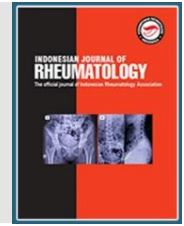




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38 Years Old Man with ANCA Negative Wegener's Granulomatosis Vasculitis with Type 2 Diabetes Mellitus and Electrolyte Imbalance: A Case Report

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ABSTRACT

Background: Wegener's granulomatosis is a very rare long-term systemic disorder, in which granuloma formation occurs and inflammation of blood vessels (vasculitis). The cause of disorder is not yet known, but genetic factors are thought to play an important role. Clinical symptoms are often similar to other disorders, making diagnosis difficult. However, early diagnosis is very important in order to provide effective management.

Objective: Diagnosis and management in a rare case of Wegener's granulomatosis vasculitis, especially it was found with other comorbidities.

Methods: This case report showed a 38-years-old-man that came to the emergency room of Dr Moewardi Hospital with complaints of swelling accompanied by redness and stiff on the face, hands and feet that worsening since 7 days ago. He also complained of fever fluctuating, nasal congestion accompanied by clear discharge and sometimes hearing loss in the right ear. Since the last 3 months, he was often experience similar complaints. History of diabetes was recognized by the patient for 5 years, but he did not regularly take medication. **Results:** In this case, examination of vital signs within normal limits. Physical examination revealed a saddle nose with clear discharge, swelling and redness around the face, hands and feet. Laboratory tests showed hemoglobin 12.9 g/dl, HbA1c 8.4%, sodium level 128 mmol/L, potassium level 3.1 mmol/L, calcium level 1.12 mmol/L. The Anti-Neutrophil Cytoplasmic Antibodies (ANCA) and Anti Nuclear Antibody (ANA) Indirect Immunofluorescence (IF) method were negative. Electrocardiogram and chest x-ray examination within normal limits. Histopathological examination revealed epidermal atrophy and multiple granulomas of the dermis. The patient underwent treatment for 10 days with tapering-off dose steroid, immunosuppressants, insulin, calcium, and potassium preparations therapy. **Conclusions:** Wegener's granulomatosis vasculitis is a rare case. Prompt and accurate diagnosis and management will prevent poor progression of them, especially it was found with other comorbidities.

Introduction

Vasculitis Wegener's Granulomatosis (VWG) is a systemic disorder that is characterized by necrotizing vasculitis of small arteries and veins. It is a rare case with the incidence estimated to be 8–10 cases per one million. This disease can occur at various age levels from children, young adults, to the elderly with a peak incidence at the age of 64–75 years. Cause of the

disorder is not yet known, but genetic factors are thought to play an important role¹. There are several etiologies that can trigger an autoimmune process resulting in this disease, including infection, environmental factors, exposure to chemicals, toxic substances or certain drugs. Clinical symptoms are often similar to other disorders, making diagnosis

difficult. The main symptoms are systemic necrotising vasculitis, necrotising granulomatous inflammation, and necrotising glomerulonephritis².

The diagnosis of GPA is made by history, physical examination, serological tests for anti-neutrophil cytoplasmic antibodies (ANCA) and histological analysis. Although a positive ANCA can immediately make a diagnosis, a negative ANCA cannot immediately rule out a diagnosis of VWG if it is clinically fulfilled³. Therapy choice for WG depends on the severity of the disease or whether the disease is limited or generalized. Currently steroids and cyclophosphamide are still the mainstay of therapy. However, early diagnosis is very important in order to provide effective management⁴.

We had an ANCA negative VWG patient with complications of diabetes mellitus and electrolyte imbalance who was hospitalized for 10 days.

