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# Granuloma Faciale-Like Lesion of the Palate: A Previously Unreported Entity

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Granuloma faciale (GF) is a rare, benign, inflammatory skin disease, usually presenting as isolated, reddish-brown to violaceous asymptomatic papules, nodules or plaques that are soft, smooth, and well-circumscribed, often showing follicular accentuation and telangiectasia (Pedace and Perry 1966). It appears as a single lesion on the face, especially on the forehead, nose, and cheeks (Radin and Mehregan 2003). However, GF can occur as multiple lesions and/or at extrafacial sites (Finnegan et al. 2024). The etiology of GF is unknown, but the disease can be considered a localized chronic fibrosing vasculitis (Carlson and LeBoit 1997). The diagnosis relies on a combination of clinical findings and confirmatory tissue biopsy. Histologically, GF shows a normal-appearing epidermis, which may be separated from the underlying inflammatory infiltrate by a *grenz zone*, i.e., a narrow area of the papillary dermis, which is spared by the underlying pathology (Abbas and Mahalingam 2013). The upper half of the dermis shows a dense and diffuse polymorphous inflammatory infiltrate of lymphocytes, histiocytes, plasma cells, eosinophils, and neutrophils, with evidence of leukocytoclasis. The inflammatory infiltrate surrounds the blood vessels, which may show evidence of fibrinoid necrosis and perivascular fibrosis (Ortonne et al. 2005). Extravasated red blood cells and hemosiderin deposits may contribute to the red-brown color seen clinically.

Here, we describe the unprecedented case of an oral lesion histologically resembling GF in a 75-year-old woman. The patient was referred by her general dentist to our Oral Medicine unit for the presence of a persistent, asymptomatic palatal lesion.

Her medical history was significant for hypertension, hypercholesterolemia, osteoporosis, and pollen allergy, and she was taking lercanidipine and atorvastatin, while she had suspended oral alendronate after the onset of the lesion 1 month prior.

At clinical examination, a single reddish, nontender, submucosal nodule with lobular appearance was noted in the middle of the posterior hard palate (Figure 1A). The patient wore a partial, removable denture that was not topographically associated with the lesion. On palpation, the nodule was soft in consistency, the overlying epithelium was not ulcerated, and the lesion appeared attached to the underlying tissues (Figure 1B). However, a CT scan of the maxilla did not reveal any involvement of the palatal bone (Figure 1C).

Differential diagnosis included minor salivary gland adenitis or neoplasm, soft tissue tumor, deep fungal infection, sarcoidosis, IgG4-related disease, Kimura disease, granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis, or hematological malignancies such as extranodal NK/T-cell lymphoma, nasal type. There were not cutaneous lesions on the face or in other parts of the body. An incisional 6-mm-punch biopsy was performed, and the excised sample was characterized by evident hemosiderin deposition in the connective tissue (Figure 1D).

The microscopic examination revealed the presence of a dense, mixed inflammatory infiltrate in the lamina propria, composed of lymphocytes, macrophages, plasma cells, neutrophils, and eosinophils (Figure 2A). The infiltrate was diffuse, with accentuation around small reactive vessels, permeating the vessel wall and showing leukocytoclasis and focal fibrinoid necrosis (Figure 2B–E). Even though a frank *grenz zone* completely devoid of inflammatory cells could not be detected due to the structural difference between the connective tissue of the skin and mucosa, the superficial lamina propria showed less inflammatory infiltrate in most areas when compared to deeper, perivascular tissues. At this level, the cellular infiltrate was mostly represented by lymphocytes, especially T-lymphocytes

