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A Patient with Granulomatosus with Polyangiitis (Wegener's Granulomatosis): A Case Report

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A B S T R A C T

Back**ground:** Granulomatosus with Polyangiitis (GPA) is an Anti-neutrophilic Cytoplasmic Antibodies (ANCA) Associated Vasculitis (AAV) which involves small to moderate-sized vessels. GPA has a variety of clinical manifestations caused by tissue ischemia and organ affected. Diagnosis of GPA remains challenging, and its actual incidence may be higher than reported. In 1990, the American College of Rheumatology (ACR) published diagnostic criteria for GPA. Guidelines of management of GPA has improved survival in last decade, but results remain unsatisfactory. Induction agents with immunosuppressive agents and glucocorticoid, and the newer agent Rituximab are recommended as first choice treatment. **Case presentation:** A 64-year-old male presented with current episode of joint pain and a history of recurrent respiratory tract infections. After a series of laboratory and radiologic examinations, lung biopsy was performed, and the result was suggestive of GPA. The patient was managed with induction remission agent and reported improvement in both clinical and laboratory parameters. **Conclusion:** Granulomatosus with Polyangiitis is a limitedly reported case. This report was presented to raise awareness of the diagnosis when faced with similar clinical symptoms. Early detection and diagnosis in GPA allow for prompt and better management with the target to achieve and maintain remission, as demonstrated in this case.

1. Introduction

Granulomatosus with Polyangiitis (GPA), previously termed Wegener's Granulomatosis, is a form of vasculitis that affects small to moderate-sized vessels. Chapel Hill Consensus Conference (CHCC) in 2012 classified GPA as an Anti-neutrophil Cytoplasmic Antibody (ANCA)-associated vasculitis (AAV).[1] In the United States, incidence of GPA was reported in about 3 per 100,000 population and could vary globally due to demographic factors.[2] Data on GPA in Indonesia are scarce. The pathogenesis of GPA is not clear and is thought to be multifactorial. The broad and unspecific clinical manifestations and disease course of GPA often pose challenges in making prompt diagnosis and implementing appropriate management. The classical triad of respiratory tract infections, suggestive alveolar hemorrhage, and glomerulonephritis could be symptoms suggestive of GPA, which are the result of tissue ischemia.[3,4] Recent medical research in GPA has improved the mortality rate and prolonged survival. An induction phase followed by maintenance phase have been proposed as a standard therapy in GPA.[5] However, due to the chronic nature of the disease, occurrence of relapses and therapy-related adverse side effects, GPA is difficult to manage and therefore, improving its awareness is essential. We report a case of a 64-year-old male with GPA who encountered difficulties in diagnosis and responded well to immunosuppressive therapy.

2. Case Presentation

A 64-year-old man came to Prof. Dr. I G N G Ngoerah General Hospital Bali in July 2021 with a chief complaint of joint pain with petechiae involving the limbs and trunk which had worsened over the past 2 weeks. The patient had experienced this complaint intermittently since one year ago. Additionally, the patient also had a history of recurrent episodes of lower respiratory tract infections since 1 year ago, with fever, hemoptysis, and non-cardiac chest pain, along with noted unintended weight loss of about 10 kg. The patient had one episode of cerebral infarction 6 months prior, which was complicated by blurry vision.

The patient had history of type 2 diabetes mellitus since 2018 which was well controlled with insulin glargine 6 units QD. He also had a history of surgery for mitral valve replacement in 2018 and was currently on oral warfarin.

Upon physical examination, vital signs were within normal limit, and a visual analog score of 1/10 in the joints. We found no saddle nose deformity and no remarkable signs from ear, nose, throat, and abdomen examination. Ronchi was found in both sides of the lower lungs. Petechiae were found in the trunk and upper and lower limbs.

