Hyperplastic lesions of the gingiva and alveolar mucosa

A study of 175 cases

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175 'epulides' were studied clinically and histologically. The lesions were histologically reclassified into three groups: granulomatous, fibromatous and giant cell lesions. The granulomatous group was four times and the giant cell group 1.5 times more frequent in females. It is suggested that the expression epulis should be abandoned as a microscopic designation for lesions in the oral mucosa, as it is only a non-specific topographico-clinical concept comprising histogenetically and histomorphologically differing lesions and therefore does not represent a uniform group. The suggested new terms for the three types of hyperplastic lesions are *oral mucosal granulomatous hyperplasias* (including such diagnostic terms as granulomatous gingivitis, gingivitis of pregnancy, granuloma gravidarium, pyogenic granuloma, epulis angiomatosa and epulis telangiectaticum), *oral mucosal fibrous hyperplasias* (including such diagnostic terms as fibrous epulis, epulis fissuratum, fibroepithelial lesions, denture injury tumor and peripheral odontogenic fibroma) and *oral mucosal giant cell hyperplasia* (including such diagnostic terms as peripheral giant cell granuloma and giant cell epulis). □ *Epulis; histopathology; terminology; periodontology; oral medicine*

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Epulis is a collective term for lesions of the oral mucosa having an intimate association with the periodontal membrane or with the periosteum of the jaw. The word epulis derives from the Greek 'epi' and 'ulon', meaning 'on the gingiva'. In clinical oral medicine the expression has thus been used to denote a process localized to the gingiva. In recent years, however, a departure has been made from earlier practice, and the term epulis is now also accepted as a designation for mucosal hyperplasias of the edentulous alveolus.

Most oral hyperplastic lesions are a response of the tissue to a nonspecific infection or other irritations. The clinical and histologic characteristics can vary to a large extent.

The variety of clinical and histopathological characteristics is presumably one of the most important reasons why lesions of epulis type have been described under such a great number of different terms in the dental and medical literature. The commonly used term, epulis, has become only a topographicoclinical concept, saying nothing about the histological structure or pathogenesis of the lesion. The term epulis should therefore be discarded as a diagnosis. The variety of other unclearly defined terms used to described epulis-type lesions has led to diagnostic confusion and uncertainty. Surprisingly little attention has been paid to this diagnostic problem in textbooks or in the dental literature, despite the fact that gingival hyperplasias are among the most commonly diagnosed and treated lesions. There is, therefore, a need to simplify and minimize the terminology of these lesions. Such a simplified classification system should, if possible, be based upon relevant both clinical and histopathological characteristics of the lesions. The aim of this study was to develop a new classification system of gingival hyperplasias based upon a clinico-pathological study of a major epulis material.

Materials and methods

The material, 175 patients, consisted of all gingival hyperplasias clinically diagnosed as epulides and collected over a 15-year period at the Department of Otolaryngology, Karolinska Hospital, Stockholm. From the patients' records, the following data were registered: age and sex of the patients, size, colour and consistency of the lesions, duration and alveolar bone involvement.

A histopathological reevaluation was made of tissue sections stained with Mayer's hematoxylin-eosin and van Gieson. The morphologic assessment was made without any knowledge of the clinical characteristics of the lesions. Each case was subjectively evaluated for the relative amount of collagen, vascularization, inflammatory cells, giant cells or bone and osteoid present (as compared to the other cases).

Results

Clinical observations

The lesions were taken from 175 patients, 110 (63%) females and 65 (37%) males. The distribution of the patients according to age and sex is illustrated in Fig. 1. The age varied between 6 and 81 years, and most of the patients were 30-49 years of age.

A classification of the examined lesions into the following three main groups was made based on the histopathological evaluation: the granulomatous, fibromatous and giant cell group.

The granulomatous group was characterized by an abundance of vascularization and inflammation. The fibromatous group was rich in collagen and had a low degree of inflammation and the giant cell group had in most cases an abundance of giant cells of the osteoclast type, low degree of inflammation and a mesenchymal stroma of embryonal type.

There were 59 granulomatous lesions and 59 fibromatous lesions and the remaining 57 cases were classified as giant cell lesions. Granulomatous lesions were 4 times (Fig. 2) and giant cell lesions (Fig. 3) 1.5 times more frequent in women. There was, however, no sex difference in the fibromatous group (Fig. 4).

The majority of patients with the granulomatous, fibromatous or giant cell lesions were between 20–39 years, 30–59 years, and 30–49 years, respectively (Figs. 2–4).

