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(CASE REPORT)

Oral ulceration as a revealing sign of granulomatosis with polyangiitis

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Abstract

Granulomatosis with polyangiitis (GPA), formerly called Wegener's granulomatosis, is a rare systemic disease of unknown etiology that can affect all areas of the body, including the oral cavity. Typical oral manifestations present as nonspecific erosive/ulcerative lesions of the oral mucosa or appear with hyperplastic gingivitis, termed “strawberry gingivitis”.

We report here a case of cheek ulceration as the first sign of recurrence of GPA in the absence of oral manifestations in the primary disease.

A 37-year-old woman was referred to our oral pathology and surgery department for oral ulcerations. The patient had already been diagnosed with GOODPASTURE syndrome (pneumorenal syndrome) two years previously and treated with cyclophosphamide and Azathioprine.

Its relapse and the appearance of oral manifestations made it possible to readjust the diagnosis and the treatment.

Keywords: Ulceration; Erosive Lesions; Oral Ulceration; Autoimmune Vasculitis

1 Introduction

Granulomatosis with polyangiitis (GPA), formerly known as Wegener's granulomatosis (WG) is a small-vessel autoimmune vasculitis strongly associated with cytoplasmic anti-neutrophil antibodies (ANCA).

GPA is diagnosed based on clinical manifestations of systemic vasculitis and histological signs of necrotizing vasculitis or granulomatous inflammation.

The manifestation of the oral cavity is present in 6 to 13% of patients during the course of the disease, but oral involvement as the first sign of the disease is found in only 2% of cases, which represents a major diagnostic pitfall for physicians. Therefore, in this report, we describe a rare case of oral mucosal GPA that corrected a previously made diagnosis.

Typical oral manifestations present as nonspecific erosive/ulcerative lesions of the oral cavity or appear with hyperplastic gingivitis, called “strawberry gingivitis”

Two types of GPA are known: diffuse forms, manifested mainly by renal and pulmonary intake, and localized forms, limited to the upper respiratory tract.

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Since the disease develops over a long period of time, it usually takes 4.7 to 15 months from the onset of symptoms to diagnosis. The American College of Rheumatology suggests that for the diagnosis of "GPA", at least two of the following criteria must be met : ulcerative lesions of the oral mucosa or nasal bleeding or swelling, nodules, infiltrates or cavities on chest X-ray, abnormal urinary sediment , or granulomatous inflammation on biopsy.

Here, we report an extremely rare case with oral ulceration and gingival papillae as early signs of GPA recurrence in the absence of oral manifestations in the primary disease.

1.1 Presentation of the case

A 37-year-old patient, diagnosed since 2017 for GOODPASTURE syndrome (pneumorenal syndrome) treated with corticosteroid (prednisone), cyclophosphamide for 6 months then immunosuppressant: Imurel (Azathioprine). Hospitalized in the internal medicine department for acute respiratory distress for 2 weeks, taken urgently to the currently stable resuscitation department, is referred for painful lesions on the left oral mucosa with edema of the ipsilateral face which have appeared for 20 days, resulting in a limitation of mouth opening. An inflammatory assessment (NFS, VS, CRP and protein electrophoresis) comes back in favor of an acute inflammation, and directs the patient to our service.

The extra-oral clinical examination is unremarkable.

Examination of the lymph nodes found no clinically palpable nodule.

The intra-oral examination shows a fetid necrotic oral ulceration, on the left side facing the absent 36 (fig.1), about 15 mm in diameter, located in the bottom of the vestibule, covered by a blue-grayish film removed by scraping with a tongue depressor, very painful on palpation, not bleeding; the surrounding oral mucosa is very inflamed.

The gingival papillae between 12-22, 26-27 and 45-46 (fig.2) have an ulcero-necrotic appearance, bleeding easily and very painful on palpation.

