

Inflammatory myofibroblastic tumor of mandible: A rare case report and review of literature

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Abstract

Inflammatory pseudotumor is a term given to different neoplastic and nonneoplastic entities that have a common histological appearance, which comprises spindle cell proliferation with a prominent chronic inflammatory cell infiltrate. Inflammatory myofibroblastic tumor (IMT) is an uncommon lesion with distinctive clinical, pathological and molecular features and is considered to be pseudotumor for the past two decades due to its appearance. IMT is an intermediate soft tissue tumor which was first observed in lungs. It was named as IMT because it mimics a malignant neoplasm clinically, radiologically and histopathologically. The most common sites are lungs, liver and gastrointestinal tract. IMT in head and neck region is exceptionally rare and the sites reported include gingiva, tongue, hard palate, mandible, buccal mucosa and submandibular salivary gland. Till now, 8 cases of intramandibular IMT were reported. Here, we report an additional case of intramandibular IMT in a 20-year-old male patient.

Keywords: Anaplastic lymphoma kinase, myofibroblasts, spindle cells

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INTRODUCTION

Inflammatory myofibroblastic tumor (IMT) is a rare neoplasm made up of various numbers of inflammatory cells as well as myofibroblastic spindle cells.^[1] It was first described by Brunn in 1939.^[2] Various terms have been described for this tumor, namely, inflammatory pseudotumor, fibrous xanthoma, plasma cell granuloma, pseudo sarcoma, lymphoid hamartoma, myxoid hamartoma, inflammatory fibrohistiocytic proliferation, benign myofibroblastoma and inflammatory fibrosarcoma.^[3]

The most common sites of involvement include lungs,^[4] liver^[5] and orbit.^[6] In the head and neck region, it has been reported in parapharyngeal spaces, maxillary sinus,

epiglottis and oral cavity. In the oral cavity, various sites such as gingiva, tongue, buccal mucosa, mandible and submandibular salivary gland are commonly involved.^[7] However, intrabony IMT's are rare; to the best of our knowledge, there are only eight reported cases of IMT involving mandible. Here, we present an additional case of intramandibular IMT and a brief discussion about clinical, radiographic and histopathological features.

CASE REPORT

A 22-year-old male patient presented with a painless enlarging mass in the lower left back tooth region for 5 months. No contributory medical history was noticed. Extraoral examination revealed facial asymmetry on the

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left side with diffuse swelling measuring approximately 7 cm × 5 cm extending anteroposteriorly 4 cm away from the angle of the mouth to the posterior border of the mandible and superoinferiorly from tragus of the ear to lower border of the mandible [Figure 1]. On palpation, swelling was firm in consistency. Restricted mouth opening (12 mm) was present. Single left submandibular lymph node was palpable measuring about 1.5 cm × 1 cm and is tender and soft in consistency.

Intraoral examination revealed swelling in the left mandibular vestibule extending anteroposteriorly from mesial aspect of 37 to anterior border of the ramus of the mandible [Figure 2]. On palpation, vestibular obliteration was present. Complete palpation of the swelling was not possible because of restricted mouth opening.

On radiographic examination, orthopantomograph (OPG) revealed irregular radiolucency extending anteroposteriorly from distal aspect of 38 to posterior border of ramus of the mandible and superoinferiorly from sigmoid notch to lower border of the mandible [Figure 3a]. Three-dimensional computed tomography scan revealed perforation at left ramus region with extensions as that of OPG [Figure 3b].

Based on clinical and radiographical findings, a provisional diagnosis of ameloblastoma was given. As there was

restricted mouth opening, complete surgical excision of the lesion was performed [Figure 4] and sent for histopathological examination.

Histopathology revealed nonencapsulated mass with fascicles of elongated spindle cells in fibrous stroma admixed with intense chronic inflammatory cell infiltrate, predominantly of lymphocytes [Figure 5a]. The spindle cells exhibited plump ovoid to tapering hyperchromatic nuclei with indistinct cell boundaries and mild nuclear atypia [Figure 5b]. No mitosis was present. In addition, immunohistochemical examination was performed with vimentin, α -smooth muscle actin (SMA), anaplastic lymphoma kinase (ALK) and S-100. Spindle cells positivity was noticed with vimentin [Figure 6a], α -SMA [Figure 6b] and ALK [Figure 6c] and negativity with respect to S-100 [Figure 6d]. Based on these findings, a diagnosis of IMT was given.

