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Case Presentation

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Granulomatosis Polyangiitis Mimicking Lung Cancer: A Case Report

Song-Jun Shao[1,3], Yu Tan[1], Shan-Shan Rao[1-3*], Xiang-ning Zhang[5*]and Yong-Shun Lin[4]

[1]Department of Respiratory and Critical Medicine, Guizhou Provincial People's, Hospital, China

[2]Academic Department, Guizhou Institute of Respiratory Diseases, China

[3]NHC Key Laboratory of Pulmonary Immune-related Diseases

[4]Department of Pathology, Guizhou Provincial People's Hospital, China

[5]Department of Pathophysiology, Guangdong Medical University, China

[*]**Corresponding author**: Shanshan Rao, Department of Respiratory and Critical Medicine, Guizhou Provincial People's Hospital, No 83, Zhogshan East Road, Guiyang, Guizhou 550002, People' Republic of China, E-mail: raoshan3@126.com

Xiang-ning Zhang, Department of Pathophysiology, Guangdong Medical University, Songshan Lake Science Park, Dongguan, Guangdong 523808, People' Republic of China, E-mail: zhangxn_06@126.com

Abstract

Background: Granulomatosis polyangiitis (GPA) is a rare and unknown etiology interstitial lung disease. It is formerly known as Wegener's granuloma. The imaging appearance is similar to tumor, so it is easy to misdiagnose tumor. This paper reports a case of GPA successfully diagnosed and treated in our department.

Case description: We present a case of GPA misdiagnosed lung cancer in a 31-year-old man patient. He went to see a doctor in local hospital because of "Intermittent chest pain accompanied by headache for 1 month". Chest computerized tomography (CT) examination results indicated "lung cancer accompanied by metastasis?" local doctor recommended hospitalization for definite diagnosis. But the patient refused to local hospitalization, he admitted to our hospital in next day. After a series of auxiliary examination, the results showed no abnormalities. Then we invited multi-disciplinary to discuss (MDD) the diagnosis and treatment plan for the patient. MDD members began to wonder whether it was a tumor or an immune system disease? So we checked the serum antinuclear antibodies and antineutrophil cytoplasmic antibody at last, the cANCA (+), anti-PR3 (++), residual antibody negative. The second lung biopsy pathological results showed chronic inflammation of lung tissue with significant proliferation of local fibrous tissue, focal aggregation of neutrophils could be seen in fibrous tissue, small vascular inflammatory changes were considered, and focal fibrinoid necrosis and focal atypical granuloma formation were observed. Final diagnosis was GPA. Because mycobacterium tuberculosis infection couldn't be ruled out, therefore we didn't treatment with plenty of prednisone acetate and cyclophosphamide. However, the patient's clinical symptoms were relieved; chest CT re-examination indicated

that the nodules and the mass in the lung were not decreased after therapies one month. Then we invited MDD to discuss the treatment plan again. And prednisone acetate was adjusted to 60 mg by mouth daily; cyclophosphamide was adjusted to 600 mg by intravenous infusion every half-month. Chest CT re-examined after treatment 2 months, the results showed that the changes of lung nodules and mass were absorbed than before.

Conclusions: GPA is a rare interstitial lung disease with high mortality and chest CT appearance similar to tumor, which is extremely difficult to identify and often misdiagnose. Correct diagnosis and time to therapy are particularly important.

Keywords: Case report; Granulomatosis polyangiitis; Lung cancer; Classification standard; Therapy

Introduction

In recent years, the incidence and mortality of lung cancer are increasing year by year, and the patients are getting younger, it is concerned by most people **[1].** GPA is a rare and unknown etiology Interstitial Lung Disease (ILD), which is also known as Wegener's granuloma **[2].** However, CT imaging of GPA is untypical, which is mimicking lung cancer or other diseases, so imaging examination alone is often easy to misdiagnose **[3]**.We reported a 31-year-old male patient who was misdiagnosed lung cancer in local hospital, until definitively diagnosed with GPA in our department in the end. Because the clinical symptoms improved significantly after treatment with prednisone acetate combined with cyclophosphamide timely, but the CT scan indicated that the lung nodules and mass were not decreased. So multi-disciplinary discussion was invited to adjust the treatment plan. When the patient was received new plan treatment2 months, re-examined chest CT indicated that lung nodules and mass partial absorbed. The patient is still returning to the hospital regularly for therapy and follow-up. Hence, patients' clinical characteristics, epidemiology, diagnostic methods, clinical treatment course and outcomes were collected and analyzed, in order to provide a reference for the clinical diagnosis and treatment of GPA, and enhancing clinicians' understanding of GPA.

