

## An Unusual Presentation of Granulomatosis with Polyangiitis

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### ABSTRACT

The granulomatosis with polyangiitis (GPA), formerly known as Wegener's granulomatosis, is a pauci-immune vasculitis involving small- and medium-sized blood vessels. Classically, the patients inflicted with this disease present with a triad of necrotizing granulomatous inflammation of the respiratory tract, cutaneous necrotizing vasculitis, and glomerulonephritis (GN). The antinuclear (ANA) and anti-neutrophil cytoplasmic antibodies (ANCA) are considered as relatively specific markers of the disease. Herein, we presented the case of a patient who initially presented with sepsis but did not respond to the conventional antibiotics and later diagnosed with GPA.

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## Introduction

The granulomatosis with polyangiitis (GPA) is a systemic vasculitis, which is characterized by destructive granulomatous lesions in the upper and lower respiratory tract and necrotizing crescentic GN. All the small- and medium-sized vessels can be affected; consequently, many potential clinical manifestations may be presented (1).

It is believed that the disease begins as a localized respiratory tract granulomatosis, which then generalizes into a vasculitis that affects small and medium-sized vessels (2).

Patient presentation varies and depends on the organ system affected. Some patients present with chronic nasal obstruction, which may be misdiagnosed as chronic sinusitis; others may present with overt acute renal or respiratory failure. Patients with pulmonary involvement often complain of cough with or without Hemoptysis, dyspnea, fever, and chest pain (2).

We present a case which initially presented as non resolving pneumonia with sepsis and later diagnosed as GPA with preserved renal function.

## Case presentation

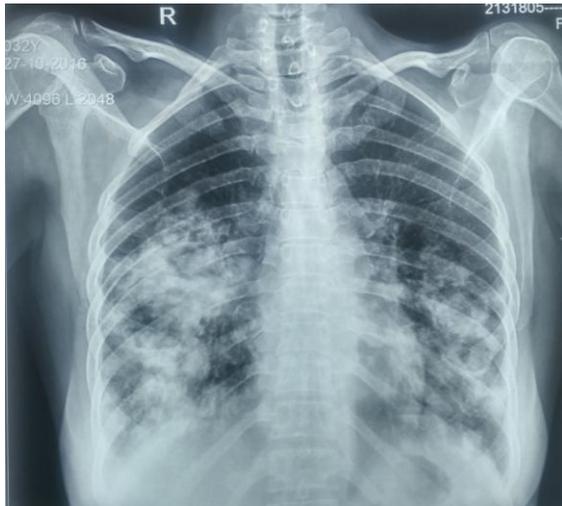
A 35-year-old female with no history of chronic diseases was referred to our institute with the complaints of generalized weakness, fever, and dyspnea having been occurred 30, 15, and 5 days before admission, respectively. Additionally, while taking the history, she complained of an ulcer on her right breast emerging from 15 days ago.

The vital signs of the patient were reported, rendering a pulse rate (PR) of about 130 bpm, blood pressure (BP) of almost 110 over 80 mmHg, and oxygen saturation level (SpO<sub>2</sub>) of 94% during the inhalation of room air. A 5×5 cm dry ulcer was

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**Figure 1.** Chest X ray of patient showing bilateral nodular opacities

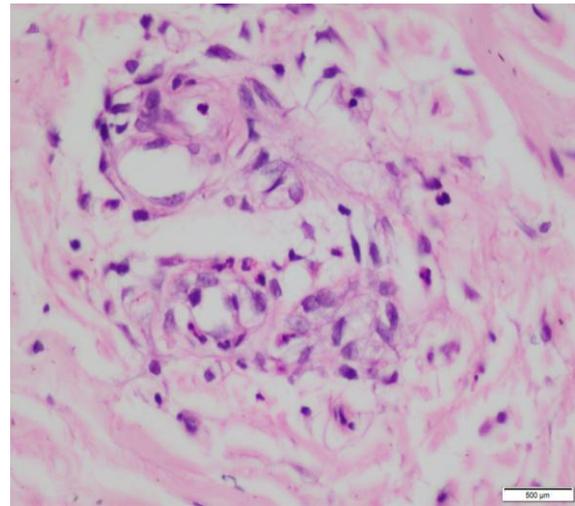
found on the lower inner quadrant of her right breast. Systemic examination was normal except for the presence of bilateral basal crepitations of the lungs.

