Case Report

Role of a dentist in early diagnosis of Granulomatosis with Polyangiitis: A rare case report

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Abstract

Granulomatosis with polyangiitis (GPA) is a rare multisystem disease characterized by a triad of necrotizing granulomas affecting the upper and lower respiratory tract, vasculitis and glomerulonephritis. Oral lesions are seen in 6–13% of cases, although not life threatening but might be the first symptoms reported by the patient. Here we present a case of gingival growth, later diagnosed as GPA owing to the timely recognition by the dentist. A 33-year-old female reported for evaluation of soft tissue growth in her lower left back tooth region present for past 3 months. She had no relevant medical or family history. Clinically it looked like a benign hypertrophic gingival enlargement. The histopathological picture was suggestive of vasculitis and nonspecific granuloma formation. On further examination altered Renal Function Test and cavitating granulomas were noted in her lungs along with a positive cytoplasmic ANCA (c-ANCA) test which led to the diagnosis of GPA.

Keywords: C-ANCA, granulomatosis with polyangiitis, oral manifestations, palatal ulcer, strawberry gingivitis, vasculitis

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INTRODUCTION

Wegener's granulomatosis was first described by German Pathologist Friedrich Wegener in 1937 and was renamed in the year 2012 as Granulomatosis with Polyangiitis(GPA).[1] In the 2012 revised Chapel Hill criteria, it is defined as a necrotizing granulomatous inflammation of the upper and lower respiratory tracts, with necrotising vasculitis of small- and medium-size vessels.[2] It is a rare autoimmune disease among the three known systemic vasculitis associated with cytoplasmic ANCA (c-ANCA) which includes microscopic polyangiitis, eosinophilic GPA (also known as Churg–Strauss syndrome) and GPA.[3] It affects both the genders equally with an estimated incidence of 3–14.4 cases per million per year. It is more prevalent in Caucasians and is common between 20 and 50 years of age.[4] It can involve various systems like upper and lower respiratory tract, kidneys, skin, mucous membrane lined cavities, central nervous system, etc., culminating in a myriad of signs and symptoms like loss of appetite, chronic fatigue, fever, sporadic pain, sinusitis, cough, haemoptysis, renal insufficiency, oedematous lungs, bronchial perforations, etc.[5] And oral signs and symptoms like gingival hyperplasia, periodontitis, facial paralysis, parotitis, delayed wound healing, ulceration and necrosis of tongue and palate, oroantral fistulas and tooth ache, rarely sublingual salivary gland inflammation

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are seen.[6] The causes of GPA are varied possibly involving genetic, environmental, drug reactions or infectious processes but antineutrophil cytoplasmic antibodies (c-ANCA are considered highly sensitive and specific in its pathogenesis.[7] The clinical presentation, a positive antineutrophil cytoplasmic antibody (ANCA) and histological presence of granulomatous inflammation and vasculitis forms the diagnostic triad of GPA.[8] It is characterised by wide spread involvement and rapid progression to multiorgan failure and death.[9] Early diagnosis is essential to prevent such progression and prolong life expectancy. Here, we present a case of a middle aged South Asian female complaining of gingival swelling and ulceration in palate, finally diagnosed with GPA due to the timely recognition of her oral symptoms.

CASE DESCRIPTION

A 33-year-old female presented with a complaint of growth in her lower left back tooth region since 3 months and pain in the left ear for which she visited the ENT ward from where she was referred to our college. Patient was apparently normal 3 months back following which she noticed growth in her left posterior mandibular region which was insidious in onset and was slow growing [Figure 1]. There was no history of associated pain or trauma in that region.

Medical and family history of the patient was noncontributory. However, 1 month back, patient was successfully treated for left parotid and submandibular abscess with cervical lymphadenopathy.

Extra oral examination showed no abnormality on inspection and palpation. No regional lymphadenopathy was noted.