Case Presentation

Chief complaints

A 31-year-old man was admitted to our department with intermittent chest pain accompanied by headache for one month.

History of present illness

One month ago, the patient had headache and the left chest pain without obvious inducement, which was obvious when standing up and inhaling, but relieved by breath-holding and supine rest. However, twenty days ago, he started to cough and expectoration, with a little white phlegm, accompanied by general fatigue. Without treatment, there was gradual aggravation of his symptoms.

History of past illness

The patient had no history of tumor, tuberculosis, or other disorders.

Personal and family history

The patient had no relevant personal and family history.

Physical examination

On admission, his vital signs are stable. The heart, lung, abdomen, skin examinations were no special.

Laboratory examinations

Laboratory examination results were as follows: serum respiratory tumor markers, T-SPOT and PPD test all negative, blood Cryptococcus capsular polysaccharide antigen test negative, the result of Next-Generation Sequencing (NGS) of alveolar lavage fluid test negative. Blood gas analysis test was normal. Blood sedimentation rate: 89 mm/h. Serum antinuclear antibodies and antineutrophil cytoplasmic antibody results showed cANCA (1:10) positive (+), anti-PR3 positive (++), antinuclear antibody negative (-).

Imaging examinations

Brain CT showed bilateral maxillary sinus and ethmoid sinus mucosa thickening and right mastoid inflammation. Enhanced chest CT scan at admission showed nodules and mass in the upper lobe of right lung accompanied by lung metastases and mediastinal lymph node enlargement, low to moderate enhancement in the center of the nodules and obvious enhancement at the edges **(Figure 1).**