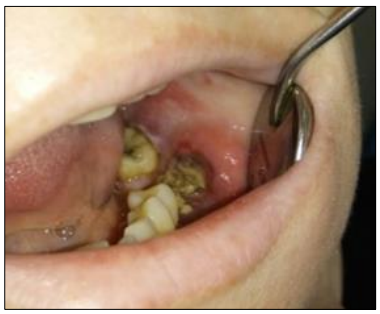


Figure 1 Necrotic oral ulceration, the surrounding cheek mucosa is very inflamed

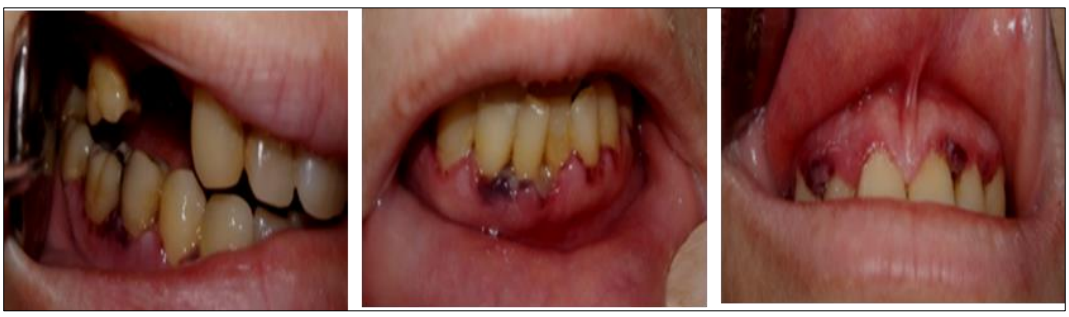


Figure 2 (A, B, C) the gingival papillae have an ulcero-necrotic appearance, bleeding easily and very painful on palpation

We are therefore faced with a 37-year-old patient, presenting with very painful mucosal ulcerations, located in the left oral region and some ulcerative-necrotic gingival papillae.

Radiological examination is unremarkable (fig.3).

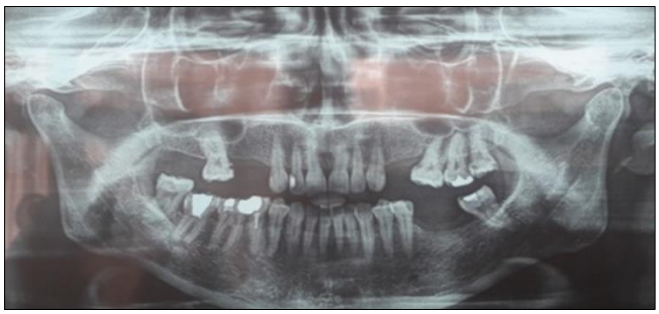


Figure 3 OPG no bone involvement

Faced with this clinical picture, several diagnoses can be evoked:

- ✓ Infectious origin: acute necrotic ulcerative gingivitis (ANUG), which is usually located at the level of the interdental papillae with respect to the gums, can be evoked especially in women, on a ground of immunosuppression but unlikely given the presence of oral ulceration.

Given the seat (inner face of the cheek and involvement of the taste buds) we can evoke a specific viral infection such as HIV, or a bacterial infection such as syphilis and tuberculosis, but these diagnoses were ruled out by a negative serology.

- ✓ A medicinal origin: cyclophosphamide is an anti-cancer drug which can cause oral ulcerations, but this diagnosis is ruled out since it has been stopped for more than a year.
- ✓ An inflammatory origin (connectivity such as Lupus) is possible but the ANA (anti-nuclear auto-antibody) test came back negative and no cutaneous signs were found clinically, so this origin is very unlikely.
- ✓ Vascular origin: Ulcerations due to vasculitis, which can give multiple ulcerations at the level of the oral mucosa, the bluish coloring can testify to the impregnation of the vessels, all the more the patient presents an inflammatory assessment which revealed a high ESR (sedimentation rate) and CRP (C reactive protein).

