

Giant-cell fibroma: Understanding the nature of the melanin-laden cells

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Abstract

Giant-cell fibroma is a localized, benign fibrous mucosal mass, which clinically mimics any other fibroepithelial growth, and its distinction from other lesions is on the basis of its peculiar histopathology. A case of giant-cell fibroma with stroma strewn with brown pigment-laden cells is presented herewith. Immunohistochemical staining aided with histochemical reaction to understand the origin of these cells was carried out. Various mechanisms that explain the presence of melanin granules in reactive lesions of giant-cell fibroma is discussed in the present report.

Keywords: Giant cells, immunohistochemistry, melanin granules, special stains

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INTRODUCTION

Giant-cell fibroma, first described by Weathers and Callihan in 1947,^[1] is a benign, sessile or pedunculated lesion of oral mucosa, seen predominately in the third decades of life with a slight female predilection.^[2] It presents as a localized reactive proliferation of fibrous tissue, which resembles irritation fibroma rather than a neoplastic proliferation.^[3] The name alludes to the characteristic cells present in the fibrous stroma that it is characterized by the presence of large stellate-shaped multinucleated fibroblasts that tend to occur near the overlying epithelium.^[4] The etiology of giant-cell fibroma remains unknown and there is no evidence to support its association due to chronic irritation.^[5] The lesion represents approximately 2%–5% of all fibrous lesions and 0.4%–1% of total biopsies, although higher percentage of its occurrence has also been reported (10.6% and 2.7%, respectively).^[6] Gingiva

is the most common site of involvement and mandible is more frequently affected than the maxilla.^[7] A case of giant-cell fibroma in a 30-year-old male, with a unique histopathological presentation of brown pigment-laden cells seemingly melanin, is presented. The origin and pathogenesis of these melanin-laden cells are discussed.

CASE REPORT

A 30-year-old male presented with the chief complaint of growth on the gingiva in the right retromolar area [Figure 1]. The patient's medical history suggested that he underwent a plate replacement following surgery about 4 years back, which has gone slack recently. Medical records of the patient confirmed that the patient was surgically treated by open reduction of an angle fracture and internal fixation for the repair of bone 10 years back, involving stainless steel plates secured with screws. Loosening of plates was noted

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about 4 years back followed by exposure of plate into the oral cavity and a purported growth in the gingiva to follow soon. On clinical examination, a growth was noted in the region of exposed plate in the right retromolar area. The lesion was about 1 cm × 0.8 cm in size, sessile, smooth surfaced and firm in consistency. Features of an underlying inflammatory reaction, including induration, tenderness and discharge, were ruled out. The patient was moderately built and nourished with other findings being noncontributory. Extraoral examination did not suggest any obvious facial asymmetry, and lymph nodes were soft and nontender. There were no other relevant dental findings. X-rays showed the presence of metal plate, which was radiopaque. A provisional diagnosis of hyperplastic gingival tissue was made and the lesion was removed in totality by excisional biopsy and sent for histopathological examination. Gross examination revealed 2 soft-tissue bits measuring 0.5 cm × 0.3 cm, firm in consistency, brownish in color.

Histopathological examination revealed a hyperplastic parakeratinized stratified squamous epithelium, acanthotic at places without any dysplastic features. The underlying connective tissue stroma was highly cellular comprising of fibroblasts, fibrocytes, a few large cells which were granular, occasionally binucleated, melanin-laden cells scattered across the stroma and chronic inflammatory cells interspersed in areas where collagen was delicate to dense and at places showing features of degeneration. The lesion was signed out as pigment rich giant cell fibroma [Figures 2 and 3].

Initially, hemosiderin pigmentation was considered as it was a lesion closely associated a loosened plate. Staining with Perls' Prussian blue was done but was negative [Figure 4]. The next logical step was to prove if the pigmentation was due to melanin using a Masson Fontana reaction. The positive Masson Fontana reaction in these cells confirmed the presence of melanin granules [Figures 5 and 6]. However, it was important to characterize these cells and confirm if they are melanocytic in origin or macrophage cells that have engulfed melanin granules. Negative staining for HMB-45 ruled out cells being melanocytes [Figure 7] and focally positive CD68, particularly in the areas of inflammation suggested the presence of macrophages with ingested melanin granules [Figure 8]. While those cells negative for CD68 were the giant fibroblasts that had engulfed the melanin granules [Figure 9].

