The giant cell fibroma

A review of 103 cases with immunohistochemical findings

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This article reports a series of 103 cases of giant cell fibromas occurring in the oral mucosa. The commonest location was the gingiva, followed by the tongue and the buccal mucosa. The mean age of the patients was 27.7 years, and the median age 21 years. Microscopically, the tumors were characterized by the presence of large stellate or angular cells, which occasionally contained several nuclei. Immunohistochemical stains showed that the cells were vimentin-positive but negative for S-100 protein, cytokeratin, leukocyte common antigen, and neurofilament. □ *Immunohistochemistry; oral mucosa; pathology*

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In 1974 Weathers & Callihan (1) reported on 108 cases of a previously undescribed tumor of the oral cavity. Histologically it was characterized by the presence of stellate, mononuclear, and multinuclear cells, and the name giant cell fibroma was proposed. The lesion was usually seen in young persons, and the commonest location was the gingiva, whereas fibrous hyperplasias were most often found in the buccal mucosa in older persons.

Houston (2) reviewed 464 cases and substantiated the findings of Weathers & Callihan (1), with minor differences. Recently, Bakos (3) reported on 116 cases. In his study a greater incidence was found in older age groups, and immunohistochemical analyses were included.

It has been questioned whether the giant cell fibroma should be regarded as a separate entity. Several fibrous lesions of the skin and mucous membranes have been shown to contain stellate and multinucleated cells (4, 5). In a study of 1550 oral fibrous hyperplasias (6) it was demonstrated that in 5% of the lesions, stellate and multinucleated cells were a dominant feature of the histologic picture. For example, 31% of the gingival fibromatoses were found to contain these characteristic cells.

In a Swedish study of 175 hyperplastic lesions of the gingiva and alveolar mucosa no giant cell fibromas were found (7). It is therefore suggested that this type of fibrous tumor might be rarer in Sweden than in other countries.

The aim of the present study was to record the occurrence of giant cell fibromas in a Swedish biopsy material and to describe the clinical, histologic, and immunohistochemical findings.

Materials and methods

The PAD files of the Department of Oral Pathology, Faculty of Odontology, University of Göteborg, were reviewed for 25,575 oral pathology reports between 1978 and 1993. In this period 4629 lesions (18.1%) were coded as fibroepithelial or fibrous hyperplasias. Of these, 103 (2.2%) could be classified as giant cell fibromas on the basis of their histologic appearance in sections stained with hematoxylin and eosin.

The material was registered by the age, sex, and localization of the lesion. Formalin-fixed sections from 10 giant cell fibromas were stained immunohistochemically with antibodies to S-100 protein (U 029), neurofilament (U 7039), cytokeratin (U 7022), leukocyte common antigen (LCA) (U 7024), and vimentin (U 7034) in accordance with DAKO's EPOS/HRP system. The incubations were performed as described in DAKO's enhanced polymer one-step staining (EPOs) immunoperoxidase staining procedure, and as a control the available negative control reagent, U 951, was used.

Results

The giant cell fibroma represented 2.2% of the biopsied fibrous lesions and 0.4% of the total biopsy specimens surveyed, whereas the fibroepithelial or fibrous hyperplasias comprised 18.1% of the total number of specimens. The mean age for patients with giant cell fibromas was 27.7 years, and the median age 21 years (range, 4–72 years). The age and sex distributions are summarized in Fig. 1 and the location in Table 1. A typical clinical