DISCUSSION

IMT is an uncommon lesion reported in various organs and mainly in soft tissues.^[3] In 1994, the WHO defined IMT as an “intermediate soft tissue tumor that is composed of myofibroblasts-differentiated spindle cells accompanied by numerous inflammatory cells, plasma cells and/or lymphocytes.”^[8]



Figure 1: Extraoral picture revealing facial asymmetry on the left side



Figure 2: Intraoral picture revealing restricted mouth opening

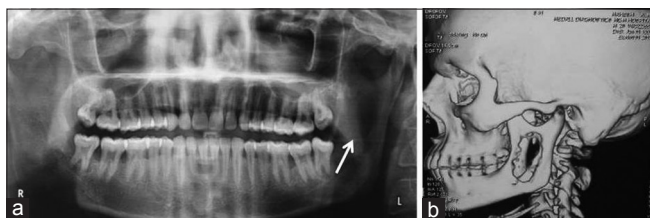


Figure 3: (a and b) Orthopantomograph and computed tomography scan revealing radiolucency at the left ramus region

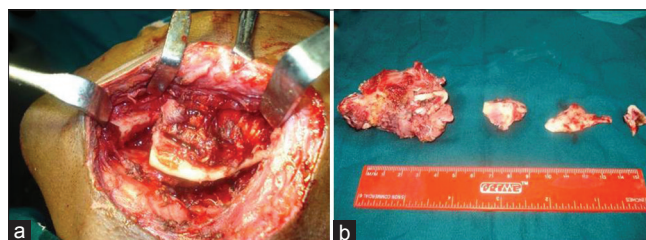


Figure 4: Excision of the tumor

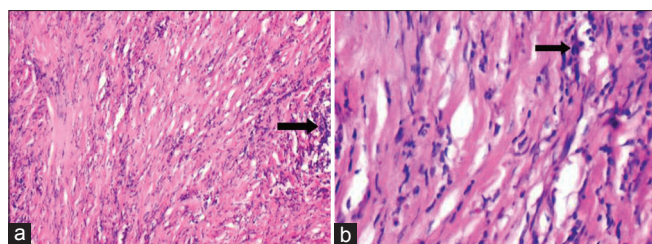


Figure 5: Histopathology revealing fascicles of elongated spindle cells admixed with dense lymphocytes (a) spindle cells are plump ovoid to tapering hyperchromatic nuclei with mild nuclear atypia (b)

The exact etiology of IMT is unknown. Various predisposing factors have been proposed which includes; reactive, infectious, autoimmune and neoplastic processes.^[7] Bacterial pathogens associated with this tumor are *Bacteroides*, *Campylobacter*, *Coxiella*, *Eikenella*, *Klebsiella* and *Pseudomonas*. However, in the published literature, none of the oral IMT has been associated with infectious etiology.^[9] An autoimmune or immunologically mediated pathogenesis has been suggested as these IMTs show regression with corticosteroids and cyclosporine A.^[10,11] With respect to neoplastic nature, dysregulation of ALK (ALK gene) has been suggested to play an important role in tumorigenesis by promoting abnormal phosphorylation of cellular substrates.^[9]

Clinically, IMT is painless with indurated mass or swelling of short duration.^[7] The present case revealed painless swelling for 5 months. In the head and neck region, it has been reported in parapharyngeal spaces, maxillary sinus, epiglottis and oral cavity. In oral cavity, various sites such as gingiva, tongue, buccal mucosa, mandible and submandibular salivary gland are commonly involved.^[7] However, central IMTs are rare. To the best of our knowledge, there are only nine reported cases (including present case) of IMT involving mandible [Table 1].^[3,7,9,12-16] Radiologically, IMTs in the head and neck region will be nonspecific and often suggest infiltrative growth, aggressive malignant lesion, or granulomatous disease.^[7]

Histologically, IMTs are characterized by a variable cellular spindle cell proliferation in myxoid to collagenous stroma intermixed with a prominent acute and chronic inflammatory cells.^[17] Coffin et al.^[18] described three basic histological patterns which are often seen in combination within the same tumor: myxoid/vascular pattern, a compact spindle cell pattern and hypocellular fibrous pattern. The myxoid or vascular pattern reveals loosely arranged plump spindle cells in an edematous or myxoid stroma with a prominent vasculature. The inflammatory infiltrate in these areas contains more neutrophils, eosinophils and fewer plasma cells as compared to other two patterns. The compact spindle cell pattern is characterized by a cellular