Laboratory examination revealed leukocyte count of 13.87 x 10^3/µL, neutrophil count of 12.29 x 10^3/µL, lymphocyte count of 1.01 x 10^3/µL, hemoglobin level of 11.6 g/dL, hematocrit of 34.9%, dan thrombocyte count of 314 x 10^3/µL. Blood chemistry showed the following results: albumin 2.65 g/dL, random blood glucose 268 mg/dL, LDH 553 U/L, BUN 19.7 mg/dL, creatinine 0.70 mg/dL, e-LFG 99.73, uric acid 3.63 mg/dL, sodium 128 mmol/L, potassium 4.2 mmol/L. APTT 37.5 s, PT 24.6 s dan INR 2.33, procalcitonin 0.11 ng/mL, HbA1C 7.4%, total cholesterol 142 mg/dL, LDL 100 mg/dL, HDL 33 mg/dL, Triglyceride 67.6 mg/dL. C Reactive protein (CRP) was elevated at 141.59 mg/dL

On admission, chest X Ray (Figure 1) suggested aortosclerois, with nodule and reticulonodular pattern in the lung, as well as right pleural effusion. Recent Computed Tomography (CT) scan of the chest showed subpleural nodule at the right lung measuring 6.9x10.5 mm, with ground glass opacity and a 12 mm cavity nodule posterolateral pleura in the left lung.

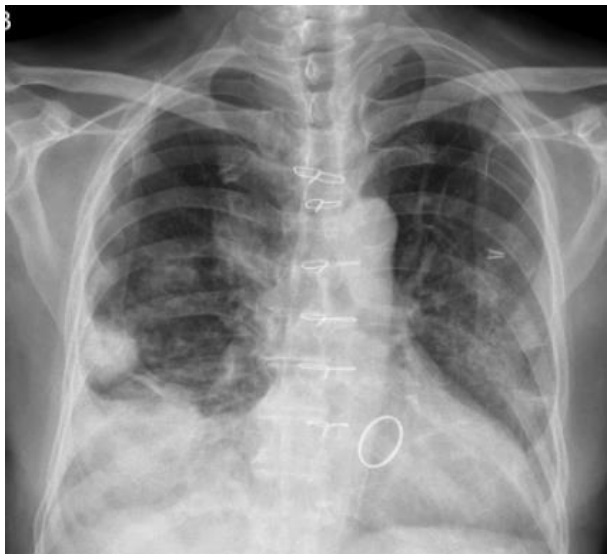

Figure 1. Chest X ray of the patient.

The patient was previously tested negative for tuberculosis (IGRA test, AFB culture), and no growth of gram culture and fungal infection was found. Patient was tested positive for p-ANCA, and lung (Figure 2). Patient was previously treated with biopsy of the left upper lobe wedge resection found necrosis with thrombosis and chronic pulmonary hemorrhage, with pathological conclusion of Granulomatosus with Polyangiitis

dexamethasone 4 mg TID.

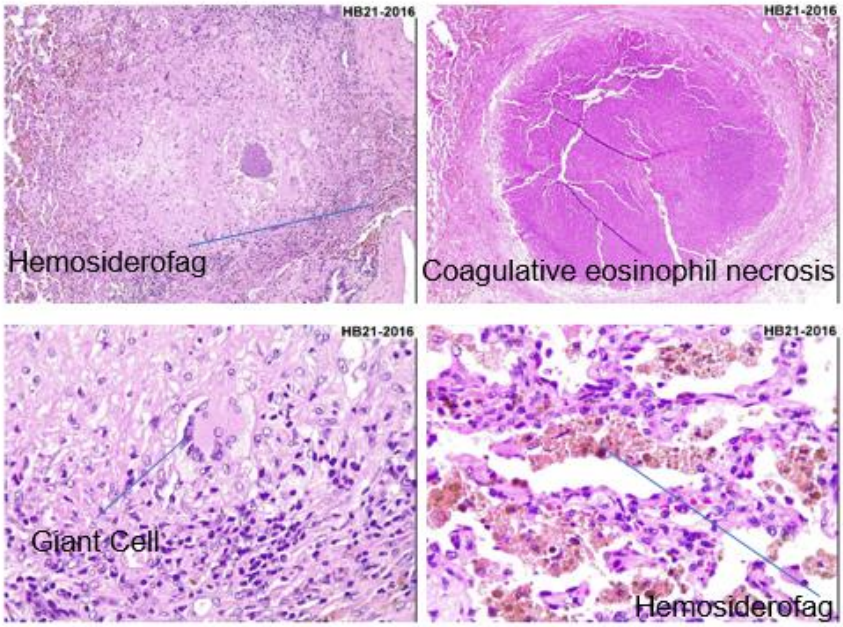

Figure 2. Histopathology of the lung. Wedge resection left upper lobe.

