Introduction
Weathers et al described the clinical and histopathologic features of giant cell fibroma in 1947 for the first time (1). Based on gender and age distribution, location, and histologic features, they separated it from the previously known entity “irritation fibroma”. It was designated as giant cell fibroma because of the presence of stellate fibroblasts with large mononuclear and multinucleated giant cells. Giant cell fibroma accounts for approximately 2% to 5% of all oral fibrous proliferations submitted for biopsy. It does not appear to have a clear etiology. In this article, we present seven cases of giant cell fibroma retrieved from the Archive of the Department of Oral and Maxillofacial Pathology, Dental Faculty, Hamadan University of Medical Sciences.

Case Presentation
Here, we present a report of seven cases of giant cell fibromas retrieved from the Archive of Department of Oral and Maxillofacial Pathology, Dental Faculty, Hamadan University of Medical Sciences from 2009 to mid-2021. There were five males and two females. The mean age of patients at the time of diagnosis was 33.9 ± 23.7 years. In our report, the lesion was mostly found on the gingiva (n = 3). The mean duration of the disease was 42.1 ± 37.9 months. The mean size of the lesions was 0.8 ± 0.26cm. Clinical differential diagnosis included irritation fibroma, squamous papilloma, mucocele, and fibroxanthoma. All demographic and clinical data of cases are summarized in Table 1. Figure 1A, B shows the clinical features.

Histopathologically, all cases showed a loosely arranged vascular fibrous connective tissue (Figure 2A). They were characterized by the presence of parakeratinized or orthokeratinized stratified squamous epithelium showing atrophy (number) with narrow and elongated rete ridges (number) (Figure 2B). In all cases, large stellate-shaped fibroblasts were seen in the connective tissue adjacent to the epithelium. The aforementioned cells showed distinct cell borders and a moderate amount of basophilic cytoplasm. Some of them contained 2-3 nuclei while some others had only one hyperchromatic nucleus or large vesicular nucleus with prominent nucleoli (Figure 2C).

Abstract
The giant cell fibroma is a fibrous tumor with characteristic clinicopathologic features. It accounts for approximately 2% to 5% of all oral fibrous proliferations submitted for biopsy. It does not appear to have a clear etiology. In this article, we present seven cases of giant cell fibroma retrieved from the Archive of the Department of Oral and Maxillofacial Pathology, Dental Faculty, Hamadan University of Medical Sciences.

Keywords: Connective tissue, Etiology, Mouth diseases, Soft tissue, Maxillofacial

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The diagnosis of giant cell fibroma was confirmed by microscopic examination. All tumors were treated by surgical excision.

**Discussion**

The giant cell fibroma is a rare non-neoplastic lesion of the oral mucosa. The etiology of this lesion remains controversial. Chronic irritation does not seem to have a role in the etiology of the lesion. Previous studies have suggested a slight female predilection. However, in this study, most of the cases were male (71%). The discrepancy may be attributed to the limited number of cases or genetic and racial differences. In the present study, the mean age of patients at the time of diagnosis was 33.9 ± 23.7 years. Previous studies have also demonstrated that the lesion usually occurs during the first three decades of life (4, 6). In the current study, most of the cases were found on the gingiva (43%). Most published papers have also
noticed that approximately 50% of all cases occur on the gingiva (5). Similar to the present study, several studies have indicated that the lesion is usually less than 1 cm in diameter (4,7). With regard to the origin of giant cell fibroma, immunohistochemical analysis has shown positive staining of stellate and multinucleated cells with vimentin and prolyl-4-hydroxylase, suggesting that these cells might originate from fibroblasts (8,9). Ultrastructural studies have revealed numerous intracellular microfibrils supporting the fibroblastic nature of the giant cells in the lesion (10). Additionally, under light microscopy, stellate morphology, vesicular nuclei with prominent nucleoli, and basophilic cytoplasm due to high mRNA content are in favor of active fibroblast differentiation (11). Giant cell fibroma must be differentiated from irritation fibroma (cases with a smooth surface) and squamous papilloma (cases with a pebbly appearance). However, in contrast to giant cell fibroma, the extracellular matrix in irritation fibroma contains elastin (12). Clinically squamous papilloma occurs in older age and the common sites are the tongue, lip, and soft palate (10,11). There is also a tumor of the skin named fibrous papule of the nose, which shares the common histologic feature of a variable number of plump stellate or spindle-shaped multinucleated cells in the dermis. Besides, immunohistochemical staining with factor XIIIa can help to differentiate these two lesions. It has been suggested that dermal dendrocytes are the putative cells of origin (13). The treatment of choice was conservative surgery. Recurrence has rarely been reported (2).

**Conclusions**

Reactive fibrous hyperplastic lesions are common in the oral cavity and have some similarities in the clinical and histopathology features. Nonetheless, the giant cell fibroma is a fibrous tumor with distinctive clinicopathologic features. The etiology is not clear. Its prognosis is similar to that of irritation fibroma. The giant cell fibroma is treated by conservative surgical excision, and its recurrence is rare.

**Authors’ Contribution**

SI: Study conception and design, supervision, manuscript preparation and editing. SJ: data collection and interpretation of results, EA: data collection and interpretation of results, draft manuscript preparation, SV: data collection PA: data collection

**Conflict of Interest Disclosures**

The authors declare that they have no conflict of interests.

**Ethical Statement**

Demographic information, medical histories, test and laboratory results and other data were published without the release of any personal information.

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