Intra oral examination revealed a solitary growth on the left lower alveolar ridge distal to 37 [Figure 1], roughly oval in shape measuring approximately 1 × 1cm with pebbly appearance. Also, on the interdental gingiva of lower anterior teeth diffuse, reddish-purple gingival enlargement with erythematous surface mucosa and petechial haemorrhage were noted resembling strawberry gingivitis [Figure 2]. On palpation the lesion was tender, haemorrhagic and soft to firm in consistency.

Radiographic examination showed no abnormality [Figure 3].

A provisional diagnosis of pyogenic granuloma was made and an incisional biopsy was sent for histopathological examination.

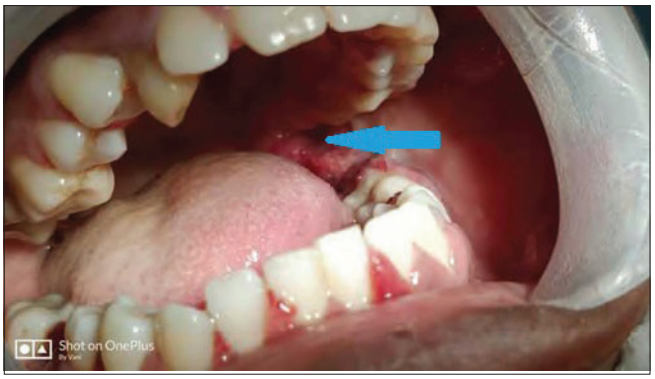

Figure 1: Arrow showing gingival growth distal to 37

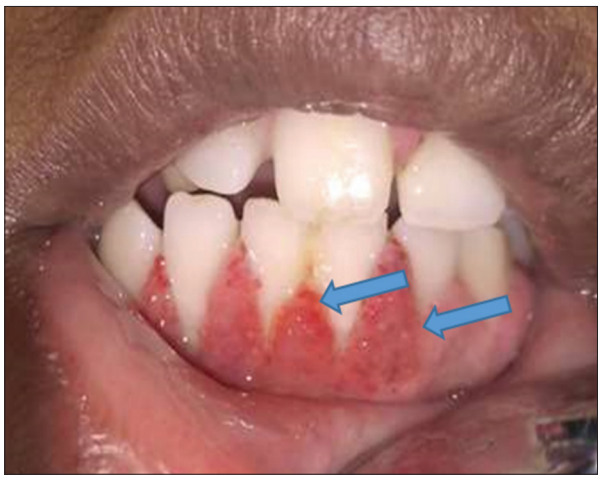

Figure 2: Arrow showing hypertrophic gingiva on labial aspect of lower anterior teeth resembling "Strawberry gingivitis"

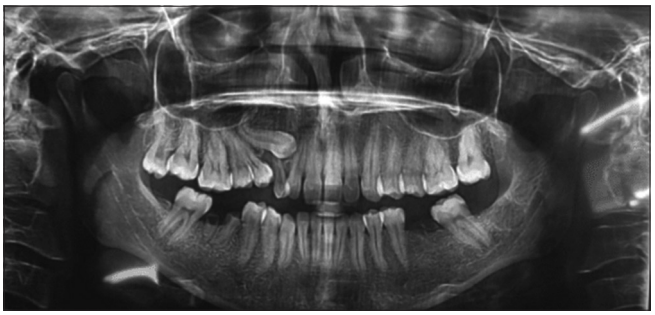

Figure 3: OPG of the patient with no significant changes with respect to lower anterior and left posterior region due to the growth

Three soft tissue bits were received of creamish brown color, in which the largest bit measured 0.6 × 0.4 × 0.3 cm [Figure 4]. Under the stereomicroscope the tissue exhibited papillary growth [Figure 5].

