

CASE REPORT

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Strawberry gingivitis - A diagnostic feature of gingival Wegener's granulomatosis!

Heera R¹, Beena VT², Kanaram Choudhary³, Rency Simon⁴

Dept of Oral Pathology & Microbiology
Govt. Dental College,
Trivandrum, Kerala, South India

Associate Professor¹
Professor & Head²
Post Graduate Student^{3&4}

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ABSTRACT:

Wegener's granulomatosis is an immunologically mediated inflammatory disease characterized by granulomatous vasculitis of the upper and lower aero-digestive tracts together with glomerulonephritis. We are reporting a rare case of gingival Wegener's granulomatosis which presented with erythematous and painful generalized gingival enlargement. Co- relation of histopathology with routine H&E and special stains (Grocott-Gomori methenamine-silver nitrate and PAS), Mantoux test, peripheral blood smear and clinical presentation were established in diagnosing this rare entity. By the above mentioned procedures and methodology we have arrived at the diagnosis of Wegener's granulomatosis limited to upper aero-digestive tract. So aim of reporting this case to emphasize that the dental surgeon often being the first person to examine the oral cavity, should be familiar with the typical appearance of gingival Wegener's granulomatosis as "strawberry gingivitis", its clinical course as well as diagnostic parameters and adequate management. Best of our knowledge it is first reported case of Wegener's granulomatosis manifesting as "strawberry gingivitis" in Indian population.

Key words: Strawberry gingivitis, Wegener's granulomatosis

Introduction

Wegener's granulomatosis (WG) is an immunologically mediated uncommon multi-system disorder, first described by Friedrich Wegener in 1936. However, detailed description of WG is given by Godman and Churg.¹ While WG typically affects the upper and lower airways and frequently the kidneys, it may involve any organ system. The granulomatous inflammation and vasculitis can affect the mouth, eyes, ear, nose, throat, lungs, skin and kidneys. The disease predominantly affects adults with mean age of 41 years, but there is no significant gender predilection.² In 1990, the American College of Rheumatology (ACR) proposed the following four specific criteria for the classification of WG. 1) Oral ulcers or nasal discharge. 2) The presence of nodules,

fixed infiltrates or cavities on a chest radiograph. 3) Abnormal urinary sediment (red blood cell casts or more than five red blood cells per high power field). 4) Granulomatous inflammation on biopsy. For the diagnosis of WG, a minimum of two criteria should be fulfilled from above mentioned (ACR 1990) criteria.^{1,3} Since the dental surgeon is often the first person to examine the oral cavity, he should be familiar with the classical appearance of gingival Wegener's granulomatosis as "strawberry gingivitis", its clinical course as well as diagnostic parameters and adequate management.

Case report

A 54 year old male patient reported to Govt. Dental College, Trivandrum, South India in the month of December 2010, with soreness of gingiva and malaise. Clinical examination revealed painful and erythematous generalized gingival enlargement

Email for correspondence:
drheerar@yahoo.co.in

involving entire maxillary gingiva, and focal areas of involvement in the mandibular gingiva, with the appearance simulating "ripe strawberry". [Figure 1] The gingiva was very friable and easily bled on touch. There was grade III mobility of maxillary anterior teeth that had spontaneously exfoliated on subsequent visit. The remaining teeth had grade I mobility. The oral hygiene status was poor and all teeth were stained with tobacco stain. The patient was a chronic smoker and alcoholic but quit the habits one year back. Panoramic radiograph revealed generalized bone loss which was more pronounced in the maxillary anterior region. Examination of specific organ system revealed that the patient had prostatic hypertrophy with slight elevation of prostate specific antigen. He was on medication (Tamsulosin+ Finasteride) for prostatic hypertrophy but serum creatinine level was normal. Patient was not on any other drugs except those mentioned above. There was no history of dyspnea, fever, night sweat or allergy to any substance. Evaluation of serum cytoplasmic antineutrophilic cytoplasmic antibody (cANCA) was done and was within normal limit. Peripheral blood smear showed neutrophilia and leucocytosis. Further, the patient was referred to department of Internal Medicine for systemic evaluation, but reports were inconclusive.

Microscopic evaluation of biopsy from gingival tissue showed parakeratinised stratified squamous epithelium with pseudoepitheliomatous hyperplasia and intraepithelial abscess, as well as abscess penetrating into the surface of epithelium. Connective tissue stroma was densely collagenous with dense diffuse infiltration of neutrophils, plasma cells and few macrophages particularly around blood vessels with dilatation and thickening of blood vessels. At one end of the section some multinucleate giant cells were also seen. [Figure 2]

A histopathological differential diagnoses of tuberculosis, deep fungal infection and Wegener's granulomatosis were made. Special staining by Grocott-Gomori methenamine-silver nitrate [Figure. 3] and PAS [Figure .4] were done, which were negative for fungal organisms. Mantoux test was done, which was negative and thus tuberculosis was ruled out.

