Granulomatosis with polyangiits associated with alveolar bone loss – Case presentation

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Abstract

Granulomatosis with polyangiitis (GPA) is a long-term systemic disorder that involves both granulomatosis and polyangiitis, if untreated can be lethal. Granulomatosis with polyangiitis is also known to cause oral mucosal lesions as nonspecific erosive- ulcerative lesions and enlargement of gingivae and alveolar bone loss.

We report a case of GPA with a severe generalized phase with oral manifestations: gingival bleeding and severe gingival inflammation. The radiographic examination of the patient revealed the periodontal bone loss and tooth loss of anterior mandibular region.

Periodontal professional care is necessary to improve the oral health of patients with GPA as a part of multidisciplinary approach.

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Introduction

Granulomatosis with polyangiitis (GPA), formerly Wegener's granulomatosis, is one of a group of blood vessel disorders called vasculitis. It is a rare multisystem autoimmune disease of unknown etiology that is pathologically characterized by an inflammatory reaction pattern (necrosis, granulomatous inflammation and vasculitis) that occurs in the upper and lower respiratory tracts and kidney.[1] The affected tissues may develop areas of inflammation called granulomas, which can affect all areas of the body: the upper respiratory tract, lungs, kidneys and other organs, including the oral cavity.[2,3]

The Chapel Hill 2012 Consensus Criteria define GPA as “necrotizing granulomatous inflammation usually involving the upper and lower respiratory tract and necrotizing vasculitis affecting predominantly small to medium vessels”.[4]

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Granulomatosis with polyangiitis (GPA) is a severe autoimmune disease which is highly associated with anti-neutrophil cytoplasmic antibodies (ANCA). GPA is mediated by a T-cell reaction,[5] where the production of pro-inflammatory cytokines TNF-α, interleukin 1-betra (IL1 β) and IFN-γ, will induce the production of anti- cytoplasmic proteinase 3 antibodies (anti –PR 3 antibodies), after the expression of surface antigens on activated neutrophil granulocytes. Under the influence of cytokines and ANCA, it will lead to degranulation of neutrophil granulocytes and will contribute to the aggression of the vessel wall and be responsible for the tissue damage.[6]

Generally, the clinical manifestation of the disease varies from patient to patient. Rapid progression in combination with multiorgan failure will lead to death if untreated.[7] Infections, environmental factors, epigenetic modifications, and a genetic predisposition may influence the risk of developing.[8,9]

GPA typically evolves into two phases: an initial phase characterized by ear, nose and throat (ENT) manifestations, such as chronic sinusitis and otitis, ulceration of the oral cavity and pharynx, as well as pulmonary nodules

and a severe generalized phase, defined by the occurrence of rapidly progressive glomerulonephritis, pulmonary hemorrhage, and arthritis.[10]

Early diagnosis and treatment of granulomatosis with polyangiitis may lead to a full recovery. Without treatment, granulomatosis with polyangiitis can be fatal.[11,12]

10% of patients with GPA have oral manifestations, and oral lesions that present as an initial manifestation of GPA are rare. The most characteristic oral lesion is hyperplastic gingivitis presenting with a “strawberry like” appearance.[13,14] Oral symptoms of Wegener Granulomatosis are: nonspecific erosive/ ulcerative lesions of oral cavity, Ulcers in oral mucosa, gingival involvement can be seen as gingival enlargement, strawberry gingivitis, erythema, pethechie, hemorrhage and necrosis.[15,16] In some cases ulcers, necrosis on tongue, bone alveolar loss, tooth loss and mobilility, ulcers on mucosa of palate, nodulare hyperplasia and desqumation of lips.[17] Osteomyelitis or necrosis of the underlying bone can develop with subsequent mobility and loss of teeth.[18] The diagnosis of GPA is made based on clinical symptoms and signs, the presence of the anti-neutrophil cytoplasmic antibody (ANCA), and a positive biopsy.[19]

We report a case of 47 –year-old female patient with GPA with oral involvement gingival bleeding and severe gingival inflammation**.**

The patient gave written informed consent. and the case had been reviewed and approved by the University Dentistry Clinical Center of Kosovo Joint Ethics Committee.

Case Report

A 47 year old female nonsmoker patient was referred to the Department of Periodontology and Oral Medicine at the University Clinical Dental Center in Prishtina, Kosovo at May 2018 with complaining of gingival swelling since approximately 1 year, soreness and bleeding from gingiva.

Patient history. The disease started as an acute, self-limited condition characterized by the abrupt onset of symmetrical fixed red papules on the skin, later on diagnosed as Erythema exudative multiformis on May 2015. After 2 weeks, her lungs were affected and she had shortness of breath, coughing, weight loss and diagnosed with interstitial pneumonia. While hospitalized, patient had cardiac manifestations of pericarditis and myocardial infarction. Within 1 month she developed rapidly progressive glomerulonephritis leading to renal failure. The patient was diagnosed with GPA in September 2015.

The histological proof of the diagnosis of GPA was obtained by kidney biopsy. Immunofluorescence of renal biopsy specimens presented negative staining (anti IgA, IgG, C3 and C1q) and all glomeruli were with crescent formation, with characteristics of pauci-immune rapidly progressive glomerulonephritis, positive ANCA where changes of renal function are observed, urinary sediment abnormalities.

When the patient was referred to our department the oral hygiene status was poor, gingival enlargement, gingival bleeding and severe gingival inflammation was observed. During the early phase of disease when there were only nonspecific symptoms, even the patient had previously oral complaint she didn’t seek periodontal opinion, and was referred only to extract teeth’s in mandibular anterior region. The patient did not receive any periodontal treatment previously.