The GPA activity was assessed as active (worsening clinical signs) and severe (presence of alveolar hemorrhage). Induction therapy was decided, and regimen was chosen with a combination of methylprednisolone 500 mg intravenous pulse dose for 3 days followed by rituximab 1000 mg intravenous on day 1 and 15. Patient showed improvement in clinical symptoms with resolution of joint pain and decrease in CRP levels (51,69 mg/dL). Subsequently, the patient was planned to receive rituximab for maintenance and oral methylprednisolone.

3. Discussion

GPA (previously termed Wegener's Granulomatosis) is a vasculitis syndrome characterized by inflammation and damage to blood vessels. The narrowing of the blood vessels causes tissue ischemia and clinical manifestations depending on the organs involved. Under the Chapel Hill Consensus Conference 2012, GPA was classified as small vessel vasculitis (SVV) with necrotizing granulomatosis that often involve upper and lower respiratory tract infections and necrotizing gromerulonephritis.[1] Although clear pathogenesis of GPA is not well understood, triggering factors may include environment, genetic, and pathogens such as *S. aureus*.[5,6] There are two phenotypes of commonly reported GPA manifestations. The first type is more commonly found in young adult women and involves the ear-nose-throat. The second type manifests more diffusely in organs such as kidneys and alveolar of lungs.[6] Various organs are involved in GPA: upper respiratory tract might show signs of rhinorrhea, sinusitis, chronic otitis media, and destruction of nasal cartilage and septum (saddle nose deformity); pulmonary manifestations range from asymptomatic nodules to chronic persistent cough with or without bloody discharge and alveolar hemorrhage with symptoms depending on the severity; kidney involvement in the form of glomerulonephritis with proteinuria, hematuria, and could rapidly progress to kidney failure; episcleritis, scleritis, corneal ulcer, mucocutaneous lesion and purpura of lower limbs, valvular heart disease, pericarditis, reduced ejection fraction of left ventricle, and cerebral infarction had also been documented previously.[6,9,10,11,12] According to the 1990 ACR criteria, GPA should meet at least two of the following criteria: 1) nasal or oral inflammation,

2) abnormal chest radiograph, 3) urinary sediment, 4) granulomatosus inflammation within wall of artery or in perivascular or extravascular area on biopsy, 5) positive antibodies to PR-3 (added to modified criteria).[7,8] Histopathology of GPA should show necrotic granulomatosus from tissue biopsy with supporting clinical signs and symptoms.

Management of GPA was divided into induction-remission phase and maintenance phase. Selection of the induction agent depends on the severity and activity of the disease. Patient should be assessed with the Birmingham Vasculitis Activity Score for GPA (BVAS/GPA) and Vasculitis Damage Index (VDI) to decide the management plan and prognosis.[5,13] For active severe GPA, rituximab and gluccocorticoid are recommended as induction-remission agents, followed by maintenance with rituximab, either methotrexate or azatioprine, and either mycophenolate mofetil (MMF) or leflunomide (LEF). Recommended rituximab dose is 375 mg/m^2 every week for 4 weeks or 1000 mg on day 1 and 15, both of which have shown similar efficacy.[14,15,16]

4. Conclusion

We report a case of a 64-year-old male diagnosed with granulomatosis with polyangiitis (GPA). Clinical symptoms of recurrent sterile respiratory tract infections prompted an invasive diagnostic approach with wedge resection and biopsy of the lung lobe, concluding the diagnosis of GPA. The patient was given induction-remission agent with rituximab and glucocorticoid, resulting in a positive response. Improvement in clinical symptoms and laboratory values were observed. Reported case of GPA in Indonesia is limited and this report aims to add value of clinical experience and knowledge, raising awareness of GPA and allowing for appropriate management of the disease.

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