Case

A 38 year old man came to the emergency room of Dr. Moewardi Hospital with complaints of reddish spots accompanied by swelling and stiffness on the face, hands and feet since 7 days before he was admitted to the hospital. Sometimes patients develop subfebrile, which is relieved temporarily with febrifuge. Patients also complain of nasal congestion and clear discharge from the nose that does not

improve, sometimes hearing loss is often reduced in the right ear. Patients often experience a similar complaint in the last 3 months, felt intermittent. The patient had received treatment at the hospital 1 month ago with the same complaint.

Other complaints such as coughing, shortness of breath, sore throat, urination and defecation disorder were denied. History of diabetes was recognized by the patient for 5 years, but he did not regularly take medication. Similar complaints to family members living in the same house were denied.

Examination of vital signs within normal limits. Physical examination revealed a saddle nose with clear discharge, swelling and redness around the face, hands and feet. Laboratory tests showed hemoglobin 12.9 g/dl, HbA1c 8.4%, sodium level 128 mmol/L, potassium level 3.1 mmol/L, calcium level 1.12 mmol/L. The Anti-Neutrophil Cytoplasmic Antibodies (ANCAs) and Anti Nuclear Antibody (ANA) Indirect Immunofluorescence (IF) method were negative. Electrocardiogram and chest x-ray examination within normal limits. Histopathological examination revealed epidermal atrophy and multiple granulomas of the dermis. The patient underwent treatment for 10 days with tapering-off dose steroid, immunosuppressants, insulin, calcium, and potassium preparations therapy.



Figure 1. Localized status in the (A) facial region, (B) palmar region, (C) plantar pedis region and (D) pedis region

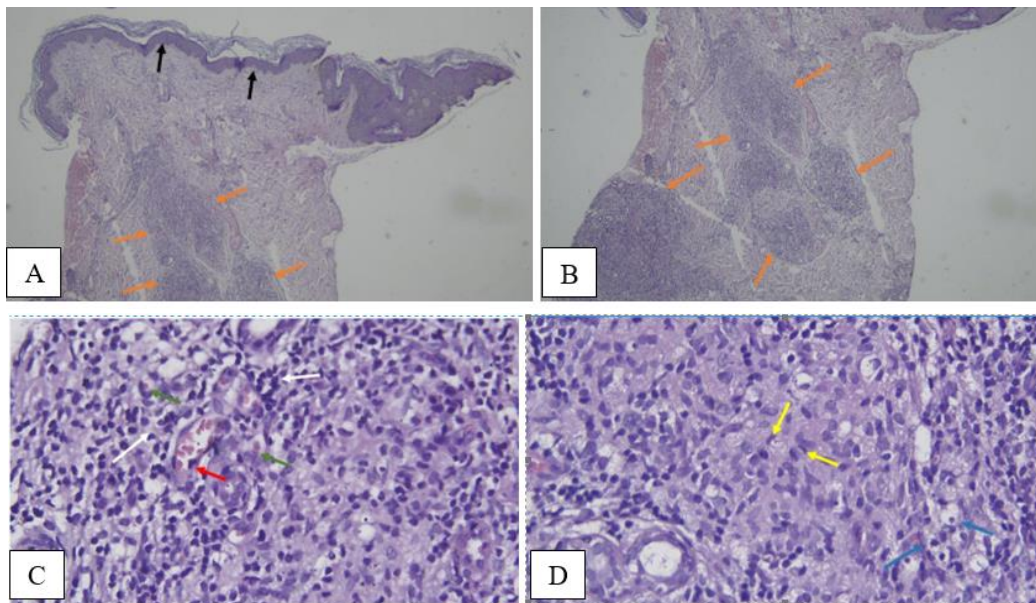


Figure 2. Histopathological features with 4-fold (A, B) and 40-fold magnification (C, D). There is epidermal atrophy (black arrow) (A) and multiple granuloma formation (orange arrow)(B). The blood vessels are damaged (red arrows) with infiltration of perivascular inflammatory cells (white arrows) and extravasation of erythrocytes (green arrows) (C), accompanied by the presence of epitheloid histiocytes (yellow arrows) and foamy macrophages (blue arrows) (D).

