Case Report

Wegener Granulomatosis with Oral Involvement as Primary Manifestation: A Case Study

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Abstract

Introduction: Wegener Granulomatosis is a rare multisystemic disease with an unknown cause, characterized by necrotic granulomatous lesions in respiratory tract, systemic vasculitis in small arteries and veins and necrotizing glomerulonephritis. Wegener can affect any organ including kidneys, eyes or other organs but classically affects upper and lower respiratory tract. One of the rare but important signs of this disease is oral involvement, generally occurring in 6-13% of patients, however, oral involvement as the primary manifestation of disease, occurs in only 5-6% of cases. The most common oral manifestation is strawberry gingivitis. **Patients:** Our patient was a 35 year-old man with gingival bleeding during brushing which began approximately 45 days before referring to the department of oral and maxillofacial diseases, Mashhad Dental School. In intraoral examination, his gingiva had a papillomatous appearance and was purple in color (strawberry appearance). Due to the presence of strawberry appearance in absence of plaque, primary diagnosis of Wegener granulomatosis was established and the patient was referred for histopathological evaluation. In laboratory tests, C-ANCA was positive and P-ANCA was negative. Finally, diagnosis of Wegener granulomatosis was confirmed and his treatment was started. Rheumatologic condition of patient's lungs was evaluated by chest X-ray and CT-scan and blood tests, biochemistry tests and urine analysis were performed for the patient. He did not have pulmonary or renal involvement. In our study, the patient was followed up after 1, 2 and 11 months from the first visit. **Discussion:** Up to now, few reports have been published on Wegener disease with oral involvement and in most of these articles, Wegener was diagnosed after respiratory symptoms and kidney or other organs involvement. Only in few studies was Wegener diagnosis confirmed on the basis of oral symptoms and gingival involvement. Immediate and aggressive administration of immunotherapy treatments are required due to the fatal nature of the disease as the survival rate of patients with untreated WG is low and 90% of these patients die within 1 year after respiratory or kidney involvement .

Keywords: Wegener granulomatosis, oral manifestation, strawberry gingivitis

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Introduction

Wegener Granulomatosis is a rare multisystemic disease (multiple organ involvement) with an unknown cause, characterized by forming necrotic granulomatous lesions in respiratory tract, systemic vasculitis in small arteries and veins and necrotizing glomerulonephritis (1). Wegener disease is very rare. Its worldwide prevalence is approximately 23.7 to 156.5 per million people with annual incidence of 3 to 14.4 per million people (2). Pathogenesis of this disease is unknown but is thought to be caused by an abnormal immune response to environmental antigens or infectious agents (1). Today, Wegener is known as a small-vessel vasculitis associated with ANCA (2).

In some cases, possibility of genetic predisposition was proposed. The average age of onset of the disease is 40-55 years with approximately equal prevalences in men and women (2)]. Wegener can affect any organ but classically affects the upper and lower respiratory tract [3],

That either can be asymptomatic or accompanied by dry cough, hemoptysis, dyspnea and chest pain. Lung involvement is shown in 45% of patients at the beginning of the disease process and 87% during the course of the disease (4). The most common pulmonary symptoms are infiltration (67%) and pulmonary nodules (58%) (4). Another frequent manifestation of this disease is kidney damage at the beginning or during the course of the disease with diverse intensities from asymptomatic involvement to renal acute glomerulonephritis, leading to end-stage renal failure (ESRD), one of the main causes of death in these patients. (4,1). Ocular involvement can occur in various forms such as keratitis, conjunctivitis, scleritis, uveitis, inflammation of the optic nerve and even blindness (8%) (4).

One of the rare but important signs of this disease is oral involvement, occurring generally in 6-13% of patients, however oral involvement as the primary manifestation of the disease, occurs only in 5-6% of cases , the most common manifestation of which is strawberry gingivitis which is a pathognomic symptom of this disease (2). Strawberry gingivitis can be localized or generalized in several quadrants. In Some cases, gingivitis can occur before renal involvement (1).

Gingival involvement can be seen as multiple, small, bulbous and fragile granular hyperplasia and bleeding bumps. These red bumps are responsible for strawberry-like appearance in this disease (1). Commom oral manifestations are written in table 1.