Of the 175 patients, 23 women (13%) were pregnant and an additional 13 women (7%)

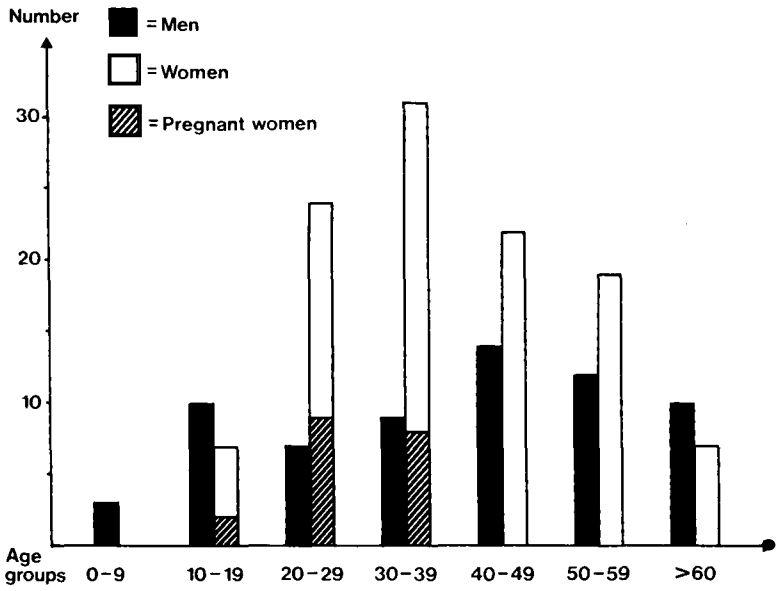

Fig. 1. Age and sex distribution of epulis patients.

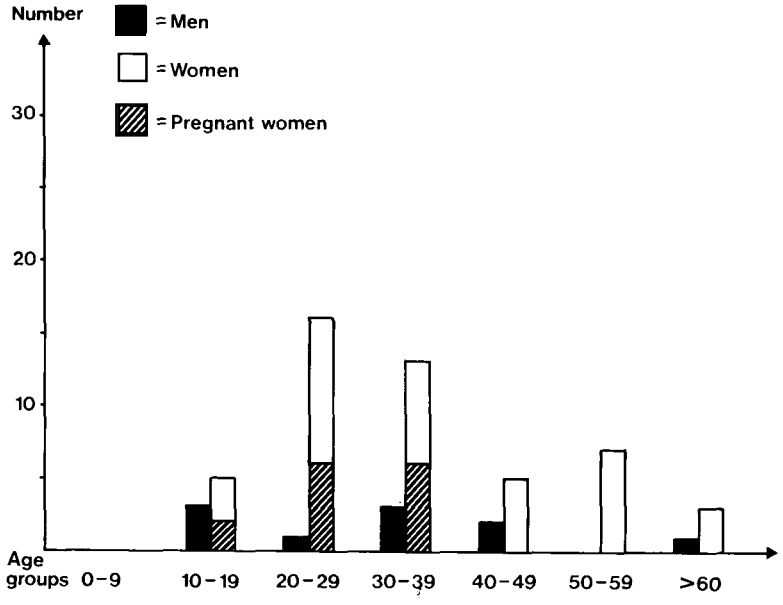

Fig. 2. Age and sex distribution of granulomatous epulis patients.

were in the lactation period. Of the 23 pregnant women, 15 (65%) had granulomatous and 7 (30%) fibromatous lesions. The remaining woman had a giant cell lesion. Of the thirteen lactating women, 9 had giant cell and 3 had granulomatous lesions.

In Figs. 5–7 the fibromatous, granulomatous and giant cell lesions are clinically illustrated.

The clinical characteristics of the lesions in terms of the form of connection to underlying tissue, the site, size, consistency, color

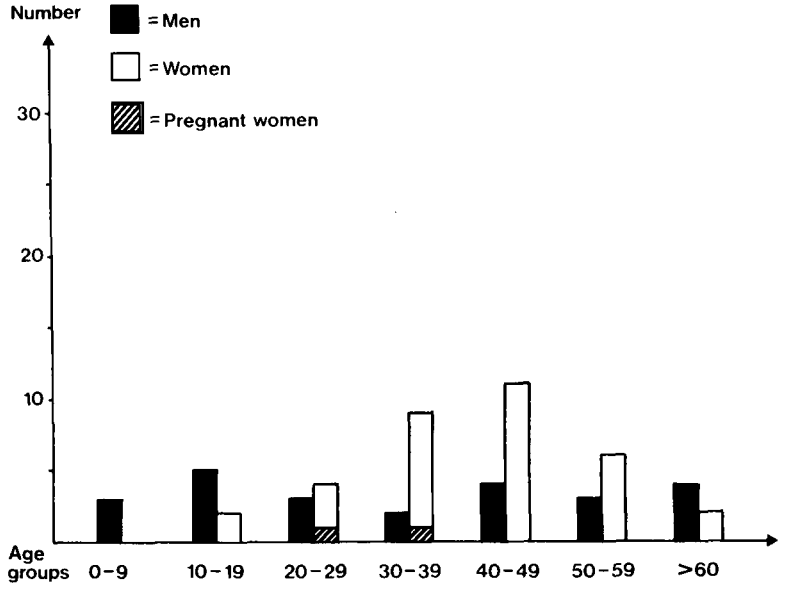

Fig. 3. Age and sex distribution of giant cell epulis patients.