Discussion

At first the patient was suspected of having scleroderma, Morbus Hansen type LL, Chug-Strauss disease, or systemic lupus erythematosus (SLE) because of the similar symptoms. However, the symptoms do not fulfill all of these diseases. The

difference between the diagnosis of VWG and MH is the absence of acid-fast bacillus on the Slit Smear examination or on the skin biopsy. In the history of Chug-Strauss disease, there is a history of allergies or respiratory disorders such as asthma, although these symptoms do not fully appear in the disease.

Besides that, the difference between VWG and Chug-Strauss disease is in the biopsy examination which shows a fairly-typical picture, namely a granulomatous picture with involvement of tissue eosinophils together with the presence of peripheral blood eosinophilia⁵. According to the lupus IRA manual, the new EULAR/ ACR criteria can be used if the ANA-IF titer is > 1:80 and there is no other possible cause than SLE. The ANA IF and ANA Profile examinations were negative, which means it could rule out suspicion of an autoimmune process⁶.

The classic symptoms of VWG are necrotizing granulomas of upper and lower respiratory system, systemic vasculitis, and necrotizing glomerulonephritis. Symptoms in the upper respiratory tract, especially symptoms of inflammation of the nose, nasal congestion, pain in the nose, rhinitis, epistaxis, brownish or mixed blood crusting, and septal perforation or septal deviation to form a saddle nose. This is in accordance with the symptoms and signs in the patient. Symptoms can appear simultaneously with the onset of most of the symptoms in the upper respiratory tract¹.

From the laboratory results, it was found that the levels of neutrophils increased by 90% and the number of lymphocytes decreased was 4.30%. Neutrophil to lymphocyte ratio (NLR) has been recently introduced and widely used to predict poor prognosis in several inflammatory diseases. Neutrophils play a role in the initial process of nonspecific systemic inflammation. An increase in the number of neutrophils can occur due to infection or use of glucocorticoids. Medical conditions such as consumption of immunosuppressive drugs can reduce neutrophil levels. Meanwhile, lymphocytes are responsible for the relatively late immune reaction. The lymphocyte count can be affected by general health and stress or various autoimmune diseases. Lymphocyte counts can be decreased in autoimmune inflammatory diseases⁷. The lymphocyte neutrophil ratio may have an important role in the pathogenesis of VWG especially in patients with ocular, cutaneous

and cardiac clinical manifestations. The ratio of neutrophils to lymphocytes together with c-ANCA can diagnose and evaluate VWG and can play a role in tissue specific and clinical characteristics⁸.

ANCA examination can support the diagnosis of VWG, but in 10-20% of cases a negative ANCA is found, as well as in this case. ANCA results reflect disease activity, with negative ANCAs having limited clinical manifestations or mild symptoms, present in more than 40% of cases. This patient's negative ANCA result was probably due to the early onset of the disease, namely three months. VWG patients who present with upper respiratory tract manifestations generally have negative ANCAs, and 83% of cases of negative ANCAs involve severe central nervous system disorders⁵.

The patient has a history of DM since 5 years ago and does not routinely take drugs. The result of HbA1c 8.4% showed poorly controlled diabetes mellitus (DM). A case of VWG in a DM patient has also been found in a 60-year-old man in Tokyo in 1982. It cannot be explained that there is a connection between DM and VWG. However, VWG steroid therapy will worsen blood sugar control in patients with DM⁹.

Conclusion

Wegener's vasculitis is a rare case, it is important to be able to diagnose and immediately initiate therapy to avoid poor progression and also shorten the occurrence of remission. Diagnosis is confirmed by ANCA and cytology, but a negative ANCA result does not exclude treatment if the history, physical examination, and other supports support Vasculitis Wegener's granulomatosis. Corticosteroids is the right, quick, and easy choice therapy, and if needed can be combined with immunosuppressants.

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