DISCUSSION

The clinical presentation and histology of most of the nonneoplastic lesions in the oral cavity are identical and



Figure 1: Clinical photograph showing growth on the gingiva in the right retromolar area

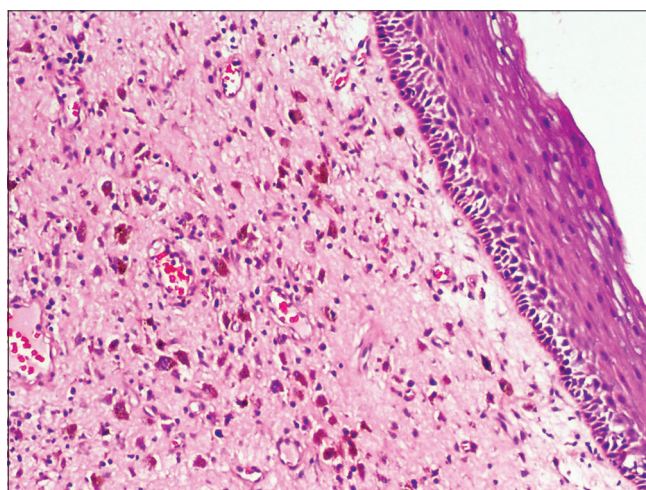


Figure 2: H&E-stained section showing parakeratinized stratified squamous epithelium with cellular connective tissue stroma comprising of stellate-shaped cells (x10)

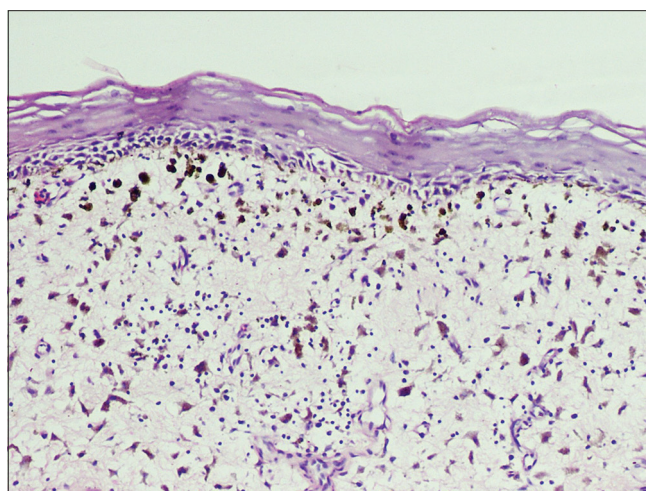


Figure 3: H&E-stained section showing pigmented cells (x20)

giant-cell fibroma, unlike other fibrous overgrowths, are seemingly innocuous although the stroma shows the

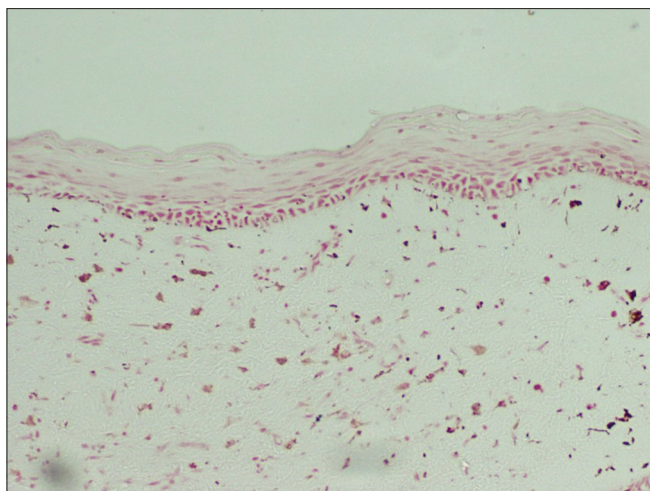


Figure 4: Staining with Perls Prussian blue which was negative (×10)