By the above mentioned clinical features, lab investigations and histopathological examination

with special stains, we arrived at the diagnosis of Wegener's granulomatosis limited to upper aerodigestive tract. Patient has been started on Prednisolone 20 mg/day on divided and tapering dose for 1 week with morning doses of 10mg after proper systemic evaluation in periodontia department. To give symptomatic relief local steroid as well astringing agents was also advised. Patient felt symptomatically better after one week follow up. After that dose of Prednisolone tapered to 10 mg/day in dividing doses with 5 mg of morning dose, unfortunately patient didn't turn for follow up.

Discussion:

Wegener's granulomatosis is a rare disease with multisystem involvement though oral presentation is vary rare. Only 6% of cases were presented with oral manifestation, that too in advanced stage of the disease and is rarely an indicator of the disease. Otorhinolaryngological involvement is more common with destruction of nasal septum resulting in palatal perforation and progressive sensorineural hearing loss. Ophthalmic symptoms may manifest as epiphora due to involvement of nasolacrimal duct. Lesion of the skin manifests as purpura, nodules and ulcers and have been reported in about 46 percent of affected patients and in 13 percent of affected patients at the onset of disease. However, limited forms of the disease have been reported in which only one or two organ systems have been involved.^{1,3}

The oral lesions may manifest either as mucosal ulcer on the tongue, buccal mucosa, gums and palate, or as gingival hyperplasia with classical "strawberry gingivitis". However, Cawson suggested that other lesions may also occur such as ulceration of the palate by extension from the nose, where destruction of the nasal septum may develop. It may also occur as small ulcer like apthae, diffuse ulcerative stomatitis, spontaneous exfoliation of the teeth as seen in our case.^{1,3,4}

Crohn's disease and sarcoidosis, deep fungal infection (candida, histoplasmosis and paracoccidioidomycosis), tuberculosis ,other granulomatous infections like midline lethal granuloma, midline NK/T-cell lymphomas, other anti-neutrophil cytoplasmic antibody (ANCA) positive

vasculitis, drug induced gingival enlargement and rarely cicatricial pemphigoid (CP) or mucous membrane pemphigoid should be included in the differential diagnosis of Wegener's granulomatosis.^{1,3,4,5,6}

Gingival manifestations of WG may have a clinical appearance similar to that of gingival leukemic infiltrates. In the reported case a peripheral blood smear examination was performed and leukemia was ruled out. Presence of multinucleated giant cells in the histopathology prompted for ruling out tuberculosis and deep fungal infection, hence Mantoux test, bacterial PCR, special staining with Grocott-Gomori methenamine-silver nitrate and PAS were performed.

In the case presented, diagnosis of Wegener's granulomatosis was made according to criteria given by American Association of Rheumatology, after careful exclusion of above mentioned lesions by appropriate systemic evaluation, lab investigation and referring the previous reported case with similar clinical and histopathological reports. Our case also fulfilled two criteria of ACR 1990 including gingival ulceration which appeared like "strawberry gingivitis" and granulomatous lesion in gingival biopsy.

Most authors acknowledge that the clinicopathological complex of "strawberry gums and the accompanying histopathological features of pseudoepitheliomatous hyperplasia, intraepithelial abscess penetrating the surface epithelium, microabscesses in connective tissue stroma, and multinucleate giant cells are "highly suggestive" of Wegener's granulomatosis. It was also suggested that there was no association of the features of this complex with any other disease process and in an appropriate clinical setting they are so characteristic of gingival Wegener's granulomatosis as to be virtually diagnostic, particularly since the classic criteria of vasculitis, granulomata, and necrosis occur only rarely in gingival biopsy specimens.⁶ The diagnosis of Wegener's granulomatosis was made in the case presented based on these particular combination of clinical and histopathologic findings.

The serological tests helped only to reinforce the clinical impression of a systemic inflammatory

process and did not confirm the diagnosis of Wegener's granulomatosis. The classical anti-neutrophil cytoplasmic antibodies (cANCA) titer, arguably the most useful investigation in cases of Wegener's granulomatosis was non-contributory in our case. Even the presence of the nasal lesion could not be considered diagnostic.^{1,6} Although few cases of Wegener's granulomatosis have been reported with classical presentation of 'strawberry gingivitis' in literature. In recent literature search a case of gum hypertrophy initially diagnosed as acute myeloid leukemia turned to be Wegener's granulomatosis reported by Kundu BK and Gadpayl AK in 2011⁷, but no case has been reported with classical presentation of strawberry gingivitis in Indian population. So reported case turned to be first one.