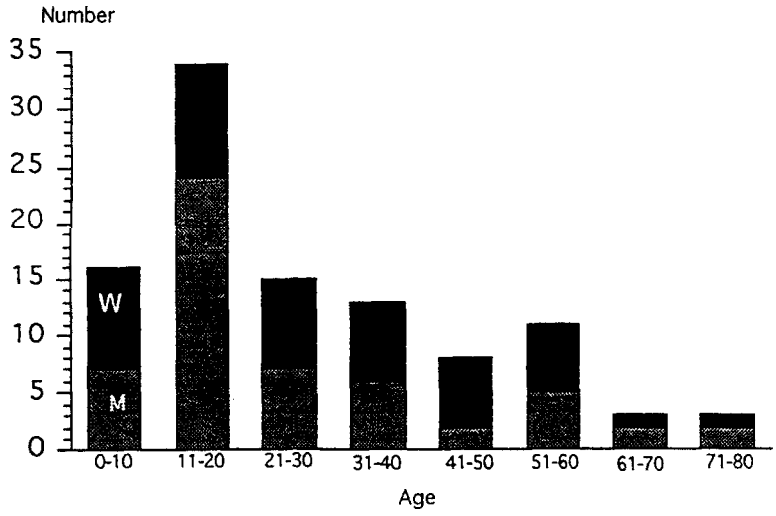

Fig. 1. Age distribution of 103 patients with giant cell fibromas. W = women; M = men.

picture of a giant cell fibroma of the gingiva is shown in Fig. 2.

Histologic and immunohistochemical findings

The giant cell fibromas were composed of a usually loosely arranged connective tissue (Fig. 3) characterized histologically by the presence of large stellate cells with a basophilic and granular cytoplasm containing vacuoles and often showing dentritic-like processes (Figs. 4 and 5). The cells usually had a single nucleus, but quite often two and occasionally several nuclei were seen (Fig. 4).

The covering epithelium often showed festooning of the rete ridges (Fig. 3), suggesting an expansive mesenchymal process. Inflammation was only seen in a minority of the cases and in the gingiva.

Immunoreactivity in the stellate cells was consistently positive for vimentin (Fig. 5), and all the 10 cases examined were negative for S-100 protein, cytokeratin, LCA, and neurofilament. All negative controls were non-reactive.

Table 1 Localization of 103 giant cell fibromas

Site	No.
Gingiva	55
Maxillary	17
Mandibular	38
Tongue	24
Buccal mucosa	12
Palate	4
Lip	1
Unknown	7

Discussion

The frequency of the lesion was in agreement with a report of Weathers & Callihan (1) but lower than those reported in other studies (3, 6). A slight female preponderance has been shown in some papers (2, 3), whereas others (1, 6), like the present one, showed no significant sex predilection. Thus the giant cell fibroma fails to show the 2:1 female sex predilection of other fibrous 'tumors' (1, 6).

The giant cell fibroma occurs most often among young people and is mainly located in the gingiva. A peak incidence in the second decade was found in our study, and this is in accordance with other studies (1, 2, 6). Bakos (3), on the other hand, found a greater