The biochemical markers revealed a high white blood cell (WBC) of 30,000, normal renal function, and slightly deranged hepatic profile. Furthermore, the evaluation of the viral markers indicated that she was positive for hepatitis C virus (HCV). Chest X-ray (CXR) revealed multiple nodular opacities, predominantly in the middle and lower zones (Figure 1). The computed tomography (CT-scan) of thorax also demonstrated multiple nodules with various sizes with cavitation and areas of consolidation (Figure 2).

No acid-fast bacilli were found in the tested sputum smear. The gram staining and culture of the sputum revealed coagulase-negative *staphylococcus aureus*. Although she was prescribed with the appropriate antibiotic based on the sensitivity testing, considering the clinical suspicion of septic emboli, she was still febrile. Therefore, she was re-evaluated to check for any missed findings. The serum samples were negative



**Figure 2.** Computed Tomogram of patient showing nodular opacities of varying sizes in both lobes a few of which cavitate



**Figure 3.** H&E: 400X: Small vessel vasculitis seen in dermis. The vessel wall is infiltrated by neutrophils and few eosinophils

for *dengue* virus and *scrub typhus* antibodies. In addition, the malaria rapid diagnostic test indicated no infection by *Plasmodium vivax* and *falciparum*. Albuminuria and microscopic hematuria were evident on urinalysis. Three hyperpigmented maculopapular dermal lesions were found on the dorsum of the right foot.

Several biopsies were obtained from these lesions, which demonstrated an epidermal necrosis due to the small vessels vasculitis (Figure 3). Additionally, ANA and ANCA were evaluated in the serum samples. According to these laboratory tests, the samples had a positive test for C-ANCA, and ANCA specific for proteinase 3 (PR3-ANCA) was found to be over 100 U/ml. The examination of the nose and the results of biopsies obtained from the nasal crusts revealed no abnormal findings. As a result, she was diagnosed as a case of Wegner's granulomatosis.

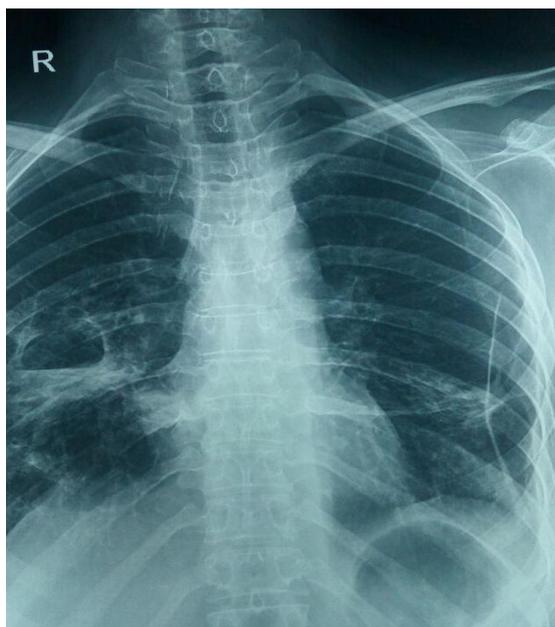
The pulse steroid therapy was not started for this patient due to leukocytosis and positive HCV. She was prescribed to consume prednisolone (0.75 mg/kg) daily through oral administration. This therapy was successful, and the patient became afebrile on the third day. Accordingly, by the end of the 15th day, the inflammation of the breast subsided completely.

Then, she was prescribed to simultaneously use mycophenolate mofetil and steroid (administered orally). After two more weeks, the patient developed a left-sided pneumothorax. Therefore, a chest tube drain was inserted, which was removed after complete pulmonary expansion and the elimination of the fistula.