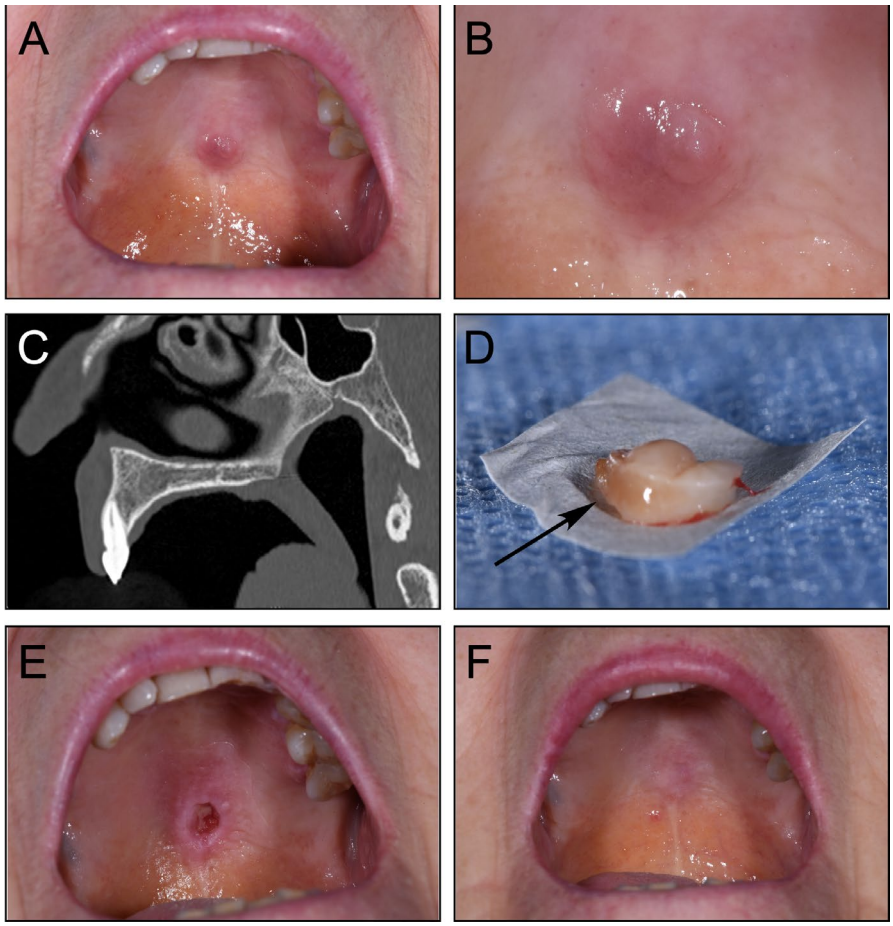


**FIGURE 1** | Granuloma faciale-like lesion of the palate, clinical features. (A) A reddish, nontender, sessile submucosal nodule in the middle of the posterior hard palate; (B) At higher magnification, the lesion showed a lobular appearance, while the overlying epithelium was not ulcerated; (C) The CT scan of the maxilla did not reveal involvement of the underlying palatal bone; (D) The bioptic sample was characterized by evident brown-colored hemosiderin deposition in the connective tissue (*arrow*); (E) Second-intention healing appearance of the lesion after 14 days from incisional biopsy; (F) Spontaneous, complete self-healing of the lesion after 1 month from incisional biopsy.

(Figure 2F,G) and macrophages (Figure 2H), while minor constituents were plasma cells, neutrophils, and eosinophils. Focal areas of fibrosis resembling a storiform pattern were detected, but there was not a well-represented IgG4-positive plasma cell component, thus excluding IgG4-RD (Figure 2I,J). Screening serology, including ANA, ENA, ANCA antibodies, and serum IgG4, provided negative results.

Therefore, a final diagnosis of Granuloma faciale-like lesion of the palate was made, and the patient was re-evaluated after 14 days and 1 month from incisional biopsy. Interestingly, the lesion completely self-healed, and there were not any signs of residual disease (Figure 1E,F). However, since GF is renowned for its high recurrence rate, a prophylactic medical treatment with topical dapsone 10% and tacrolimus 0.1% galenic oral gels were prescribed for 30 days (Van de Kerkhof 1994; Mitchell 2004). After 3 months, recurrence did not occur.

To date, this is the first report of an isolated GF-like lesion in the oral cavity. Only one paper reported a similar case on the gingiva of an inferior third molar, but in this instance, there were multiple lesions also on the skin and in the nasal cavity; thus, a final diagnosis of eosinophilic angiocentric fibrosis (EAF) was provided (Nigar et al. 2007).

Eosinophilic angiocentric fibrosis is considered by some authors as the mucosal counterpart of GF and is defined as a rare, locally destructive disease with a predilection for the sinonasal tract, even though involvement of the orbit, lung, and subglottic region were reported (Karligkiotis et al. 2013). Histologically, EAF is characterized by the presence of numerous scattered eosinophils and perivascular concentric fibrosis showing "onion-skin" pattern (Narayan and Douglas-Jones 2005; Javadirad, Roozbahani, and Sadafi 2022), while fibrinoid necrosis is usually not observed. In 2011, it has been hypothesized that EAF lies on the spectrum of IgG4-RD, but this issue is still under investigation (Deshpande et al. 2011; Bal and Deshpande 2024). In our case, the inflammatory component was predominant over the fibrotic process, there were signs of vasculitis along with fibrinoid necrosis, a full-blown onion-skin pattern of collagenous fibrosis was absent, and there were very few, scattered IgG4-positive plasma cells. For these reasons, we considered our case as a unique case of mucosal GF-like lesion, reflecting more the clinical and histopathological features of GF rather than those of EAF. Interestingly, a specular report in the literature reported a case of EAF of the skin, reflecting the fact that the two diseases share many features and may show overlapping features (Rashidghamat, Groves, and Robson 2015).