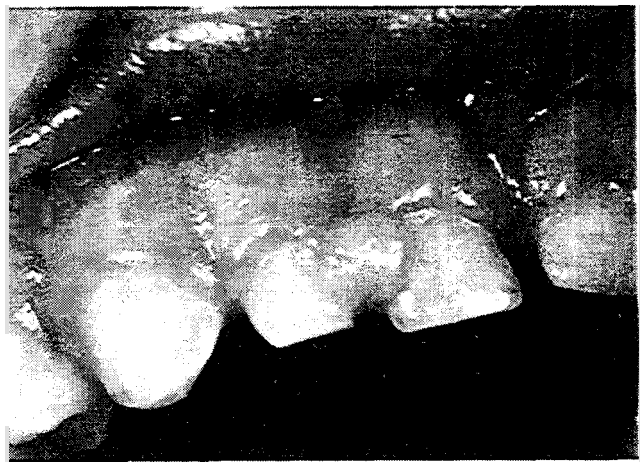

Fig. 2. Giant cell fibroma in the gingiva in a 7-year-old boy

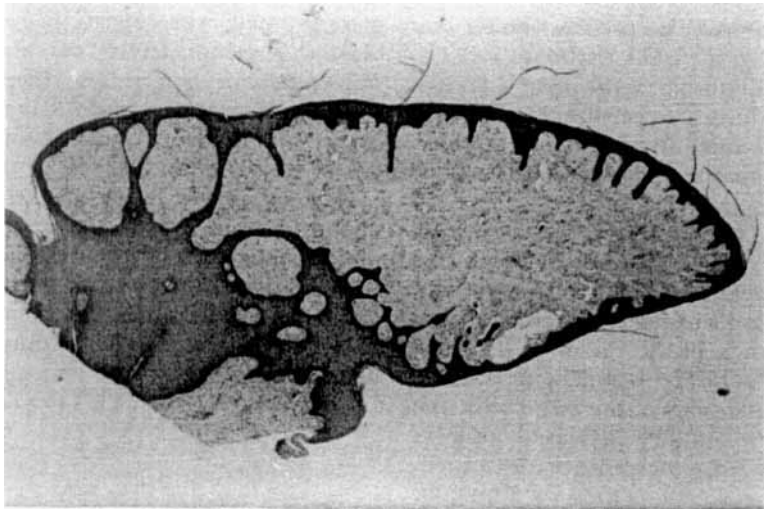

Fig. 3. Low magnification of a typical giant cell fibroma. The covering epithelium shows festooning of the rete ridges, and the stroma is fibrous with a loosely arranged collagen (hematoxylin and eosin stain; original magnification, ×50).

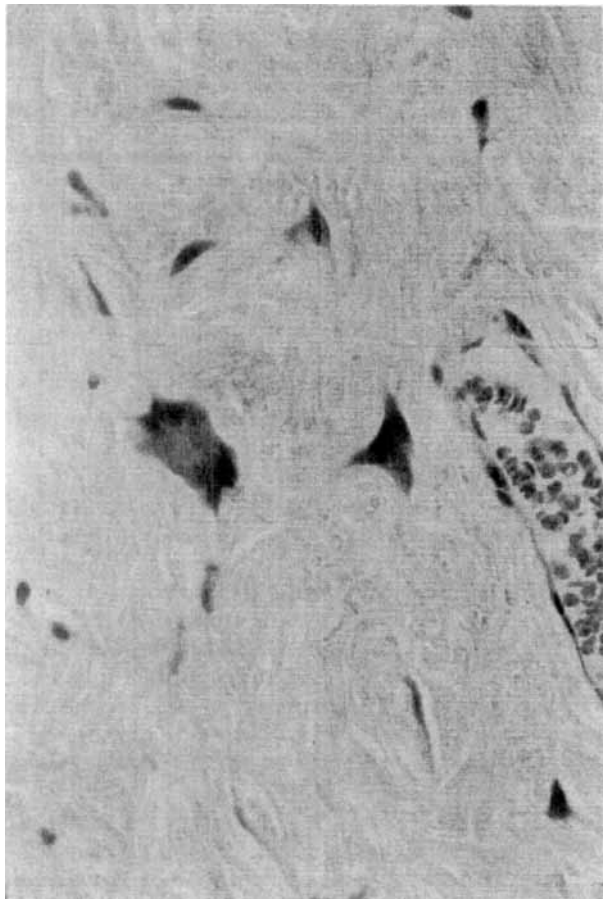

Fig. 4. Characteristic stellate and giant cells of giant cell fibroma (hematoxylin and eosin stain; original magnification, ×320).