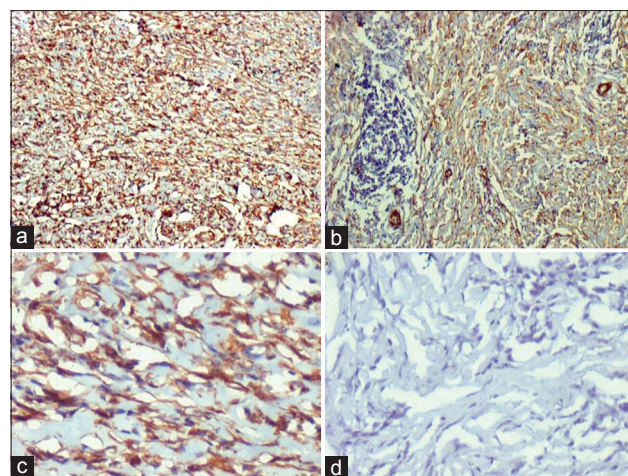


Figure 6: Immunohistochemistry revealing positivity for vimentin (a), smooth muscle actin (b), anaplastic lymphoma kinase (c) and negativity for s-100 (d)

Table 1: List of inflammatory myofibroblastic tumor cases reported in mandible

Author	Age	Sex	Location	Reference number
Ide et al., 1998	43	Female	Mandible retromolar region	[12]
Jordan and Regezi, 2003	23	Male	Mandible	[13]
Fang and Dym, 2004	23	Male	Mandible retromolar region and body and masseter muscle	[14]
Brooks et al., 2004	82	Female	Mandible	[9]
Poh et al., 2005	42	Female	Mandible	[3]
Johann et al., 2008	33	Male	Mandible	[15]
Oh et al., 2008	20	Female	Mandible	[16]
Palaskar et al., 2011	19	Male	Mandible	[7]
Korlepara et al.	22	Male	Mandible	Present case

proliferation of spindle cells with a fascicular or storiform pattern in a collagenous stroma. These foci typically show numerous plasma cells and lymphocytes admixed with spindle cells, but discrete lymphoid follicles and aggregates of plasma cells are also common. The fibromatosis-like pattern is relatively hypocellular with elongated rather than plump spindle cells in a densely collagenous background containing scattered lymphocytes, plasma cells and eosinophils. The present case revealed the features of compact spindle cell proliferation pattern.

The differential diagnosis includes nodular fasciitis, solitary fibrous tumor, benign fibrous histiocytoma, fibrosarcoma and leiomyosarcoma. Histopathologically, nodular fasciitis can be differentiated from IMTs by the presence of “C-” shaped fascicles and mucin-rich stroma giving characteristic “tissue culture like or feathery” appearance with minimal inflammatory cell infiltrate.^[19] Solitary fibrous tumor was excluded due to the absence of hemangiopericytoma-like areas and strong CD34 immunoreactivity.^[3] Benign fibrous

histiocytoma was not considered due to the presence of storiform pattern and ALK positivity.^[7] Fibrosarcoma was differentiated due to lack of characteristic “herring bone” pattern and minimal inflammatory infiltrate.^[3] Leiomyosarcoma was not considered due to the absence of spindle cells with cigar-shaped nuclei.^[17]

Immunoprofiling is important in the establishment of diagnosis of IMT, especially with identification of myofibroblasts. Approximately 50% of IMTs are ALK-positive with reactivity ranging from 36% to 71%.^[17] The present case revealed a diffuse positivity for ALK. ALK expression in IMT relatively predicts the presence of an ALK gene rearrangement.^[20] The pattern of ALK immunostaining correlates with specific gene fusion partners such as TPM3, TPM4, CARS, ATIC and SEC3 reveals diffuse cytoplasmic staining; RAN binding protein two and nuclear pore protein reveals nuclear membrane staining; Clathrin heavy chain gene (CLTC) fusion partner gives granular cytoplasmic staining.^[17,20] The present case revealed diffuse granular cytoplasmic staining.

The histopathological features for the diagnosis of IMT are the presence of diffuse inflammatory cell infiltrate predominantly consisting of plasma cells, lymphocytes, mild nuclear atypia, low mitotic rate without atypical forms and ALK positivity by immunohistochemistry (IHC).^[17]

Management of oral IMTs includes complete surgical resection,^[9] and continuous follow-up is needed as these are classified as tumors of intermediate biological potential.^[17] However, there is no evidence of recurrence or metastasis reported with oral IMTs till date.^[2]

CONCLUSION

IMTs are low-grade rare benign tumors which show variable clinical and radiological presentation. Only histological and IHC features can confirm the diagnosis which reveals characteristic features such as fascicles of spindle cells in an inflammatory cell background and ALK positivity.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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