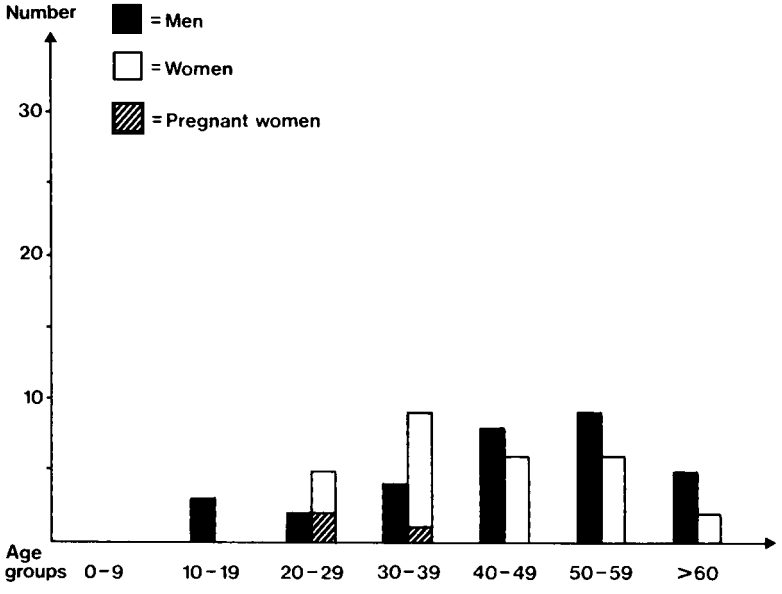

Fig. 4. Age and sex distribution of fibromatous epulis patients.

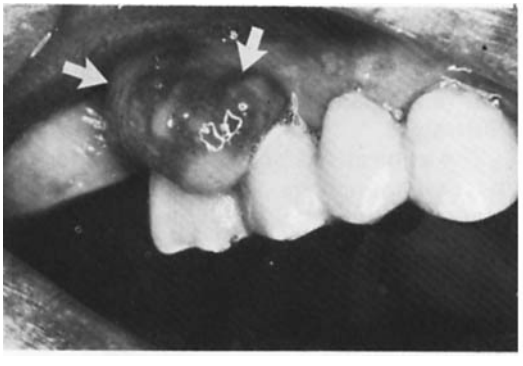

Fig. 5. A hyperplastic fibromatous lesion (epulis) in the area of the maxillary right first molar in a 37-year-old male.

Fig. 7. A hyperplastic giant cell lesion (epulis) in the area of the maxillary right canine in a 52-year-old male.

Fig. 6. A hyperplastic granulomatous lesion (epulis) in the area of the maxillary right first premolar in a 42-year-old female.

and duration of the lesions are illustrated in Tables 1–4.

Of the 175 examined lesions, 98 (56%) cases were located in the anterior part of the maxilla or mandible, while the remaining 77 (44%) cases were located in the posterior part (Table 1). The granulomatous and fibromatous lesions were predominantly localized to the anterior maxilla and mandible while the giant cell lesions were mostly located in the posterior regions (Table 1). The lesions were located to the gingiva in 140 (80%) of the cases, while the remaining 35 (20%) of the lesions were found on edentulous alveolar mucosa.

Table 1. Location of 175 granulomatous, fibromatous and giant cell lesions

Site	Granulomatous group	Fibromatous group	Giant cell group	Total no.
Maxillae, anterior part	24	16	9	49
Maxillae, posterior part	10	7	15	32
Mandibulae, anterior part	13	23	13	49
Mandibulae, posterior part	12	13	20	45
Total no.	59	59	57	175

Table 2. Size of 175 granulomatous, fibromatous and giant cell lesions

Size	Granulomatous group	Fibromatous group	Giant cell group	Total no.
< 0.5 cm	22	15	13	50
0.5–1 cm	29	30	21	80
1–2 cm	2	6	13	21
> 2 cm	0	3	5	8
No data available	6	5	5	16
Total no.	59	59	57	175

Table 3. Connection to underlying tissue, consistency and color in 175 granulomatous, fibromatous and giant cell lesions