Different treatment protocols were given including prednisolone, prednisolone and cyclophosphamide (CYC), azothiopurine (AZT). Glucocorticoids combined with CYC or methotrexate (MTX) are the only two regimens that have thus far been shown to induce remission of active WG affecting a major organ. Patients with alveolar hemorrhage, rapidly progressive glomerulonephritis, central nervous system disease, or other manifestations that are immediately life threatening should initially be treated with CYC and glucocorticoids. Once remission has been induced, consideration can be given to stopping CYC and beginning AZA or MTX treatment to maintain remission. Maintenance therapy should be based on medication, contraindications and toxicity profiles, on the patient's relapse and disease history, and on the physician's experience with each medication. Monitoring and prevention of therapeutic toxicity play an important role in overall patient management. This includes pneumocystis prophylaxis and osteoporosis prevention regimens with concurrent glucocorticoid treatment. Some authors also suggested co-trimoxazole to avoid the side effects of immunosuppressive therapy. Although substantial progress has been made, challenges remain in the search for newer and better regimens that reduce disease relapse and therapeutic toxicity. Good prognosis with long term remissions have been reported with combination therapy.^{8,9,10} Reported case responded with steroid therapy.

If left untreated, WG often is fatal within the first year of onset. Mean survival is reported as 5 years for untreated cases. The condition has a more favourable prognosis in the absence of renal involvement.⁵

The characteristic gingival lesion with the combination of histopathology might be diagnostic of WG, and early diagnosis accompanied by aggressive treatment is important for a better outcome in this potentially lethal disease.

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Figure 1. Clinical picture showing "ripe strawberry gingiva"

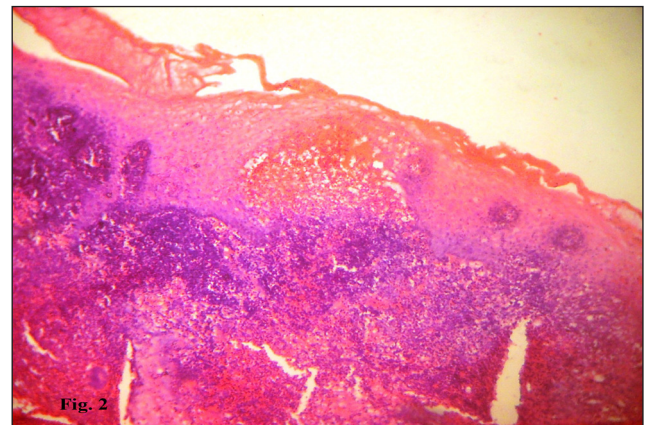


Figure 2. Histopathological picture showing intraepithelial abscess and abscess penetrating to surface. (10x).

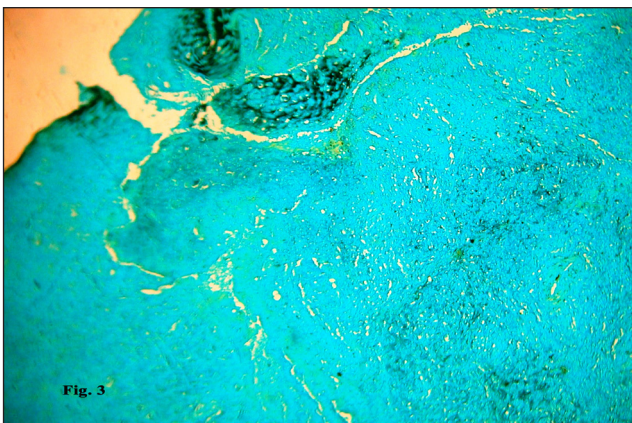


Figure 3. Grocott-Gomori methenamine-silver nitrate stain of section (10x)

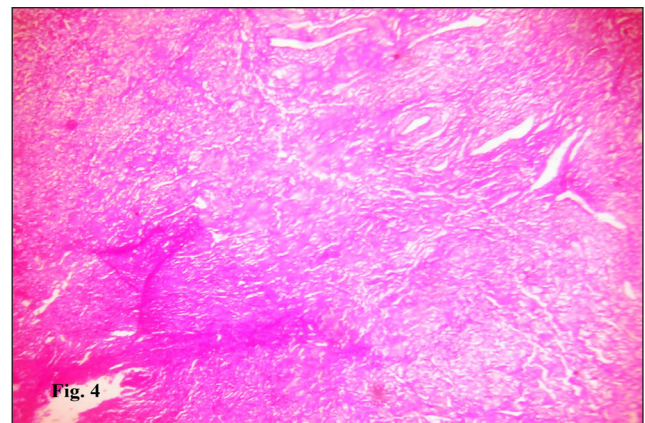


Figure 4. PAS stain of section (10x)