Table 1. Oral symptoms of Wegener Granulomatosis [2]

Oral symptoms	Affected part
Ulcers, delayed healing of dental sockets	Oral mucosa
Gingival enlargement, strawberry gingivitis, erythema, petechiae, hemorrhage, necrosis	Gingiva
Ulcers, necrosis	Tongue
Osteomyelitis, bone loss	Alveolar bone
Ulcers, osteonecrosis, oral-antral fistula	Palate
Tooth loss and mobility	Tooth
Ulcer	Oropharynx
Nodular hyperplasia, swelling and desquamation	Lips

So far, few Wegener cases with oral involvement have been reported and in most of these studies, oral involvement occurred after respiratory symptoms and kidney or other organs involvements (4-10). Only in a few studies, was Wegener diagnosis primarily approved based on oral symptoms and gingival involvement (5 and 11-13). The present case is one in which oral manifestations preceded systemic involvement. In all except one of the cases (7), patients' ages were between 50-70 years, but in the present study, the age of the patient was 35 years, which is considered too young among most of the other reported cases.

Diagnosis of Wegener at an early stage can dramatically increase treatment success and survival rate of patients.

In this paper, a case of Wegener that was primarily diagnosed on the basis of oral manifestations is reported.

Patient

A 35 year-old man with complaint of gingiva bleeding during brushing was referred to the Department of Oral and Maxillofacial diseases, Dental School, Mashhad, by a periodontal specialist in spring 2015. Patient's history revealed that he noticed bleeding gingiva approximately 45 days earlier. For this reason, he stopped brushing since 5-6 days before and used mouthwash; the bleeding was stopped, but started again when he restarted toothbrushing.

On seeing a periodontal specialist, scaling was done for the patient. In review of systems, the patient said that he had a high blood pressure since 5 years earlier and consumed 50 mg Metoral (half in the morning and half in the evening). The patient stated that he suffered from grade 1 fatty liver and kidney stones. In the laboratory tests of the patient (including complete blood count, urinalysis, liver enzymes, lipids, FBS, kidney evaluations and coagulation tests) which was conducted one month earlier, only liver enzymes (ALT and AST) and total and direct bilirubin was higher than normal.

In urine analysis, urea crystals were found only in trace amounts and other parametres were normal.

In extraoral examination, the face, skin and neck were all normal.

Intraoral examination: Papillomatous and purple gingiva (strawberry appearance) was observed in the following regions: buccal gingivae of the maxillary teeth, from the left incisor to the left second molar and right incisor to the second molar (teeth 2 to 15); palatal gingivae of the maxillary teeth, from right lateral to the right canine (teeth 6,7); buccal gingivae of the mandibular teeth, from the left lateral to the first left premolar(teeth 21 to 23) and from the right lateral to the second molar(teeth 26 to 31); lingual gingivae of the mandibular teeth, from the first left premolar to the second left molar(teeth 21 to 18) and from the first right premolar to the second right molar(teeth 28 to 31. (Diagram1)

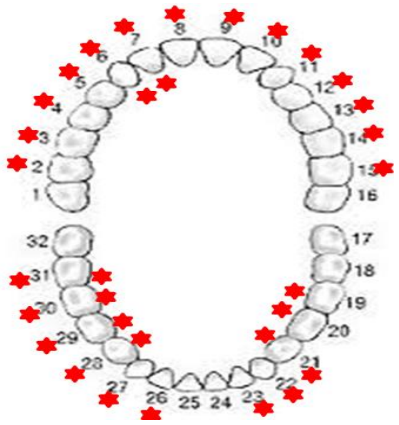

Diagram1. Gingival involvement in our patient (demonstrated by universal numbering system)

In the buccal gingival region of the first right mandibular molars, necrosis was seen (Fig1and 2).