Clinical data	Granulomatous group	Fibromatous group	Giant cell group	Total no.
Connection to underlying tissue				
Stalk, thin	25	13	8	46
Stalk, thick	22	23	26	53
Broad base	7	23	23	71
No information available	5	—	—	5
Consistency				
Firm	20	26	9	55
Half-firm	25	30	26	81
Soft	14	3	22	39
Color				
Normal	45	47	44	136
Reddish and/or cyanotic	14	12	13	39

Table 4. Duration of 175 granulomatous, fibramatous and giant cell lesions

Duration	Granulomatous group	Fibromatous group	Giant cell group	Total no.
1–2 months	20	8	14	42
3–6 months	15	9	17	41
7–12 months	9	10	9	28
> 1 year	9	30	12	51
No information available	6	2	5	13
Total no.	59	59	57	175

Table 5. Histopathologic characteristics in 175 granulomatous, fibromatous and giant cell oral mucosal lesions. Percentage figures within parentheses

Type of lesion	Collagen			Inflammation degree				Vascularization			Giant cell			Bone formation			
	Little	Moder.	Abund.	None	Mild	Moder.	Severe	Slight	Moder.	Abund.	None	Few	Moder.	Abund.	None	Few	Moder.	Abund.
Granulomatous lesion (n=59)	44 (74)	14 (24)	1 (2)	—	16 (27)	29 (49)	14 (24)	4 (7)	29 (49)	26 (44)	57 (96)	2 (4)	—	—	38 (64)	11 (19)	9 (15)	1 (2)
Fibromatous lesion (n=59)	3 (5)	33 (55)	23 (40)	1 (2)	31 (52)	24 (41)	3 (5)	46 (78)	12 (20)	1 (2)	59 (100)	—	—	—	40 (58)	13 (22)	3 (5)	3 (5)
Giant cell lesion (n=57)	44 (77)	11 (19)	2 (4)	1 (2)	46 (81)	9 (15)	1 (2)	14 (24)	41 (72)	2 (4)	—	6 (10)	11 (19)	40 (71)	29 (51)	14 (25)	7 (12)	7 (12)
Total number (n=175)	91 (52)	58 (33)	26 (15)	2 (1)	93 (53)	62 (36)	18 (10)	64 (37)	82 (47)	29 (16)	116 (66)	8 (5)	11 (6)	40 (23)	107 (61)	38 (22)	19 (11)	11 (6)

In consistency the giant cell lesions (39%) and the granulomatous lesions (24%) were more commonly described as soft than the fibromatous group (5%). The giant cell lesions were rarely (16%) described as firm.

No case was associated with the flanges of ill-fitting dentures (epulis fissuratum).

No difference between the groups of lesions concerning color was noticed (Table 3). The most common color of the mucosa covering the lesions was in all groups a clinically normal, pale color.

By roentgenographic examination, adjacent alveolar bone destruction was found in 23 (13%) of the lesions. Of these 23 cases, 15 (65%) belonged to the giant cell, 5 (22%) to the granulomatous and 3 (13%) to the fibromatous group.

The duration of the lesions varied considerably (Table 4). Thirty-five (66%) of the granulomatous lesions and 31 (60%) of the giant cell lesions had a duration time of less than 6 months, while the corresponding figure for the fibromatous lesions was 17 months (30%). Thirty (53%) of the fibromatous lesions had been present for longer than 1 year.

Histological observations

After histopathological evaluation, the 175 'epulides' could usually be easily classified into three groups: granulomatous, fibromatous and giant cell lesions. Occasionally lesions had histopathological features of more than one group. For example, sometimes fibrogranulomatous would have been the most accurate description. Such lesions, however, were assigned to the group corresponding to the predominant histopathologic pattern. The relative histopathological characteristics of the examined lesions were compiled in Table 5.

Granulomatous group. This group comprised 59 (33.5%) of the cases and their histopathologic features are summarized in Table 5. These lesions were histopathologically characterized entirely or predominantly by loose granulation tissue rich in capillary vessels with more or less pronounced endothelial cell proliferations (Fig. 8). Immature fibroblasts, lymphocytes, plasma