The haematoxylin and eosin stained section revealed parakeratinised stratified squamous epithelium and subepithelial connective tissue. The epithelium exhibited hyperplasia at some regions with broad rete ridges [Figure 6]. Underlying stroma showed dense mixed inflammatory cell infiltrate comprising of neutrophils, lymphocytes, plasma

cells, eosinophils and macrophages [Figure 7]. Few areas of necrosis surrounded by palisading epitheloid cells, histiocytes, foreign body and langhans type multinucleated giant cells and other inflammatory cells like lymphocytes were seen resembling granulomas [Figure 8]. Intervening connective tissue showed numerous blood vessels surrounded and infiltrated by inflammatory cells suggestive of vasculitis [Figure 9]. Large areas of haemorrhage were also noted. Histopathological impression of Necrotizing granulomatous inflammation was given.

On follow-up visit after 1 month the patient had developed a solitary and painless ulcer on the right side of hard palate measuring approximately 0.5 × 0.7 cm that seemed to be perforating the palate [Figure 10].

To rule out other diagnosis, several investigations were performed that showed normal haemoglobin, normal bleeding and clotting time. Whereas elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels raised an alarm. Also an altered Renal Function Test arose suspicion and confusion. Hence we decided to refer the patient to a general physician to rule out GPA. The physician advised a chest computed tomography (CT) scan, that revealed well-defined smooth-walled cavitating granulomas in the upper and lower lobe of right lung measuring 1.3 × 1.2 cm and 0.8 × 0.7 cm, respectively. Finally an ANCA test was performed which turned out to be positive for c-ANCA.

Hence, on the basis of all the clinicopathological findings a final diagnosis of GPA was made and the appropriate treatment was started for the patient at the earliest.

DISCUSSION

GPA is a rare chronic disease with episodes of remissions and relapses. Early diagnosis is of utmost important in preventing long-term complications such as permanent

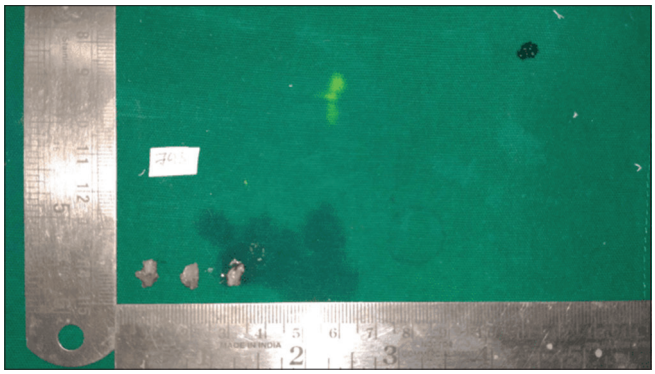

Figure 4: Grossing image of the soft tissue bits

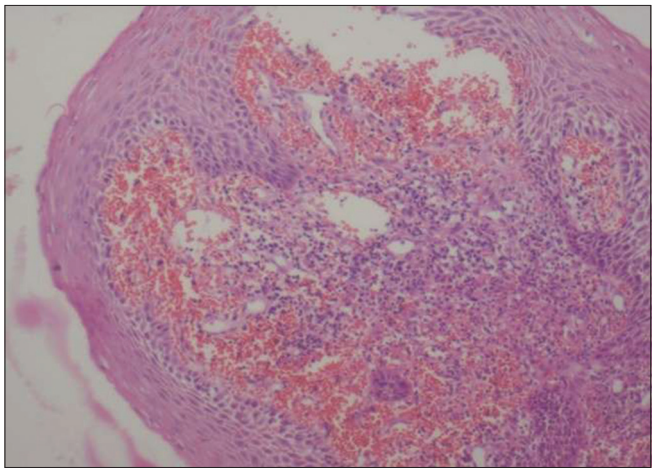

Figure 6: Parakeratinized stratified squamous epithelium and underlying inflammed connective tissue (original magnification –100x; Haematoxylin and eosin stained section)

