Clinical Case Report

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Orofacial granulomatosis

A case report of three cases may be caused by apical periodontitis

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Abstract

Rationale: Orofacial granulomatosis (OFG) is a rare disease characterized by noncaseating granulomatous inflammation. The most common clinical presentation is persistent swelling of the soft tissues in the oral and maxillofacial regions. The precise cause of OFG is unknown. Corticosteroids are the first-line and best treatment, but there is lack of uniform treatment prescription and standard. It is important to identify the pathogen in order to improve treatment specificity.

Patient concerns: Three patients presented with recurring lip swelling and cobblestone formation on buccal mucosa, complained of toothache or dental caries for many years. They had very similar and characteristic clinical signs, especially the corresponding location with infected teeth, which suffered from apical periodontitis.

Diagnoses: The three patients were all diagnosed with typical clinical signs and non-caseating epithelioid cell granulomas histologically.

Interventions: The teeth with apical periodontitis were extracted or treated and corticosteroids were prescribed locally or/and systematically.

Outcomes: A complete resolution of lip swelling and cobblestone formation were shown after treatment.

Lessons: This is the first report to highlight that apical periodontitis may intrigue the pathogenesis of OFG, which suggested that dental infection may be the direct and initial etiology of OFG. Removal of infected teeth should be performed as soon as possible in order to reduce the dosage of corticosteroids and occcurence rate of OFG.

Abbreviation: OFG = orofacial granulomatosis.

Keywords: apical peiodontitis, dental infection, orofacial granulomatosis

1. Introduction

The term orofacial granulomatosis (OFG) was introduced by Wiesenfeld in 1985.[1] Typically, OFG presents as labial swellings that persist or recur. It is also associated with oral ulceration, gingival overgrowth and a cobblestone appearance of the buccal mucosa.[2] The diagnosis can be confirmed by histopathological identification of noncaseating granulomas.[3]

The precise etiology of OFG is unknown. Genetics, allergies (food, dental materials), microbiological agents, or immunology were suggested as potential causative agents.[4,5] There has not been a case report to demonstrate that OFG was caused by dental infection. To successfully treat this disease entity, we believe it is imperative to properly identify the root cause of OFG individually. Herein, we report 3 cases of OFG with similar clinical signs. The potential effect of dental infection on OFG and proper treatment of the infected teeth as the first step in treating OFG are discussed.

2. Case reports

2.1. Case 1

A 52-year-old woman was referred to our hospital in 2013 for treatment of 6-month swelling of left lower lip. She complained of previous swelling and mild itching but did not seek treatment. She also complained of dental caries since young age, and several teeth had been extracted, whereas others were decayed. The patient had no history of systemic diseases and denied any food or drug allergy.

Clinical examination revealed redness and high temperature of left chin skin. Intraorally, there were cobblestone formation on the left buccal mucosa and several residual roots in the left mandible (Fig. 1A and B). Panoramic x-ray demonstrated apical radiolucency around the residual roots (Fig. 1C). Hence, a clinical diagnosis of OFG was made and was confirmed later by biopsy of the left cobblestone formation, non-necrotizing granulomas with multinucleated giant cells (Fig. 1D and E).

One week after extraction of the residual roots, the extraction wound healed without any complication. Local injection on left

Editor: Li Wu Zheng.

Ethical review and informed consent: This case report was approved by the Clinical Research Ethics Committee of Qingdao stomatological hospital (board's name: Yanling Yu). The three patients provided their written informed consents for the publication of this case report.

The authors declare that they have no conflict of interest.

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Medicine (2017) 96:39(e8102)