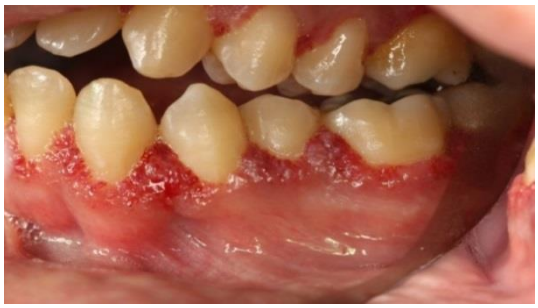

Fig1: Patient's gingivae in the first visit

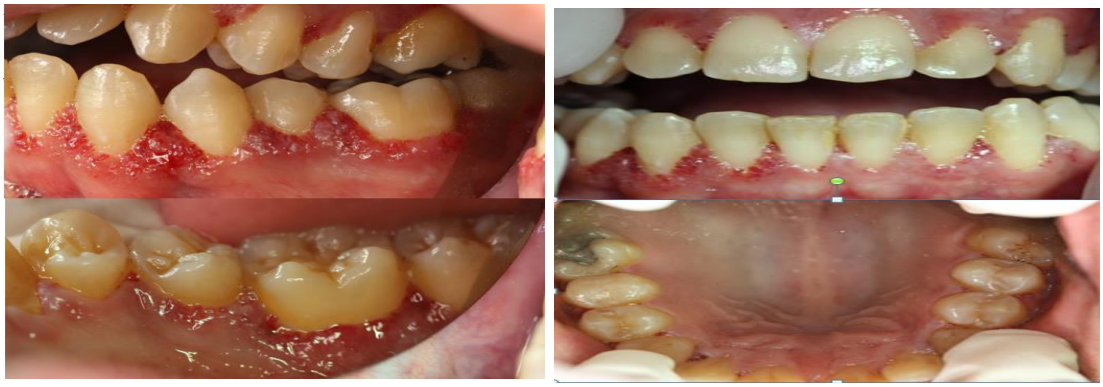

Fig2. Patient's gingivae in the first visit

The consistency of gingivae was soft and could be removed with minimal manipulation. In the panoramic view, no abnormality was found. Because of the strawberry appearance of gingivae and absence of plaque, the patient was referred for histopathological evaluation with primary diagnosis of Wegener granulomatosis.

Differential diagnosis included hyper sensitivity, periodontal and vesiculobullous diseases with no strawberry gingivitis appearance. Furthermore, the patient did not have any ulcer, dental plaque or history of any new substance or drug application.

In histopathologic examination of mucosal sections, the specimens were spongeotic squamous, edematous, chorionic with vascular congestion and severe infiltration of lymphoplasmosites and hystosites and polynuclears of neutrophils and eosinophils (clarify) with slight changes of vasculitis were observed. Geographic necrosis and giant cells were not observed in the submitted sample (Fig 3).

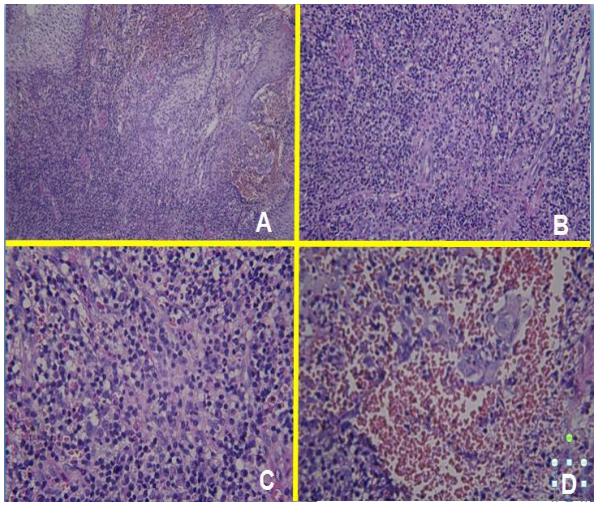

Fig3. Histologic features of gingival biopsy

A-40X, hyperplastic epithelium and chronic inflammatory chorion

B-100X, severely inflamed chorion with lymphoplasmacytic infiltration with abundant blood vessels

C-400X, severely infiltration of chronic inflammatory cells and vasculitis

D-400X, obvious destruction of blood vessels because of infiltration of inflammatory cells due to vasculitis

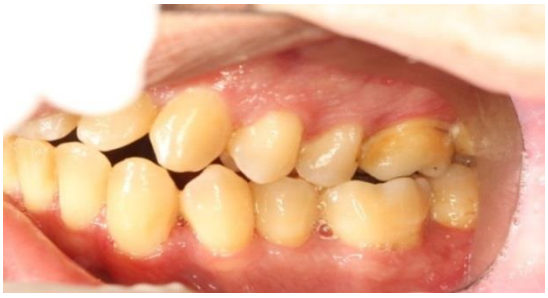

Fig 4. Patient's gingivae in follow-up visit.