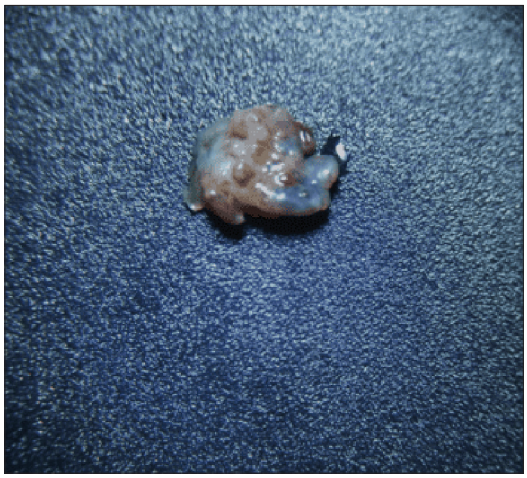

Figure 5: Stereomicroscopic view of the soft tissue bit showing smooth and papillary surface

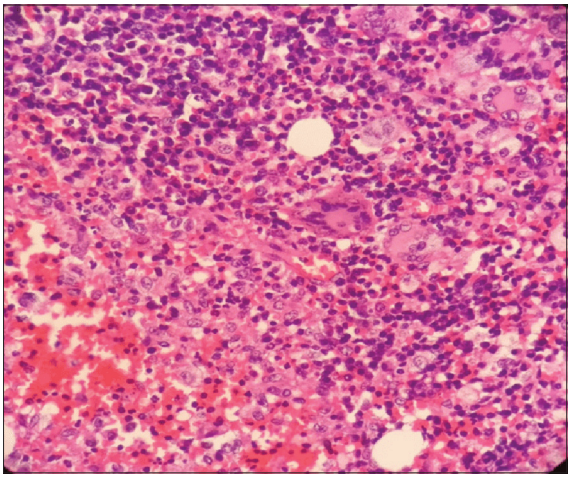

Figure 7: Inflammatory cells like neutrophils, lymphocytes, plasma cells, eosinophils and macrophages in the background of mature connective tissue (original magnification –400x; Haematoxylin and eosin stained section)

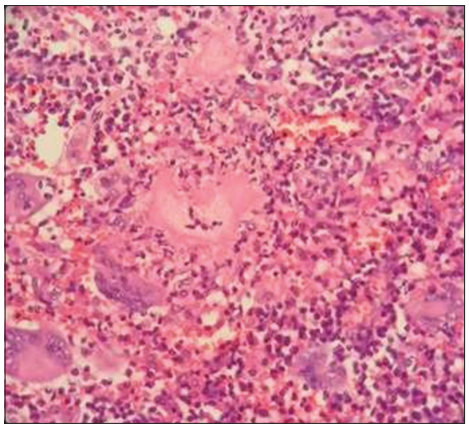

Figure 8: Central areas of necrosis surrounded by epitheloid cells, histiocytes and multinucleated giant cells resembling granuloma formation (original magnification –400x; Haematoxylin and eosin stained section)

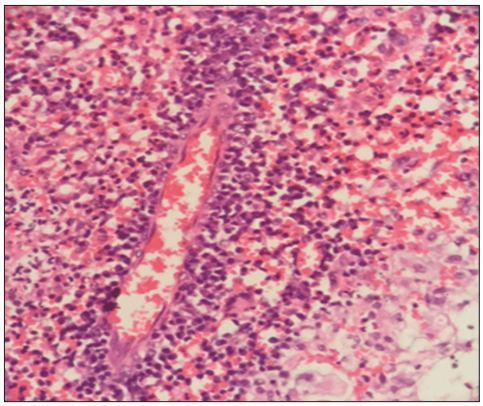

Figure 9: Blood vessel completely surrounded and infiltrated by inflammatory cells suggestive of vasculitis (original magnification –400x; Haematoxylin and eosin stained section)