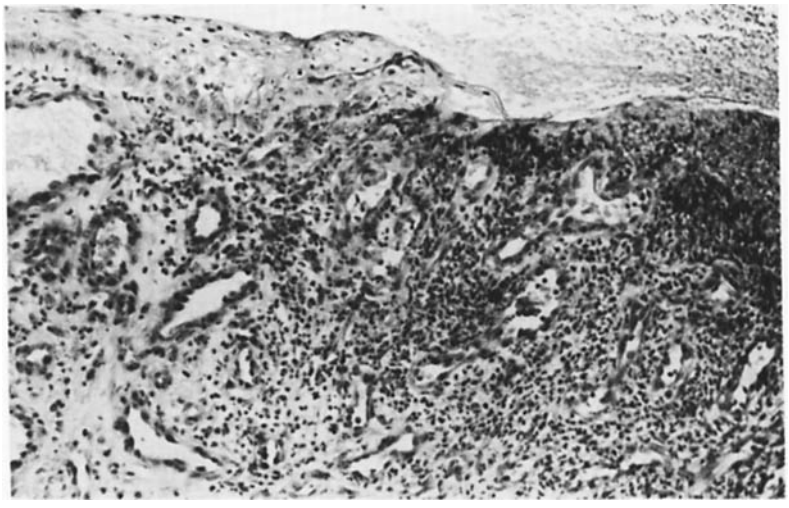

Fig. 8. The hyperplastic lesion (epulis) is histopathologically characterized by loose granulation tissue rich in capillary vessels with more or less pronounced endothelial cell proliferation. The lesion shows an ulceration covered by a pyogenic, fibrous, leucocyte-bearing membrane. Hematoxylin-eosin staining.

cells and polymorphonuclear leucocytes were also observed in the tissue.

Occasional giant cells occurred in only two cases, which due to the structure of the stroma were considered not to represent genuine giant cell lesions. Metaplastic bone formation, usually in small amounts, was observed in 36% of the cases.

In 19 (32%) cases, the lesions contained angiomatous and/or telangiectatic elements, and were histologically characterized by a granulation tissue containing an abnormal number of large, thin-walled blood vessels, a dense infiltration of lymphocytes, plasma cell and polymorphonuclear leucocytes, and very little collagen (Fig. 9). Histological differential diagnosis between these lesions and other types of granulomatous lesions, however, proved difficult. Hence, all granulomas and granuloma-like lesions were recorded as one group.

Granulomatous lesions of the 15 pregnant women were characterized by more pronounced inflammation and vascularization and less collagen. Bone formation (47%) and angioma-like patterns or telangiectasia-like structures (60%) were more common in this group than in the

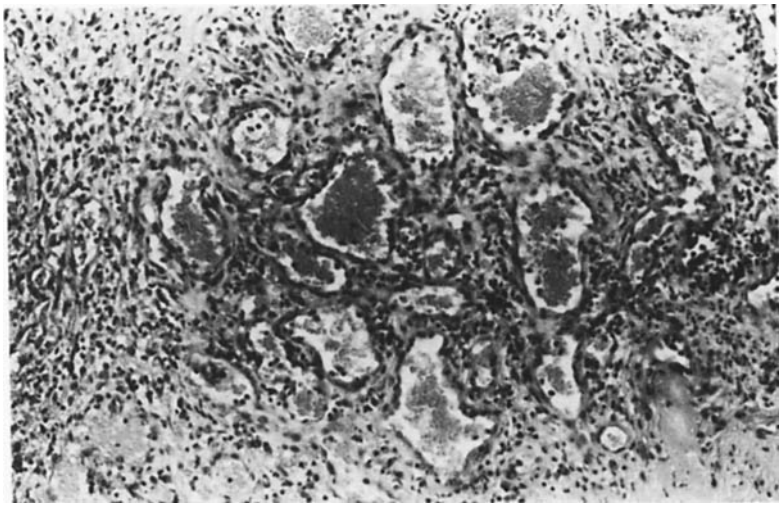

Fig. 9. A hyperplastic, granulomatous lesion (epulis) containing angiomatous and/or telangiectatic elements. The lesion is histologically characterized by granulation tissue containing an abnormal number of large thin-walled blood vessels. Hematoxylin-eosin staining.

Fig. 10. A hyperplastic, fibromatous lesion (epulis). The collagen is abundant and the number of fibroblasts few in this group of lesions. Hematoxylin-eosin staining.

granulomatous lesions of patients who were not pregnant.

The epithelium covering the granulomatous lesions was thin and frequently had ulcerations which were covered with a pyogenic, fibrinous, leukocyte-bearing membrane (Fig. 8). Acanthosis as well as proliferation of rete ridges was, in other areas, however, a common morphological feature.

Fibromatous group. This group comprised 59 (33%) of the cases. These lesions, whose histopathological features are illustrated in Fig. 10 and summarized in Table 5, were characterized by a dense collagenous connective tissue with a mostly mild chronic inflammatory reaction and a slight vascularization.

Giant cells were observed in no case. Metaplastic bone formation of varying extent occurred in 32% of the cases.

The epithelium covering the fibromatous lesions often exhibited acanthosis and proliferation of rete ridges. Hyperorthokeratinization and hyperparakeratinization were observed in some areas.