Emergency treatment is instituted to relieve the patient. Thus, symptomatic medical treatment was prescribed based on the analgesic Paracetamol 1g and an anesthetic gel such as xylocaine 1% in order to allow him to eat.

An anatomopathological examination (fig.4, 5), is essential for the positive diagnosis, a biopsy of the cheek lesion must be performed.

It is also essential to motivate the patient to maintain good oral hygiene.

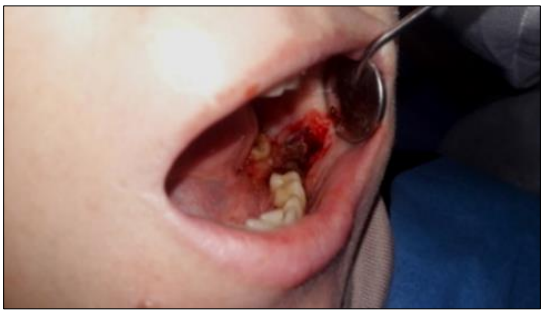
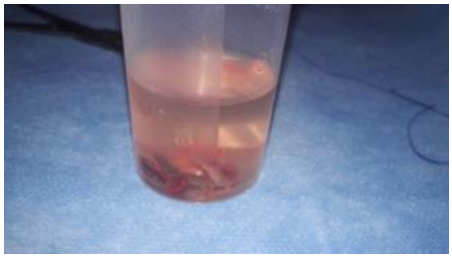


Figure 4 The biopsy was performed in the oral region



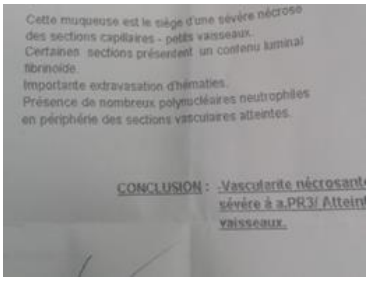


Figure 5 Sending of the piece in anapath **Figure 6 H**istological result

Histological examination of this mucosa shows severe necrosis of the capillary sections of small vessels. Some sections show fibrinoid luminal content.

Significant extravasation of red blood cells, presence of numerous neutrophils in the periphery of the affected vascular sections.

This histological result is in favor of a vasculitis of the small vessels with necrosis of the capillary sections (fig.6).

The indirect immunofluorescence reaction against the cytoplasmic ANCA was positive, as well as the immuno-enzymatic test with proteinase 3 ANCA. Kidney tests were abnormal, chest x-ray and computed tomography (CT) showed diffuse areas of opacification in both lungs.

In addition, the ENT and ophthalmological, neurological and digestive examinations are unremarkable.

Clinical, microscopic, radiographic and laboratory findings were consistent with the diagnosis of GPA.

The patient was therefore straightened out in the internal medicine department, to establish a treatment protocol,

The treatment of wegener'sgranulomatosis is based on the prescription of corticosteroids alone or associated with immunosuppressants.

Faced with the relapse, rituximab was introduced. At the follow-up visit, the patient showed complete remission of the oral ulceration and gingival papillae. His general condition is also stable.

2 Discussion

GPA is a rare chronic inflammatory disease of unknown etiopathogenesis with an autoimmune background. It was formerly known as Wegener's granulomatosis, described by German physician Friedreich Wegener in 1936 as a distinctive form of vasculitis. GPA is characterized by systemic vasculitis associated with the presence of ANCA in patient serum. The pathogenetic cause of GPA is mediated by a T cell reaction leading to the production and release of pro-inflammatory cytokines like TNF-α and IFN-γ which induce the expression of surface antigens on the cells. Activated neutrophil granulocytes. One of these antigens is proteinase 3 which is the target of anti-neutrophil cytoplasmic antibodies (c-ANCA).

The disease affects many organs, including the upper respiratory tract including the trachea, sinuses and nose, but also the lungs, kidneys, nervous system, eyes, ears, heart, skin and oral cavity.