This patient is still under follow-up with acceptable clinical and radiological responses as demonstrated in Figure 4.

## Discussion

The American College of Rheumatology has



**Figure 4.** Follow up chest x ray of patient showing resolution of lesions .left sided pneumothorax is also seen

suggested the diagnostic criteria for GPA, including oral or nasal ulcers or purulent bloody flux, CXR findings (e.g., pulmonary nodules or cavitation), abnormal urinary sediment, and extravascular granulomas (3). The presence of two or more of these items has a sensitivity of 88% and a specificity of 99% in the diagnosis of GPA (1, 3). Our patient met the criteria for two items, namely, abnormal findings on CXR and vasculitis due to skin biopsy.

In a study, out of all GPA cases, about 70-90%, 25-30%, 70-80%, and 80-90% of the patients experienced the sinus and nasal, pleural, and renal involvement, as well as pulmonary lesions throughout the course of the disease, respectively (4). Several studies demonstrated that dermal manifestations might appear in 16 to 77% of the cases (5). Papulonecrotic tuberculid is the most common lesion, which emerge mainly in the lower limbs (5).

Pathologically, GPA is characterized by necrotizing granulomatous inflammation of small- and medium-sized vessels, leading to the necrosis in the wall of the vessels (4). The GPA may inflict the patients at any age, but occurs most often at the age of 40 to 55 years old. The prevalence of the disease is the same for both males and females (4).

The C-ANCA was detected in the blood samples of more than 90% of the GPA patients (6). The PR3-ANCA is implicated in GPA; therefore, it should be specified in the diagnosis of this disease (7). This antibody was detected in blood samples of 85% and 30 to 40% of the patients with active disease and in the remission time, respectively (6, 7). In our case, the levels of

C- and PR3-ANCA were highly elevated.

The GPA is a necrotizing vasculitis with variable presentations in the mediastina, which are best depicted on high resolution CT-scan. CXR findings might include nodules, thin or thick-walled cavitation, ground-glass opacity secondary to the diffused alveolar hemorrhage, tracheobronchial stenosis, the halo sign in CT-scan (ground-glass opacity surrounding a pulmonary nodule or mass and represents hemorrhage), or reverse halo sign (also known as atoll sign) (8). Our patient had multiple bilateral nodules with few pulmonary cavities. Active Wegener's granulomatosis can mimic numerous of the diseases such as pneumonia, septic emboli, and metastasis (9).

The GPA is a rare disease with varied clinical presentations; therefore, the initial diagnosis is often delayed and only thought of when the conventional therapies failed. In our case, the patient presented with cutaneous lesions and pulmonary nodules. She did not have any nasal symptoms and her renal function was normal; accordingly, it was difficult to diagnose GPA at the onset. She was treated in the lines of septic emboli. It was only suspected when she did not respond to the therapies.

More than 90% of the GPA patients, treated with glucocorticoids and daily cyclophosphamide (CYC), experience a complete remission or significant bettering (10). However, in the clinical trials in which CYC therapy was continued for at least one year after remission, the disease recurrence eventually occurred in 50% of the patients (11).

Although the treatment with the repeated courses of CYC is very effective, adverse effects of this medicine including infertility, myeloproliferative disorders, and transitional cell carcinoma of the bladder were observed in several patients (11).

Recently, mycophenolate mofetil, which is an immunosuppressive agent, was considered as an appropriate alternative for the treatment of autoimmune diseases in general and particularly the GPA (12).

Our patient was prescribed mycophenolate mofetil (MMF) with the dose of 500 mg daily with steroids. She is still under our follow up till writing of this report and was going well.

## Conclusion

GPA can present in various clinicoradiological manifestations. It should always be kept in the differentials of non resolving pneumonia if patient is not responding to conventional antibiotics. If left untreated, it can be fatal too.

## Conflict of Interest

The authors declare no conflict of interest.

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