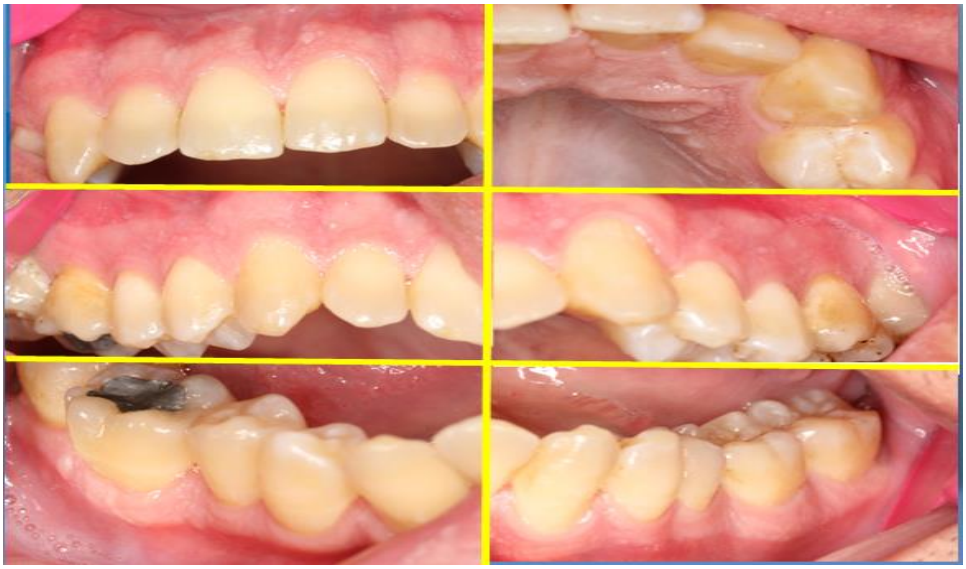

Fig 5. Patient's gingivae in follow-up visit

According to the criteria of American College of Rheumatology for confirmation of Wegener diagnosis, just two of the following four criteria must exist in patients (10 and 14). 1. Ulcerative lesions of the oral mucosa or inflammation and bleeding from the nose, 2. Nodules, fixed infiltration or cavity on chest radiograph, 3. Abnormal urinary sediment (red cell cast or >5 RBC per high power field) (3) and 4. Granulomatous inflammation on biopsy specimens. Items 1 and 4 were positive in the present patient (10 and 14).

In the patient's blood tests, C-ANCA was positive and P-ANCA was negative. C-ANCA sensitivity and specificity was 92 and 96%, respectively [6]. Given that P-ANCA in diseases other than Wegener (including: microscopic polyangitis, Churg-Strauss syndrome, glomerulonephritis and Hodgkin's lymphoma) is also positive [7], and taking into account the specificity of C-ANCA and the results of the biopsy, the patient was diagnosed with Wegener and referred to a rheumatologist for further investigations and treatment.

According to rheumatologist, the patient's lungs condition was evaluated by chest X-ray and CT-scan, and blood tests, biochemistry tests and urine analysis were performed for the patient. He did not have pulmonary or renal involvement. Finally, diagnosis of Wegener granulomatosis was confirmed and his treatment was started.

Oral lesions had full recovery at follow-up visit (28 days after treatment) (Fig 4 and 5).

The patient was followed up after 1, 2 and 11 months from the first visit. Oral lesions were not observed and the gingiva looked healthy (Fig 6). The medical condition of the patient was initially treated with prednisolone and methotrexate. After 5 months, due to lack of systemic symptoms (such as kidney and lung involvement, etc.), methotrexate was interrupted and prednisolone was continued. After 9 months, rash-like lesions on patient's feet (Fig 7), proteinuria and joint pain developed and the patient was hospitalized. In the hospital, the patient received systemic corticosteroid therapy and rituximab. Currently, the patient is under observation of a rheumatologist and no particular oral problem exists.