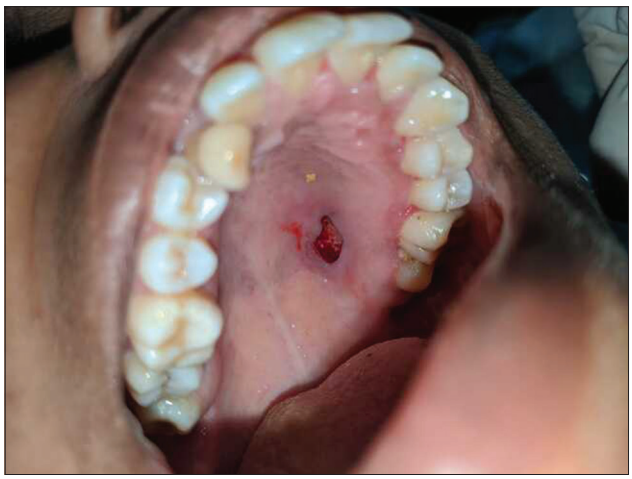

Figure 10: Palatal ulceration on the left side of the hard palate

hearing loss, facial nerve paralysis, chronic kidney disorders, lung failure, etc.[10] Oral manifestations are reported as first signs in only 2% of the cases.[11] In our case presence of gingival hypertrophy resembling strawberry gingivitis and palatal ulceration were the only symptoms reported by the patient though her lower respiratory tract and kidneys were involved much before the oral signs showed up. Diagnosis of GPA is difficult due to its indefinite presentation. Hence, initially we considered various differential diagnosis such as tuberculosis, foreign body reaction, systemic fungal infection, sarcoidosis, rheumatic vasculitis, drug-induced gingival enlargement or secondary lesions due to immunodeficiency which were ruled out eventually. GPA is brought about by a T-cell reaction which produces and releases proinflammatory cytokines like tumor necrosis factor-alpha (TNF-α) and interferon-gamma (IFN-γ) which induces the expression of surface antigens on activated neutrophils.[12] One such antigen is proteinase 3 that becomes the target of antineutrophil cytoplasmic antibodies (c-ANCA). It is a protein that is present in azurophilic granules of neutrophils, its secretory vesicles and plasma membrane. It helps in degradation of extracellular proteins at the site of inflammation and acts as an inflammatory mediator.[12,13] ANCA activates neutrophils, increases their ability of adherence to endothelial cells causing release of oxygen and lytic enzymes thereby causing vasculitis. Hence, it leads to small and medium vessel vasculitis which can culminate in multiorgan damage.[2]

We followed the diagnostic system known as the ELK (E for ears, nose and throat or upper respiratory tract; L for lung; and K for kidney) classification system which utilises ANCA results. According to this system, any typical manifestation in the E, L or K supported by typical histopathology or a positive cytoplasmic ANCA (c-ANCA) test qualifies for the diagnosis of GPA.[14] Another diagnostic criteria given by The American College of Rheumatology proposes that two or more of the findings should be fulfilled to give a diagnosis of GPA: (i) ulcerative lesions in the oral mucosa or nasal bleeding or swelling (ii) nodules, infiltrates or cavities on chest radiograph (iii) abnormal urinary sediment or (iv) granulomatous inflammation on biopsy.[15] This criteria also confirmed the diagnosis of GPA in our case.

Histopathologically the lesions show infiltrates of acute and chronic inflammatory cells, areas of microabscess, haemorrhage, multinucleated giant cells and pseudoepitheliomatous hyperplasia of the epithelium. The histopathological findings are nonspecific and needs to be confirmed with other findings like ANCA which is said to show high sensitivity of 91% and specificity of 98%.[8]

When treating oral manifestations in such patients' physician's consent should be obtained and treated like any other immunocompromised patient. Regular oral prophylaxis, antimicrobial mouth wash and antibiotic

prophylaxis is recommended before any procedure. Only emergency treatment is advised during acute phases of the disease.[7] Our patient is on regular follow-up and being treated with methotrexate, prednisolone and other supplements as per the patient's requirement. The patient is able to lead a normal life owing to the early diagnosis and intervention. The dentist might be the first one being consulted by the patient or referred from general practitioners with oral symptoms such as gingival hyperplasia or mucosal ulcerations, hence he or she should be acquainted with various manifestations of systemic diseases to be able to identify and refer a patient quickly to other medical specialists for early intervention and treatment.

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Conflicts of interest

There are no conflicts of interest.

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