Giant cell group. The giant cell lesions constituted 57 (33%) of the cases. These lesions were morphologically characterized by the occurrence of giant cells which were of osteoclast type and localized in a mesenchymal stroma. The giant cells were mostly centrally located. They were of osteoclast type and often occurred in association with osteoblasts as a morphological expression of a metaplastic transformation of the tissue in an osteogenic direction (Fig. 11). The histopathological picture of the giant cell lesions, the morphological character-

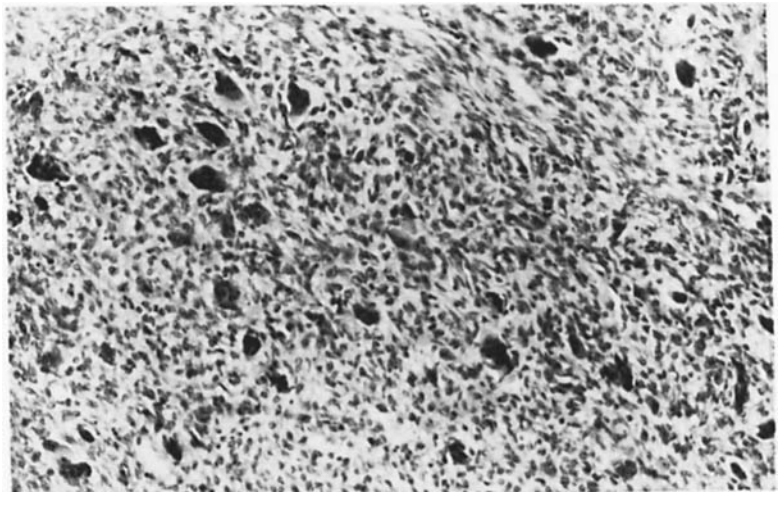

Fig. 11. A hyperplastic, giant cell lesion (epulis) with several giant cells of osteoclast type. Hematoxylin-eosin staining.

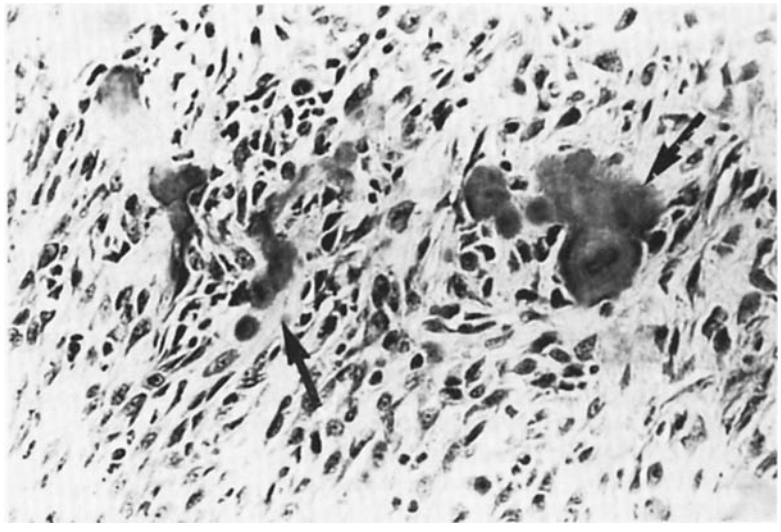

Fig. 12. A hyperplastic, giant cell lesion (epulis) with an embryonal stroma showing fibroblasts. The stroma exhibits the potential for differentiation in an osteogenic direction (arrows). Hematoxylin-eosin staining.

istics of which are compiled in Table 5, was also characterized by a primitive mesenchymal stroma of embyronal, often myxoid type with presence of fibroblasts (Figs. 12 and 13).

Adjoining the multilayered epithelium on the surface of the lesion there was usually normal fibrous connective tissue. In four cases angioma-like structures and in three cases fibromatous structures were observed adjoining the giant cell tissue proper. Hemosiderin pigment was commonly observed in the cases with abundant giant cells.

Discussion

Granulomatous lesions

In the present study the frequency of granulomatous lesions in females, which included such lesions as pyogenic granulomas (5, 14) as well as pregnancy tumors (7, 8, 16, 21) was four times that of men. The female predominancy which was in agreement with other studies (15) indicates that the pathogenesis of many of these lesions has been influenced by hormonal factors. If the pregnant and lactating women were excluded, the female to male ratio still was 2:1. The