Radiographic examination revealed generalized horizontal/ vertical bone loss on November 2016 (Figure 1) and widespread horizontal/vertical severe bone loss was more pronounced in the mandibular anterior region on January 2018 (Figure 2)). Incisors of mandibular region with terminal alveolar bone loss were extracted. Comparing the radiographic examinations, the severe periodontal destruction or early tooth loss can be observed. In this period of time the patient did not received periodontal treatment.

After including oral hygiene instructions, scaling and root planning using both hand and ultrasonic instruments, the periodontal parameters improved (Figure 3 & Figure 4).

Due to her current diagnosis with GPA, Insufficienta renalis chr grade III, hypertension, Hypothyreosis, Arthritis, her current medications are: immunosuppressant’s, oral corticosteroids, antihypertensive drugs, hypothyroidism drugs.

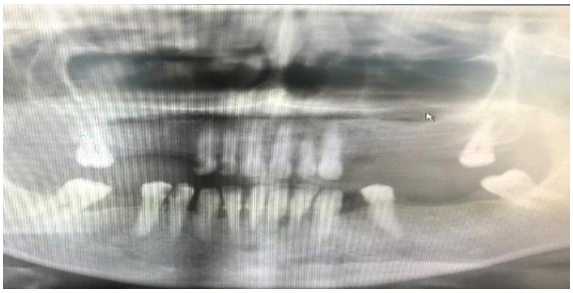

Figure 1. Radiograhy of the patient with GPA demonstrating general horizontal/vertical bone loss. (November 2016).

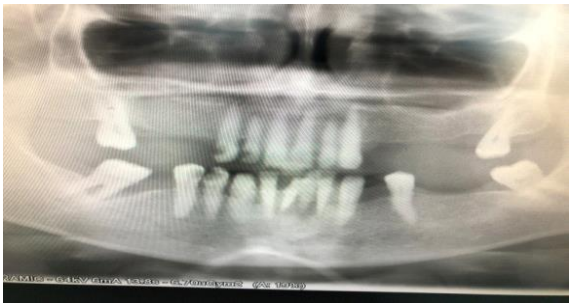

Figure 2. Radiograhy of the patient with GPA demonstrating vertical destrucition of anterior maxillary region and interradicular bone loss in the maxillary first right molar (Januay 2018).

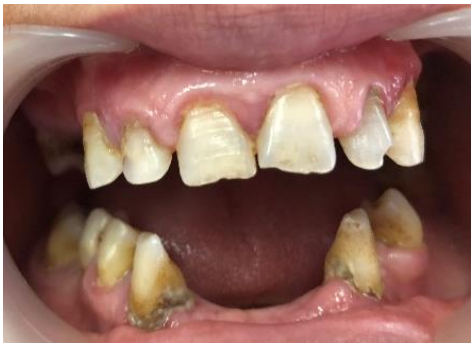

Figure 3. Pretreatment periodontal condition of patient with GPA.

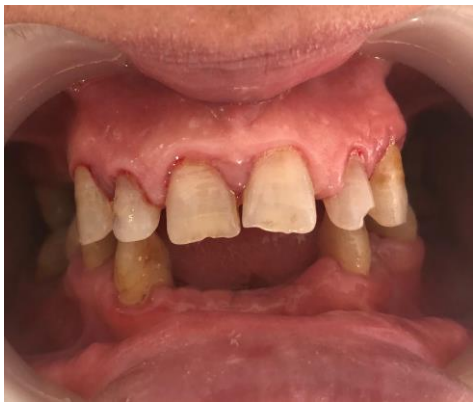

Figure 4. Post treatment periodontal condition of patient with GPA.

Discussion

The diagnostic criteria, as defined by the American College of Rheumatology for the diagnosis of WG requires at least 2 of the following 4 criteria: (1) oral ulcers or nasal manifestation, (2) the presence of nodules, fixed infiltrate, or cavities on a chest radiograph, (3) nephritic urinary sediment (red cell cast or >5 red blood cell per high power field), and (4) granulomatous inflammation on a biopsy (20). Although oral ulceration is one of the criteria required by the ACR in the diagnosis of WG, it usually occurs late in the disease.

Proteinase 3 (PR3) is a multifunctional neutrophil-derived serine protease influencing cell cycle, differentiation, and cell death. This molecule is the main target antigen of autoantibodies in Wegener's granulomatosis (WG) known as antineutrophil cytoplasmic antibodies (PR3-ANCA).[21] Anti-neutrophilic cytoplasmic antibodies with a cytoplasmic staining pattern (c-ANCA) have been found to have a high degree of sensitivity and specificity for Wegener's granulomatosis.[22] But they are not considered diagnostic criteria according to the "The American College of Rheumatology", they have 96% specifity and a 92% sensitivity.[23,24] If the c- ANCA are negative they do not necessarily exclude disease, but they play role once the treatment has been started.

In recent times mortality due to GPA has been significantly reduced by the use of cytotoxic therapy with cyclophosphamide and glucocorticoids.[25,26]

Several systemic diseases exhibit characteristic oral manifestations, which dentists can identify or diagnose. Causes of gingival swelling can be a feature of chronic gingivitis and may be caused by local and systemic causes. The changes in periodontal health of patient with GPA can be improved and it requires periodontal professional care.[27,28]

Conclusions

Health professionals should be familiar with clinical picture of GPA. The diagnosis and therapeutic treatment should be managed by a multi-disciplinary team and multidisciplinary approach involving all specialists, as well as strategies to facilitate prompt disease

recognition and to provide continued oral health care to these medically complex patients. Failure to recognize the diagnostic clinical picture of GPA is unfortunately common and this often leads to serious morbidity or even fatal outcomes.

Conflict of Interest

The authors state that there were no conflicts of interest related to this study.

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