Granulomatosis with polyangiitis is most frequently diagnosed in adult patients of middle age between 40 and 55 years, but cases affecting children are also described. There is no predilection for sex and the disease can be classified as localized or generalized depending on the extent of the process and the involvement of vital organs.

Constitutional symptoms such as pulmonary involvement (alveolar hemorrhage revealed by acute respiratory distress), renal involvement (proteinuria and hematuria without renal insufficiency) can be observed as shown in our case and hematological examinations can reveal non-specific alterations. Like lymphopenia, eosinophilia and hyperimmunoglobulinemia E. which are absent in our patient, anemia is also a possible discovery as this case illustrates.

Current diagnostic criteria for GPA include identification of at least two of the following features: nasal or oral inflammation; presence of an abnormal chest X-ray; abnormal urine sediment; and the presence of granulomatous inflammation in a biopsy. In the present case, the cheek ulceration and the gingival lesions were compatible with this diagnosis. In addition, oral biopsy demonstrated severe necrosis of capillary sections of small vessels. Some sections show fibrinoid luminal content and significant extravasation of red blood cells, presence of numerous neutrophils around the periphery of the affected vascular sections. X-ray,

Cases of GPA with oral symptoms have been described in several reports. Comparable to our case, the oral ulceration was evident only in case of recurrence in this single reported case. The standard treatment for initial GPA was glucocorticoids or cyclophosphamide, or a combination of both. Although the standard treatment improves the survival rate of patients. Unlike standard treatment for initial GPA, there are reports of successful treatment of refractory GPA of the head and neck with rituximab (14). Rituximab is a chimeric monoclonal antibody targeting the CD20 antigen expressed by B cells.

Successful treatment with rituximab leading to complete remission is reported in 62% of all patients treated by Martinez et al. Typical oral manifestations of GPA are nonspecific erosive lesions of the oral mucosa or hyperplastic gingivitis, such as indicated here. The differential diagnosis of ulceration could be made with ANUG which is usually localized at the level of the interdental papillae, with a specific viral infection such as HIV, or a bacterial infection such as syphilis and tuberculosis, they can be of drug origin. (cyclophosphamide), Or of inflammatory origin (connectivity such as Lupus)

Since oral lesions can be localized long before multiorgan involvement actually occurs, the often overlooked oral manifestation can be interpreted as the first sign of GPA and could be pathognomonic for the disease.

The histopathological pattern of GPA includes granulomatous inflammation, vasculitis, necrosis, and multinucleated giant cells. Additionally, rare diseases with oral components are known to benefit more from early diagnosis than rare diseases without oral components. Misdiagnosed oral manifestations that are often overlooked by physicians and dentists may be interpreted as the first evidence of a resurgence of GPA in general and could therefore be pathognomonic for the disease. A dental specialist has a high chance of identifying GPA based on the characteristics of the oral findings. In addition, the dentist may be the first to be consulted by the patient with oral manifestations such as ulceration of the oral mucosa and gingival hyperplasia. Gingival hyperplasia that is not associated with remission after periodontal therapy or drug administration should then be investigated with respect to internal diseases such as GPA or leukemia. This example affirms why healthcare professionals should be familiar with the orofacial manifestations of rare diseases such as GPA. Hence, faster referrals to other medical specialists like the rheumatologist. On the other hand, dentists may receive referrals from doctors to assess oral symptoms.

Generally, the clinical manifestation of the disease varies from patient to patient. Rapid progression associated with multiple organ failure will result in death if untreated.

3 Conclusion

The often overlooked oral manifestation can be interpreted as the first evidence of resurgent GPA in general and could therefore be pathognomonic for the disease. This case affirms the need for healthcare professionals to become familiar with the orofacial manifestations of rare diseases such as GPA. As a result, dentists will be able to help in the diagnosis of GPA more easily, which will improve the prognosis of patients suffering from this disease.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

The patient was hospitalized after obtaining informed consent and compliance with the ethical protocol.

Statement of informed consent

Informed consent was obtained from all subjects involved in the study.

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