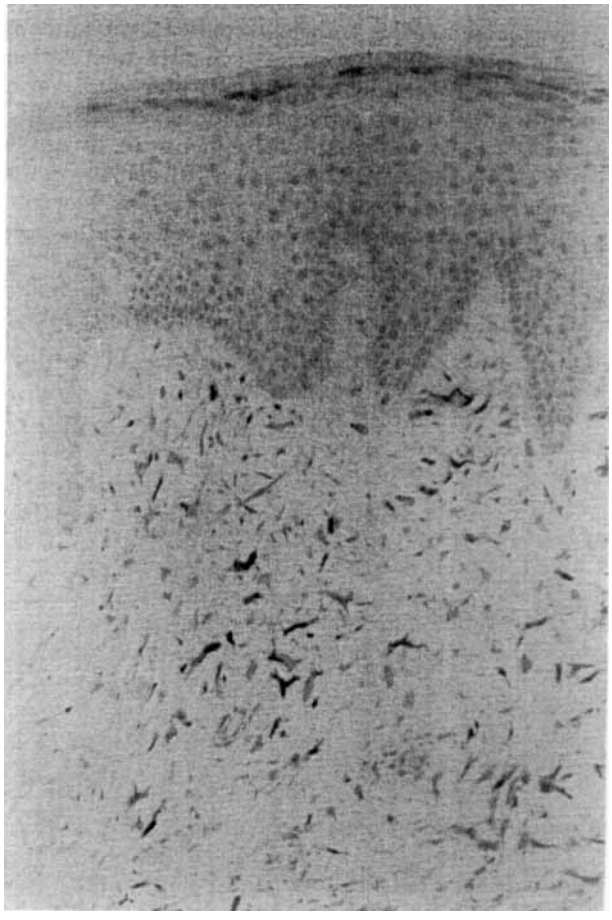

Fig. 5. Immunohistochemical staining for vimentin in giant cell fibroma. Strong positive staining is seen in spindle-shaped, stellate, and multinucleated connective tissue cells (hematoxylin counterstain; original magnification, ×125).

incidence in older age groups. The predilection for the gingiva is in agreement with earlier findings (1–3, 6). In contrast to the giant cell fibromas, the more common irritation hyperplasias (fibrous hyperplasias, fibroepithelial hyperplasias, fibromas) are commoner in older age groups, and the commonest localization is in the buccal mucosa (1, 6).

The histopathologic characteristics were also in agreement with earlier studies: distinct mononuclear and sometimes multinuclear large cells were seen. The mononuclear cells often had a fusiform or stellate shape.

With regard to the origin of the tumor cells, it has been suggested that they might be melanocytes (1). The dendritic cytoplasmic extensions of the large cells, the presence of melanin (1, 2), and their increased numbers near the epithelium suggest a melanocytic derivation. However, the present result with negative staining for S-100 protein does not confirm this suggestion and also makes a relationship to Langerhans cells unlikely. Negative staining for neurofilament and for S-100 protein suggests that the cells are not of peripheral nerve origin, which is in agreement with an earlier study (3). In this study it was also shown that the cells were negative for factor VIII and lectin (indicates no relation to endothelial cells), lysozyme (suggests no relation to giant cells of granulation tissue), and cytokeratin (indicates no relation to squamous epithelial cells). The profile with positive staining for vimentin is in agreement with the result of Regezi et al. (8). These results indicate that the stellate cells are of fibroblastic origin. An ultrastructural study has also intimated that the cells are unusual fibroblasts (5). However, Regezi et al. found positivity also for antichymotrysin and often also for HLA-DR and suggested that the cells were primitive mesenchymal cells capable of macrophage and fibroblast differentiation. In the present study the cells stained negatively for LCA. However, this reagent only reacts with histiocytes and macrophages to a variable extent, and thus the result does not exclude the hypothesis of Regezi et al. (5).

Various fibrous lesions of the skin and the mucous membranes have been shown to contain stellate and multinucleated cells of presumed fibroblastic origin (2, 5, 6). Thus, the presence of these cells is not unique for giant cell fibromas, and therefore the lesions are likely to be reactive or hamartomatous rather than true neoplasms.

References

1. Weathers DR, Callihan MD. Giant cell fibroma. Oral Surg Oral Med Oral Pathol 1974;37:374–84.
2. Houston GD. The giant cell fibroma: a review of 464 cases. Oral Surg Oral Med Oral Pathol 1982;53:582–7.
3. Bakos LH. The giant cell fibroma: a review of 116 cases. Ann Dent 1992;5:32–5.
4. Buchner A, Merell PW, Hansen LS, Leider AS. The retrocuspid papilla of the mandibular lingual gingiva. J Periodontol 1990;61: 586–90.
5. Regezi JA, Zarbo RJ, Tomich CE, Lloyd RV, Coutney RM, Crissman JD. Immunoprofile of benign and malignant fibrohistiocytic tumors. J Oral Pathol 1987;16:260–5.
6. Reibel J. Oral fibrous hyperplasias containing stellate and multinucleated cells. Scand J Dent Res 1982;90:217–26.
7. Anneroth G, Sigurdson Å. Hyperplastic lesions of the gingiva and alveloar mucosa. Acta Odontol Scand 1983;41:75–86.
8. Regezi JA, Courtney RM, Kerr DA. Fibrous lesions of skin and mucous membranes which contain stellate and multinucleated cells. Oral Surg Oral Med Oral Pathol 1975;39:605–14.

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