Received: 3 July 2017 / Received in final form: 26 August 2017 / Accepted: 29 August 2017

http://dx.doi.org/10.1097/MD.0000000000008102

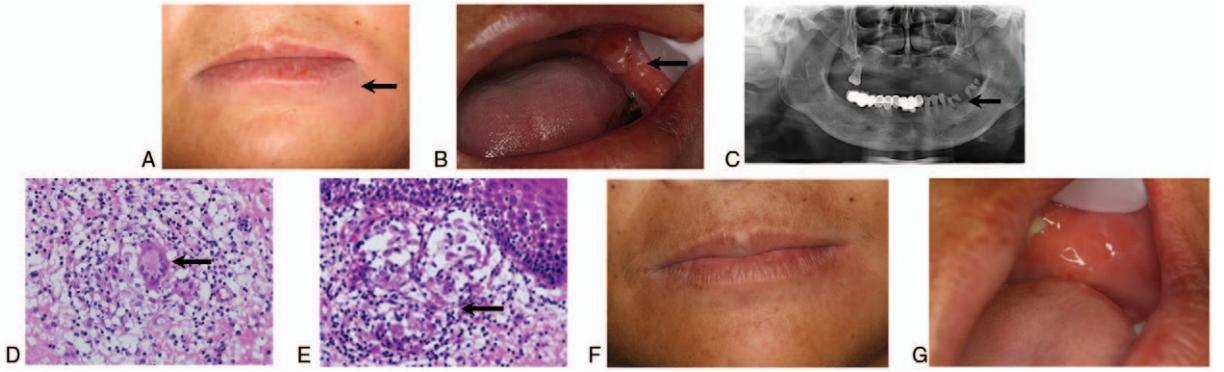

Figure 1. (A) The left lower lip showed diffuse edema, and the left chin skin was red with hot temperature; (B) cobblestone formation was visible on the left buccal mucosa. Note that the mandibular molars developed black residual roots; (C) residual roots were present in the mandibular molars, and x-ray shadow around roots suggested apical periodontitis; (D and E) high-power magnification demonstrated granulomatous inflammation (E, arrow) beneath the cobblestone mucosa with multinucleated giant cells (D, arrow); (F and G) the swelling and redness disappeared on the lower lip and left chin, and cobblestone formation was invisible on the left buccal mucosa after treatment.

lower lip (triamcinolone acetonide 40 mg/dose every week) and systemic corticosteroid therapy (methylprednisolone at an initial dosage of 12 mg, tapering to 4 mg every week) was started, and was well tolerated. After 3 weeks of treatment, lip swelling, redness of skin, and mucosal hyperplasia completely disappeared (Fig. 1F and G) and thus the medications after were suspended. One month later, the patient notified us of mild lower lip swelling, but did not visit the hospital. In her 1-year follow up, she reported no recurrence of swelling and was not taking any drugs.

2.2. Case 2

A 42-year-old woman visited our department in 2014 because of a lump on her right buccal mucosa for 1 year. She often felt hot on the right side of her face and had swelling lip for 1 year. The mandibular posterior teeth were painful for several years and had decayed. She did not see any dentist before visiting our hospital. She reported no intestinal problems suggestive of Crohn disease, or complaints of chronic fatigue. There was no history of tuberculosis.

Upon clinical examination, the right perioral and cheek skin was blush with a higher temperature than the left. There was swelling in the right lower lip and a cobblestone formation on the right buccal mucosa intraorally. There were residual roots in the right mandibular teeth and a sinus tract on the buccal gingiva of tooth #24 (Fig. 2A–C). Panoramic x-ray showed apparent periapical radiolucency suggestive of apical periodontitis (Fig. 2D and E). The routine blood test showed mild anemia (hemoglobin 107 g/L, mean corpuscular volume 74.2 fL, mean corpuscular hemoglobin 291 g/L), but the patient felt no discomfort. We performed a biopsy from the hyperplasia of the right buccal mucosa and histopathologically diagnosed OFG (Fig. 2F).

The first treatment step was to remove all dental infection, including root canal therapy of tooth #24, and extraction of residual roots. Then the patient was prescribed methylprednisolone at an initial dosage of 12 mg/day. After 1 month of treatment, the right cheek swelling and blush reduced (Fig. 2G and H). Unfortunately, the patient did not return for further follow-up.