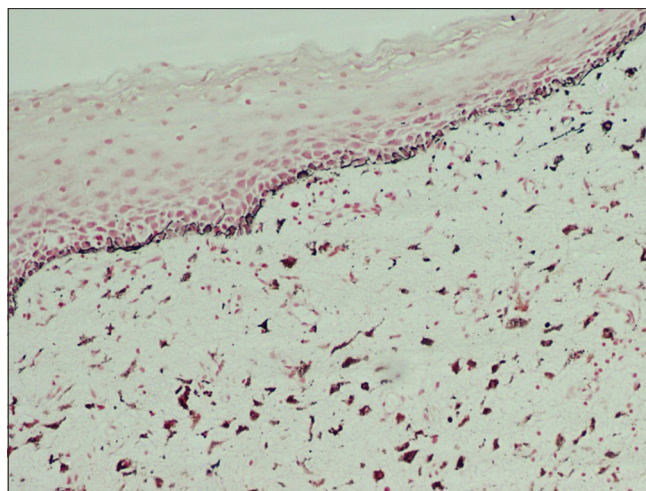


Figure 5: Brown pigment-laden cells (Masson Fontana, ×10)

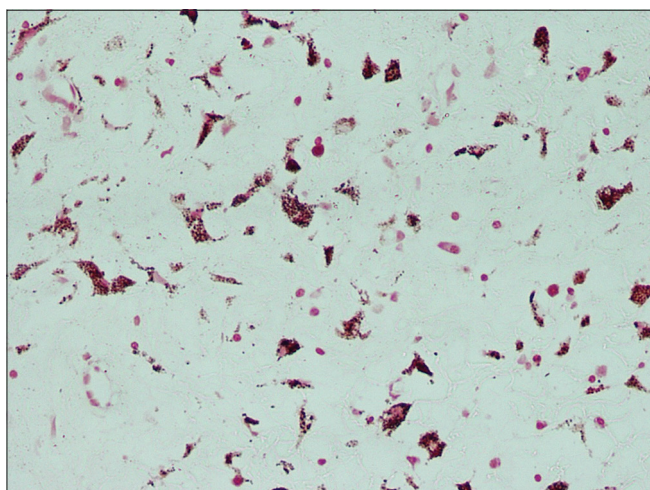


Figure 6: Giant cells that have phagocytosed melanin granules (Masson Fontana, ×20)

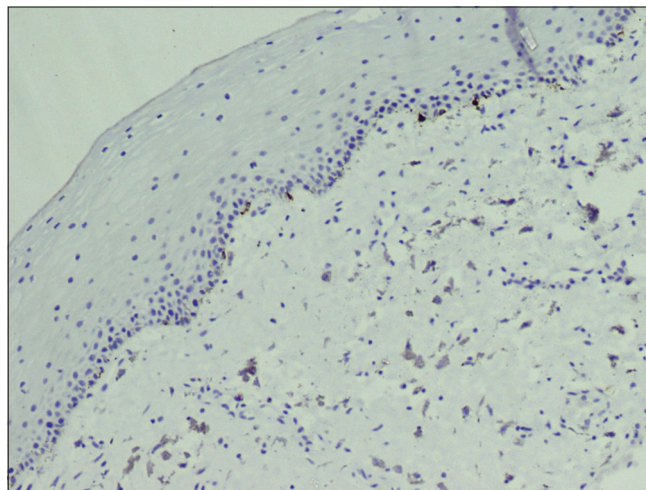


Figure 7: Immunohistochemical staining for HMB-45 which was negative (×10)

characteristic presence of giant fibroblasts. These are stellate or spindle-shaped fibroblasts, binucleated or even trinucleated, mostly vesicular with the cytoplasm being granular disposed of in a stroma which is collagenous. Melanin granules, which are usually demonstrated in these cells,^[5] coincide with the present case.

Investigators have ruled out myofibroblastic origin of these cells, as they are negative for alpha-smooth muscle actin.^[8] Positive staining with vimentin and prolyl 4-hydroxylase has established the cells to have a fibroblast lineage. In a report by Okamura *et al.*^[9] the giant fibroblasts in giant cell fibroma were considered to be of macrophage - monocytic lineage. In another report by Regezi *et al.*^[10] these fibroblasts were described to be mesenchymal cells which possessed the properties of both macrophage and fibroblast. What remained a mystery however was the reason for the presence of melanin granules in these cells although a number of possible mechanisms have been described

to discuss the same. The simplistic view is that gingiva being the most common site of melanin pigmentation, melanocytes residing in the gingival basement membrane produce melanin granules, and the fibroblasts which have a multifunctional role of tissue repair and protein synthesis could have ingested these granules.^[5,11]

The other plausible explanation is the mechanical wearing out of the metal implant, which releases particles and induces a foreign body reaction. The metallic debris being gray black is however different to melanin granules, which appear finely granular and is distributed in the cytoplasm of the cell.^[12]