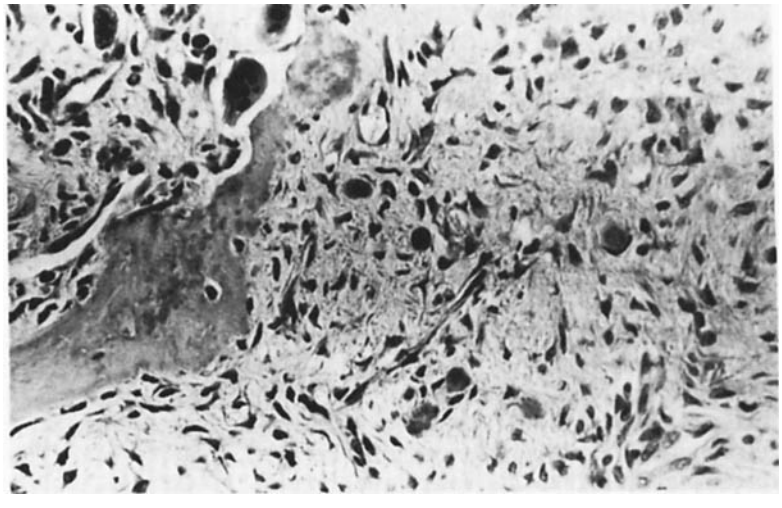

Fig. 13. A hyperplastic giant cell lesion (epulis) with a primitive mesenchymal stroma, fibroblasts, giant cells of osteoclast type and osteoid trabeculae. Hematoxylin-eosin staining.

female predominance was more accentuated in this study than in other published series (6, 14).

The histological characteristics of pyogenic granulomas, pregnancy tumors and certain other angiomatous proliferations of the oral mucous membrane are identical (21). Histologically these lesions are granulation tissue particularly rich in capillary blood vessels. The etiologic factors presumably may be anything which stimulates vascular proliferation; for example, trauma and/or infection. The hormonal influence in some of these cases may enhance the tissue reaction to these etiologic factors, thus explaining the often rapid growth of pregnancy tumors.

Fibromatous lesions

Fibromatous epulides have been discussed in the literature under different terms such as peripheral fibroma (5), peripheral fibroma with calcification (5), fibrous epulis (9) and fibroma (17). The term fibroma, however, according to the authors' opinion, is used to designate a benign connective tissue tumor, which originates from fibroblasts. Fibroma is a neoplastic growth of fibroblast type and is very rare in the oral cavity (9, 20). The fibromatous epulides, on the other hand, are hyperplastic reactive lesions, the majority of which represent more or less abundant masses of collagen.

A special type of fibrous tumor, the giant-cell fibroma, has been reported to occur mainly on the gingiva (22). This type of lesion, which contains two characteristic cell types, a spindle or stellate cell and a multinucleated giant cell, was not found in the material investigated in the present study.

The majority of patients with fibromatous lesions in the present study were between 30 and 59 years and there was no sex predilection. These findings were in agreement with a previous report (17) and with the result of a survey of the literature presented by Bhaskar & Jacoway (6).

In the present study the duration of the fibromatous lesions was longer and the age of the patient higher than in the granulomatous group. These findings support the suggestion that long-standing granulomatous lesions may undergo maturation into more fibrous type lesions (14).

Giant cell lesions

The giant cell epulides constituted a group that was histopathologically separated from the granulomatous and fibromatous lesions. The connective tissue stroma of the giant cell lesions had a distinct primitive mesenchymal or embryonal character with occurrence of fibroblasts. These lesions may have the potential ability of differentiating in different directions into a myxoid tissue or a fibroblast-rich and osteoblast-rich tissue forming bone and/or osteoid trabeculae. The giant cells were of the osteoclast type with little evidence of phagocytosis. The fact that they occurred together with osteoblasts could be interpreted as a morphological expression of metaplastic transformation of the tissue in an osteogenic direction. Bone or osteoid formation was more frequently found in this group than in the granulomatous and fibromatous groups. The osteoclast characteristic of the giant cells has also been pointed out in electron microscopic examinations (1, 2). The fibrogenic and osteogenic quality of the stroma cells of giant cell lesions has been confirmed in light microscopic (4, 10) as well as in electron microscopic studies (18). These cells were ultrastructurally found to be compatible with various stages of differentiating osteoprogenitor cells (18, 19). From the histopathological aspect, the giant cell lesions might be presumed to constitute a primitive mesenchymal tissue proliferation of an embryonal nature with the potential for differentiation in various directions. The osteoprogenitor cells could, by the hyperplastic reactive inflammatory response, be stimulated to differentiate into osteoblastic and/or osteoclastic cells (18).

The myxoid character of the giant cell lesions is presumably reminiscent of the primitive mesenchymal tissue that characterizes the mesoderma of foeti. Correspondingly, embryonally induced tumor-like proliferations have been described in other

locations, such as the lung, pylorus, etc., and have been denoted hamartomas. These are not considered to constitute genuine neoplasms. The giant cell lesion was earlier described as a true neoplasm, but its clinical behavior and histopathological characteristics have led most investigators to consider it a reactive, hyperplastic response of the tissue to injury (10, 13).