2.3. Case 3

A 61-year-old man was referred to our hospital in 2016 with swelling of the left upper lip for 3 months. He had multiple tooth extractions and experienced toothache on left mandibular

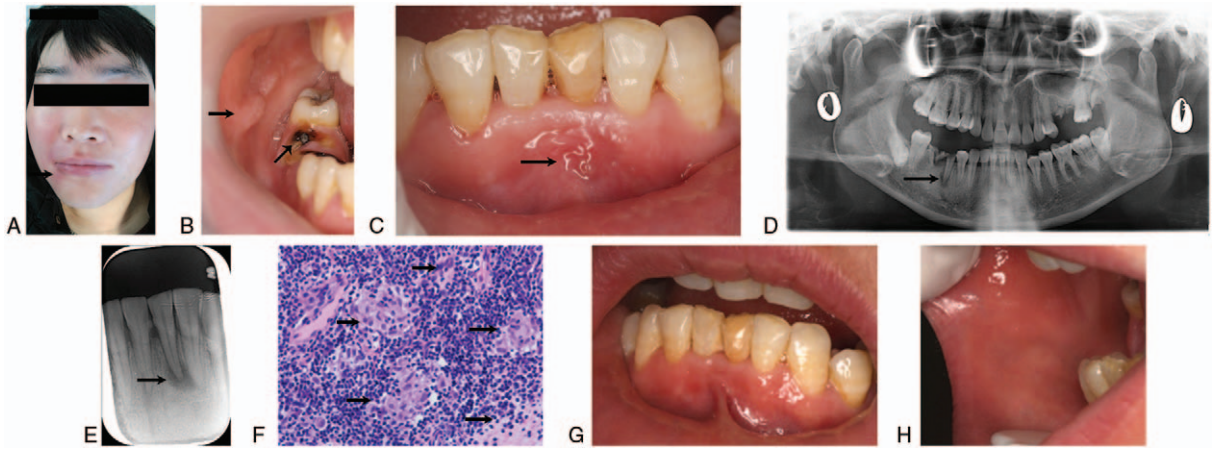

Figure 2. (A) The right side of the face was apparently blush and the right lower lip was swollen; (B and C) the residual roots and cobblestone formation were homolateral. There was a fistula on the surface of buccal gingiva, the color of tooth #24 was dark yellow; (D and E) periapical shadows were visible in tooth #24 and #30; (F) several noncaseating epithelioid granulomas along with inflammatory infiltrate were visible in the photomicrograph (arrows) (hematoxylin and eosin; original magnification ×200); (G and H) the sinus tract in teeth #24 disappeared, and cobblestone formation on buccal mucosa was invisible after treatment.

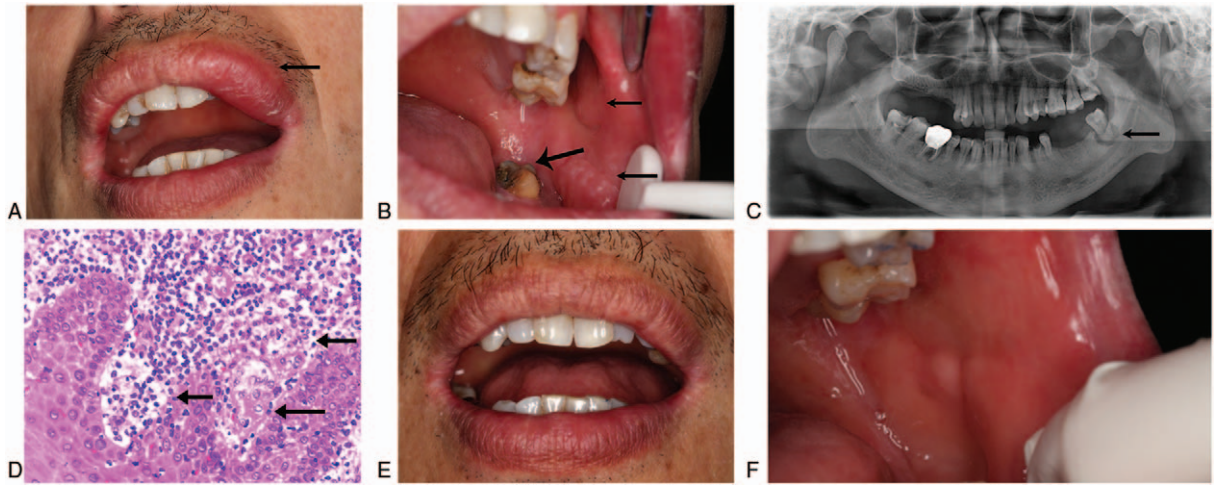

Figure 3. (A and B) The left upper lip was blush and swollen (A), cobblestone formation was seen on the left buccal mucosa, tooth #17 had extensive caries and second-degree mobility (B); (C) a translucent zone around the root of tooth #17 was seen in the radiograph (arrow). (D) Several noncaseating epithelioid granulomas under epithelium were visible in the photomicrograph (arrows) (hematoxylin and eosin; original magnification ×200). (E and F) Upper lip edema, and cobblestone formation of mucosa disappeared after treatment.

teeth while chewing food. The patient had no systemic diseases and his medical history was noncontributory.