Oral postinflammatory pigmentation is another condition that represents discoloration of oral mucosa due to excess melanin deposition within the basal layer of epithelium and connective tissue of areas that are affected by chronic inflammation. This condition may be due to increased

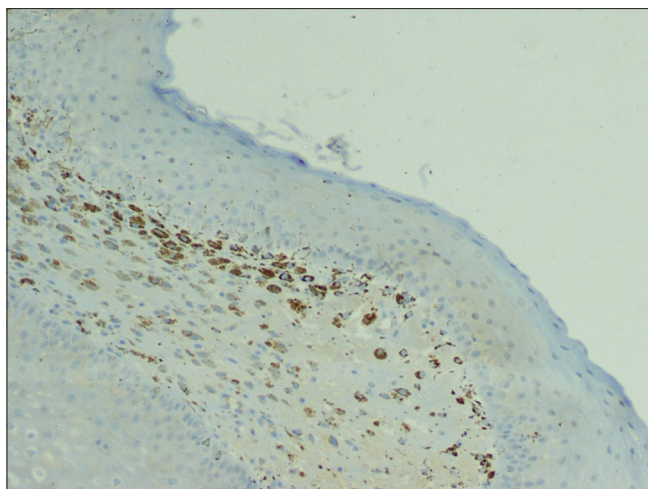


Figure 8: Immunohistochemical staining for CD68 was positive in the areas of inflammation which are the macrophages that have engulfed the melanin granules (x20)

melanin production or abnormal distribution of melanin pigment.^[12] An account by Papa and Kligman stated that the keratinocytes have the property and willingness to receive extraneous melanin in inflammatory conditions. Direct stimulation of melanocytes by inflammatory mediators (arachidonic acid) causes postinflammatory pigmentation.^[12,13] Keratinocyte growth factor released from fibroblasts is stimulated by interleukin-1 alpha, which binds to receptors on epithelial cells inducing uptake of melanosomes, thus suggesting that the specimens with postinflammatory hyperpigmentation show the presence of melanin-laden macrophage in the connective tissue, where the melanin has been phagocytized by the melanophage.^[13,14]

The differential diagnosis for giant-cell fibroma should include irritation fibroma, retrocuspid papillae, papilloma, peripheral ossifying fibroma, focal fibrous hyperplasia, peripheral odontogenic fibroma, odontogenic hamartoma, neurofibroma, peripheral adenomatoid odontogenic tumor, lipoma, peripheral ameloblastoma, intraoral neurilemmoma and peripheral calcifying odontogenic cyst.^[5,15,16] The presence of giant fibroblasts histopathologically distinguishes this lesion from others.

Surgical excision is the choice of treatment for these lesions, and in pediatric cases, electrosurgery or laser excision is preferred.^[4]

CONCLUSION

Giant-cell fibroma is a rare entity, distinguished from other exophytic growth in the oral cavity based on its peculiar histopathology which shows functional fibroblastic

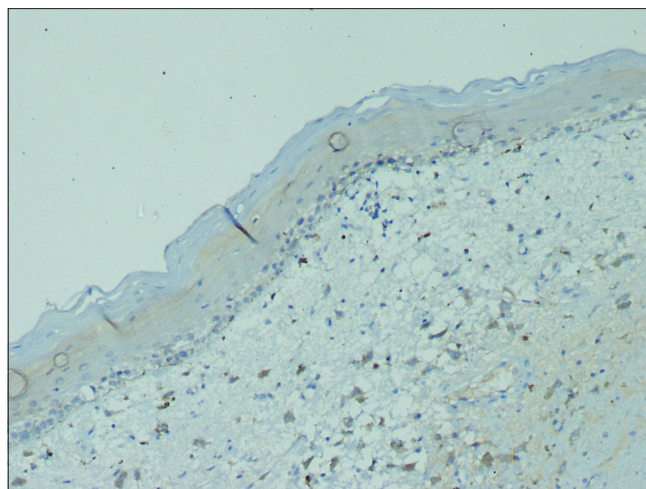


Figure 9: Immunohistochemical staining for CD68 was negative in other areas which are the fibroblasts that have engulfed the melanin granules (x20)

differentiation and some of these fibroblasts phagocytized these melanin granules that are responsible for the giant nature of the cells. The origin of these melanin granules might be from the melanocytes residing in the gingival basement membrane, and in the areas of inflammation, these melanin granules were engulfed by macrophages.

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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