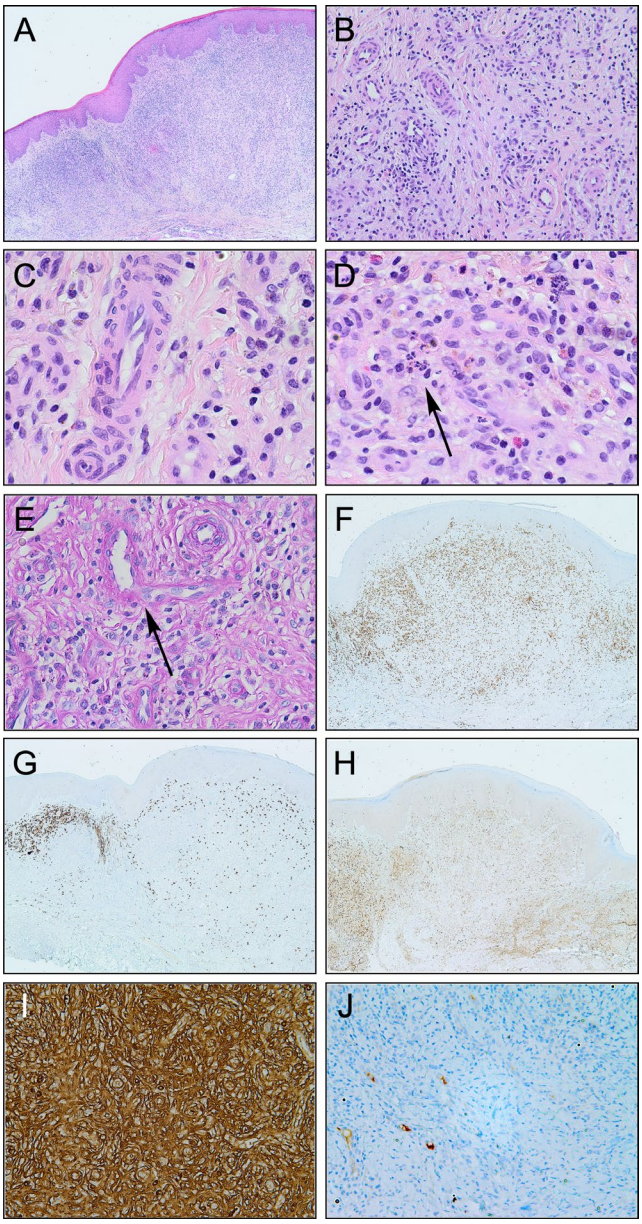


**FIGURE 2** | Histopathological features of the Granuloma faciale-like lesion. (A) The histopathological examination of the lesion revealed the presence of a dense, diffuse, mixed inflammatory infiltrate in the connective tissue. The most superficial aspect of the lamina propria showed less inflammation in most areas, resembling the *grenz zone* commonly observed in the skin (H&E, 40×); (B) The inflammatory infiltrate was diffuse but mainly concentrated around small reactive vessels (H&E, 200×); (C) At higher magnification, a perivascular infiltrate and vasculitis with inflammatory cells permeating the vessel wall could be appreciated. Of notice, the eosinophils did not represent a significant component of the cellular infiltrate (H&E, 600×); (D) Areas of leukocytoclasis with nuclear debris (*arrow*) (H&E, 600×); (E) Focal areas with fibrinoid necrosis in the vessel wall (arrow) (PAS, 400×); (F) The inflammatory infiltrate was mainly composed of T-lymphocytes (CD3+, 40×); (G) The B-lymphocyte component was less represented, mainly in superficial lamina propria (CD20+, 40×); (H) There was a significant proportion of cells of the mononuclear-macrophage line (CD68+, 40×); (I, J) IgG4-bearing plasma cells (J) were very scarse when compared with total IgG-positive plasma cells (I). This feature excluded IgG4-RD.

Interestingly, the spontaneous healing observed after biopsy is a rare feature observed for only few cases of GF (Ludwig et al. 2003). Indeed, treatment usually requires a combination of both medical and surgical approaches due to the high rate of recurrence (Lindhaus and Elsner 2018).

## Author Contributions

**Francesca Magnoli:** investigation, writing – review and editing, methodology, supervision, conceptualization. **Alessandro D'Aiuto:** investigation, data curation. **Cristina Ciardiello:** investigation. **Fabio Brusamolino:** investigation. **Michele Cerati:** supervision; writing – review and editing. **Lorenzo Azzi:** conceptualization; investigation; writing – original draft; visualization; data curation.

## Conflicts of Interest

The authors declare no conflicts of interest.

## Data Availability Statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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