	Female	Hard palate	1.8×1.8	8 weeks	8 weeks NA
Ideet al.	27	Male	Tongue	1.7	4 months	NA
Pankajand Uma	-	-	Tongue	-	-	NA
Jordan andRegezi	23	Male	Mandible	1	1 month	NA
Fangand Dym	23	Male	Retromolar area and masseter muscle	2.5×4×5	1 month	6 months; NED
Brooks et al.	82	Female	Mandible	5×5	2 months	18 months; NED
Pohet al.	42	Female	Mandible	3×3	-	6 months; NED
Deshingkaret al.	30	Female	Maxilla	3×4	8 months	NA
Johann et al.	33	Male	Mandible	3×2×2	-	28 months; NED
Oh et al.	20	Female	Mandible	-	3-4 months	22 months; NED
Xavier et al.	23	Female	Floor of mouth	3×3	3 weeks	2 years; NED
Eleyand Watt-Smith	29	Male	Maxilla	5×5	1 month	6 years; NED
Satomi et al.	14	Female	Gingiva	3×2	3 months	10 years; NED
Binmadi et al.	40	Female	Gingiva	1.5×1.2	-	4 months; NED
Palaskar et al.	19	Male	Mandible	-	3 months	6 months; NED
Rautava et al.	11	Female	Maxilla	-	-	3 years; NED
Yucel Ekici et al.	75	Male	Tongue	4	4 months	NA
Sah et al.	30	Male	Mandible	7x5	1 month	7 months; NED
Stringer et al.	16	Male	Mandible	-	3.5	6 months; NED
Rahman et al.	36	Female	Upper alveolus	7x4.5x3	1 month	18 months; NED
Shetty et al.	29	Male	Maxilla	3x2.5	13 months	NA
Our case	58	Female	Buccalmucosa	9.5x8x3.5	8 months	3 months; NED

NA = Not available, NED = No evidence of disease.

In the oral cavity, a total of 31 cases had been reported with the case, with lesions occurring over a wide age range of 2-82 years, with a median age of 32.9 years. Tumors show an 8:7 female predilection. When examined from the aspect of tumor size most of the tumors are smaller than 5 cm except for two other cases and ours. In this perspective, our case had the largest IMT in the oral cavity ever reported.

As a result, IMTs are tumors that rare in the oral cavity but can mimic malignancies due to their clinically and radiologically aggressive appearance. For this reason, recognizing the tumors is important and the differential diagnosis from other benign and malignant oral spindle cell tumors should be made with the help of histopathological and immunohistochemical methods. We found it appropriate to submit this case because of its rarity and rapid growth; also, it is the largest oral cavity IMT that has been reported so far.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Funding

None.

Consent for publication

Written consent was obtained from the patient.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

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Summary of the case

1	**Patient (gender, age)**	Female, 58-year-old
2	**Final diagnosis**	Inflammatory myofibroblastic tumor
3	**Symptoms**	Mass in left buccal mucosa
4	**Medications**	None
5	**Clinical procedure**	Surgical excision
6	**Specialty**	Pathology