Clinically, the patient presented recurring labial swellings and firm cobblestone appearance on the left buccal mucosa (Fig. 3A and B). Results of routine blood tests were within normal limits. Panoramic x-ray showed periapical radiolucency around the root of tooth #17, suggestive of apical periodontitis (Fig. 3C). A biopsy from the hyperplasia of the left buccal mucosa and histopathologically diagnosed OFG (Fig. 3D).

First, we advised the patient to immediately extract tooth #17. Ten days later, lip swelling apparently alleviated, but the lesion on buccal mucosa remained unchanged. Then, we prescribed methylprednisolone at an initial dosage of 12 mg/day. The cobblestone formation on the left cheek narrowed after 3 weeks. One year follow-up showed a complete resolution of lip swelling and cobblestone formation (Fig. 3E and F).

3. Discussion

OFG is an increasingly recognized entity; however, its exact etiology remains unclear. Traditionally, the first-line treatment is to prescribe systemic corticosteroids.[6] If we can identify the cause responsible for OFG and effectively remove it, it might not only alleviate the symptoms sooner but also reduce the dosage and duration of steroid treatment.

The involvement of microbial agents in the pathogenesis of OFG has been suggested in similar chronic granulomatous conditions, such as Crohn disease, sarcoidosis, and turberculosis.[2] Some kinds of bacteria, such as *Mycobacterium tubersulosis, M paratuberculosis, Saccharomyces cerevisiae, Spirochetes, Mycobacteria, Borrelia burgdorferi*, have been detected in OFG.[7–9] Gibson et al[10] reported one OFG patient suffering from oral staphylococcal infection, but the cause-and-effect relationship between oral infection and OFG was uncertain. However, it has been demonstrated that periapical lesions can produce numerous bacteria and 2 types of viruses.[11–14] Besides interleukin (IL)-1 family, markers of T-helper subsets markers are also expressed in periapical lesions, and elevated IL-1 and tumor necrosis factor-α can be detected in the blood of apical periodontitis patients.[15] These types of local irritations may trigger homolateral mucosal granulomatosis. To our knowledge, there has been no case report to associate dental infections, such as apical periodontitis to OFG. Therefore, we hypothesized that bacteria from infected root canal and/or periapical lesions may elicit inflammatory cytokines to stimulate mucosal swelling and hyperplasia.

The 3 cases in this report had very similar and characteristic clinical signs, especially the corresponding location with infected teeth, which suffered from apical periodontitis. Especially for the patient in case 3, his left upper lip swelling alleviated greatly only 10 days after extracting the homolateral infected tooth without usage of any drug. Even the patient suspended to take methylprednisolone 3 weeks later, the mucosal cobblestone formation and lip swelling disappeared completely while following up 1 year later. Hence, the hypothesis that OFG caused by apical periodontitis appeared more solidly. However, it is unlikely to demonstrate etiology of disease based on a case report, our article is aimed to proposing this hypothesis, reminding peers of the possibility, and providing a new treatment for OFG.

Whether OFG is a mere manifestation of systemic diseases or a separate disease entity itself remains controversial.[2] The limitation of our report is that we did not ask the 3 patients to undergo specific examinations to exclude other systemic diseases and possible allergies, mainly based on their medical histories. Based on previous reports[2,7] and our clinical experience, there is no standard corticosteroids treatment protocol for OFG. The 3 patients seemed to tolerate our treatment protocol well without any significant side-effects during their treatment repectively neither after long-term follow-up.

4. Conclusion

The 3 cases presented in this report suggested a potential and direct relationship between OFG and apical periodontitis. However, more clinical cases and studies are needed in the future to confirm our hypothesis.

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