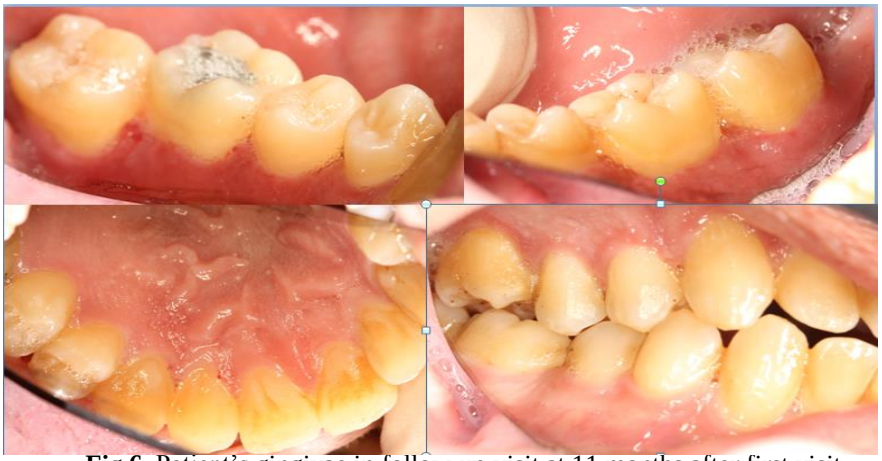

Fig 6. Patient's gingivae in follow-up visit at 11 months after first visit

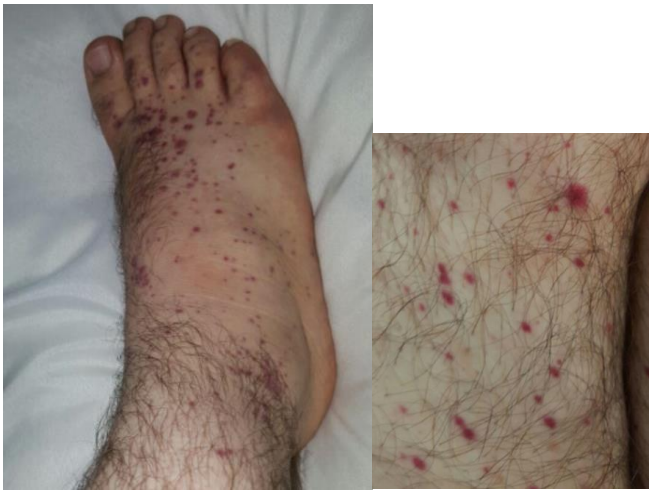

Fig 7. rash-like lesions in patient's feet after 9 months of the first visit

Discussion

Wegener was first recognized in 1933 by Klinger and was later studied more by other researchers, including Rossele (1933), Wegener (1936, 1939) and Ringertz (1948). It is a dangerous and life-threatening vasculitic disorder, which classically involves the upper and lower respiratory tract and the kidneys. Other areas affected include heart, eyes, central nervous system and skin. Involvement of gastrointestinal system, including the mouth, is very rare in this disease and rarely occurs as the first signs of vasculitis. In this study, gingival involvement was the initial manifestation of the disease, which was observed before other organs' symptoms, including the kidneys.

The average time between onset of symptoms and diagnosis is 4.7 to 15 months; however, in this patient, due to on-time referral, the interval between the incidence of bleeding gingiva and diagnosis was about one month and a half. This disease, ifnot treated immediatly, causes death within one year from diagnosis (3). Therefore, early diagnosis and treatment must be considered to prevent serious complications (16). Delays in diagnosis are often due to lack of specific symptoms of this disease (3). However, in the present case, because of visiting the relevant center, the gap between referral and diagnosis of the disease was about 15 days.

Up to now, few reports have been published on Wegener disease with oral involvement and in most of these articles, Wegener was diagnosed after involvement of respiratory symptoms and kidney or other organs and only in few studies (8 articles) was Wegener diagnosis confirmed based on oral symptoms and gingival involvement. In all the studies except two (7 and 15), reports are on patients of 25 to 32 years; the age range in other articles is between 40-70 years. In the current case, the patient's age was 35 years, which is considered quite young for Wegener disease.

Gender differences have not been proven in epidemiological studies on Wegener disease; however, in report of cases published so far (about 17 cases), 10 patients were male and 7 were female which may indicate a slightly higher prevalence of the disease in men.

Immediate and aggressive administration of immunotherapy treatments is required due to the fatal nature of the disease because the survival rate of patients with untreated WG is low and 90% of these patients die within 1 year of having respiratory or kidney diseases [4].

Wegener initial treatment involves a combination of cyclophosphamide and strong-acting corticosteroids taken orally or intravenously. This treatment can bring up to 90% of patients into remission phase and, 75% of patients, with strong acting treatments, may enter the complete remission phase.

The average duration for generating complete remission is 12 months, but in some patients, it may take up to 2 years (4).

Other treatments include administering methotrexate and prednisone to patients with no or mild kidney involvement [4]. One of the new drugs with confirmed positive and beneficial effects is Rituximab, which is considered as a promising treatment option, particularly in patients with refractory Wegener (2).

Currently, the patient is under medical control. It is hoped that the treatment becomes effective.

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