The relatively higher incidence of bone destruction associated with lesions in the giant cell group was interesting with respect to the findings reported by Hellstrom (12), who showed that epulide-like lesions of giant cell type often occurred in connection with disturbance in the function of the parathyroid glands. A determination of serum Ca and P values is indicated in cases of peripheral giant cell lesions of the oral mucosa, as well as of central giant cell granuloma, to rule out the possibility of primary or secondary hyperparathyroidism.

Giant cell lesions may recur, and of the lesions in this study exhibiting adjacent alveolar bone destruction 65% belonged to the giant cell group. For these reasons, giant cell lesions may require more radical excision comprising not only extirpation of the stem alone but also of the underlying periosteum and when necessary, a superficial layer of cortical bone.

Terminology

Gingival tumors described clinically as epulides are usually not true neoplasms but hyperplasias resulting from multiplication of epithelial and/or connective tissue cells. Hyperplasia is defined as a self-limiting process resulting from a reaction to stimulation or irritation. After removal of the causative factor the process usually regresses. A neoplasm does not have this self-limiting character and continues to grow even after the causative factor has been eliminated. The histopathological appearance of oral mucosal hyperplasias, however, is often indiscernible from lesions which in the textbooks are called neoplasms (19, 20). Most of the lesions are a response of the tissue to a nonspecific infection or to other stimulants and irritants, which either stimulate the proliferation of such cell elements as epithelial cells, fibroblasts, collagen and vascular endothelial cells or lead to the destruction of tissue. Depending on local causative factors and modifying systemic factors, both the clinical and histological characteristics of gingival hyperplasias can vary to a large extent. Clinical variables include 1) nature of attachment (pedunculated vs. sessile), 2) presence or absence of ulceration, 3) consistency, 4) color, and 5) associated bone destruction. The histopathological pattern exhibits varying degrees of inflammation and vascularization and varying amounts of fibroblasts, collagen, bone, osteoid and giant cells. The variety of clinical and histopathological characteristics presumably is one of the most important reasons why gingival hyperplasias have been described under such a great number of different terms in the dental and medical literature. Since the present plethora of diagnostic concepts has created disorder and uncertainty, there is undoubtedly a need for more concise and pertinent classification of these oral mucosal hyperplasias. The hitherto most commonly used term, epulis, has become a nonspecific clinical topographical term, indicating solely that the lesions are sited in the gingiva. This term should therefore be abandoned in microscopic diagnosis. The results of the histological evaluation in the present study suggest that a histological classification of so-called 'epulides' in three distinct groups was possible: the granulomatous, fibromatous and the giant cell groups.

The results of the clinical observations, however, indicated that none of these three histological groups had any specific clinical characteristics. There were to some extent some minor differences in localization, consistency and relation to the subjacent tissue. Variation within each group, however, and overlap between groups prevent the differences in clinical characteristics from forming a basis for classification. The histopathological characteristics alone must therefore serve as a basis for a new classification of the lesions.

Of the three types of gingival hyperplasias discussed in the present study, only the giant cell lesion deserves the designation epulis as it exclusively occurs on the gingiva and

alveolar process (19, 20). The term epulis as a general diagnosis for any proliferative lesion of the gingiva should, therefore be discarded. It may therefore, be advisable to use the term suggested by WHO (23) 'peripheral giant cell granuloma' for this lesion, even though the histopathologic characteristics certainly are not in accordance with a granuloma. A granuloma is considered to be a more obvious inflammatory lesion. An alternative diagnostic term, might be *oral mucosal giant cell hyperplasia.*

The other lesions can be divided into two main groups, the granulomatous and fibromatous groups. As these lesions are reactive hyperplasias it is suggested that they should be called, *oral mucosal granulomatous hyperplasia* (including such diagnostic terms as granulomatous gingivitis, gingivitis of pregnancy, pregnancy tumor, epulis gravidarum, pyogenic granuloma, epulis angiomatosa, epulis telangiectaticum) and *oral mucosal fibrous hyperplasia* (including such diagnostic terms as fibrous epulis, epulis fissuratum, fibroepithelial lesions, denture injury tumor). If osteoid and/or bone formation occur in the lesion one should add *'with ossification'* to the suggested terms.

As oral granulomatous and fibromatous hyperplasias are not confined to the gingiva and alveolar ridge, it is the authors' opinion that the suggested diagnostic terms of oral mucosal fibrous hyperplasia and oral mucosal granulomatous hyperplasia should be used to designate lesions of appropriate histology irrespective of intraoral location.

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