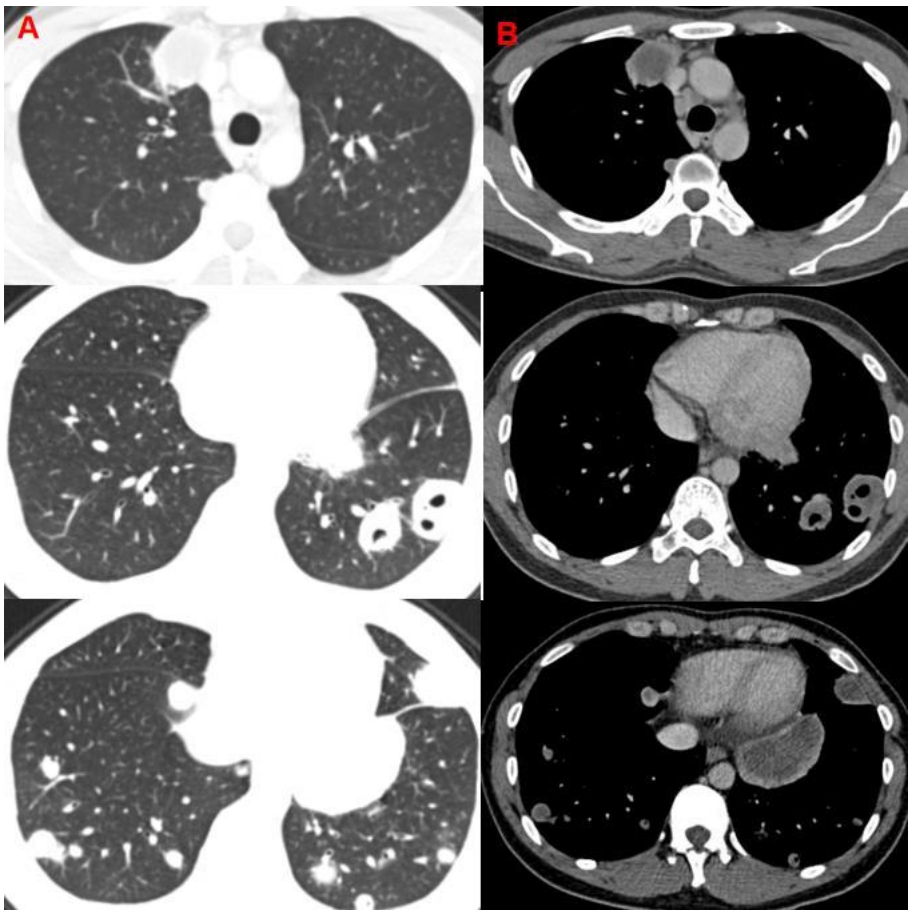

Figure 1: Enhanced chest CT scan displayed variously sized masses with voids in both lungs on 14th January 2022. A) Pulmonary window. B) Mediastinal window.

Pathological examinations

Bronchoscopy and percutaneous lung biopsy pathological finding revealed chronic inflammation of lung tissues with significant proliferation of local fibrous tissues, focal aggregation of neutrophils could be seen in fibrous tissues, small vascular inflammatory changes were considered, focal fibrinoid necrosis and focal atypical granuloma formation were observed **(Figure 2).**

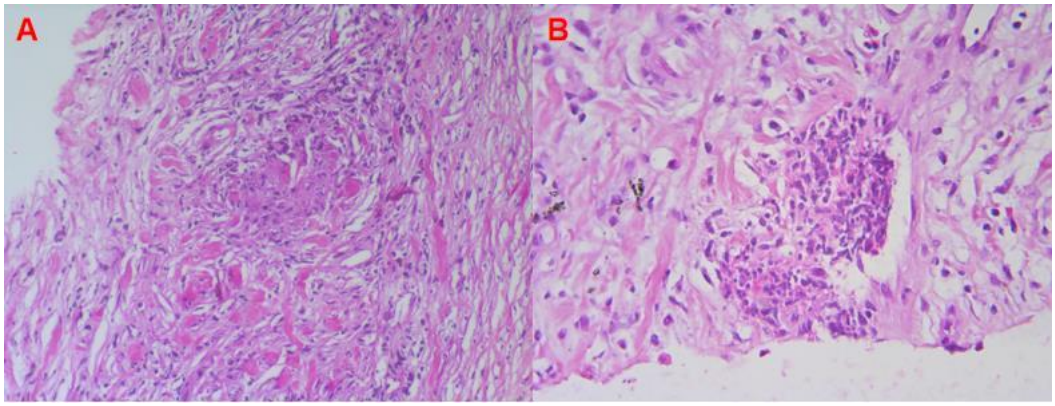

Figure 2: Lung biopsy pathological results (HE staining ×100): Hyperplasia of fibrous tissue, focal aggregation of neutrophils and inflammatory changes of small blood vessels were observed. Focal atypical granuloma formation. A) The first time of lung biopsy on right upper lobe. B. The second time of lung biopsy on left lower lobe.

Final diagnosis

We combined with the history, clinical symptoms, laboratory examinations, chest CT and pathological results, and based on the American College of Rheumatology in 1990 **[4]** and **[5]** (ACR/EULAR) of Granulomatous polyvasculitis (GPA) in 2017, and finally diagnosed granulomatous polyvasculitis.

Treatment

On the day after admission, the patient was given symptomatic treatment such as relieving cough and resolving phlegm. After the diagnosis of GPA, according to the latest American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Antineutrophil Cytoplasmic Antibody-Associated Vasculitis in 2021 **[6],** we administered 30 mg/d prednisone acetate tablet orally and 500 mg cyclophosphamide is given intravenously at the first, and received approximately 500 mg of cyclophosphamide treatment on twice a month.

Outcome and follow-up

The patient was discharged with the clinical symptoms improved significantly. Three month later, the patient was stable condition still and alive with adequate quality of life. Compared to the first CT results, the follow-up chest CT showed: 1. Multiple space-occupying lesions in both lungs were significantly smaller than before (the larger lesions in the upper lobe of the right lung were significantly smaller). 2. Mediastinum and hilar lymph nodes were smaller than before **(Figure 3).** Up to now, he has been treated and followed-up to date.

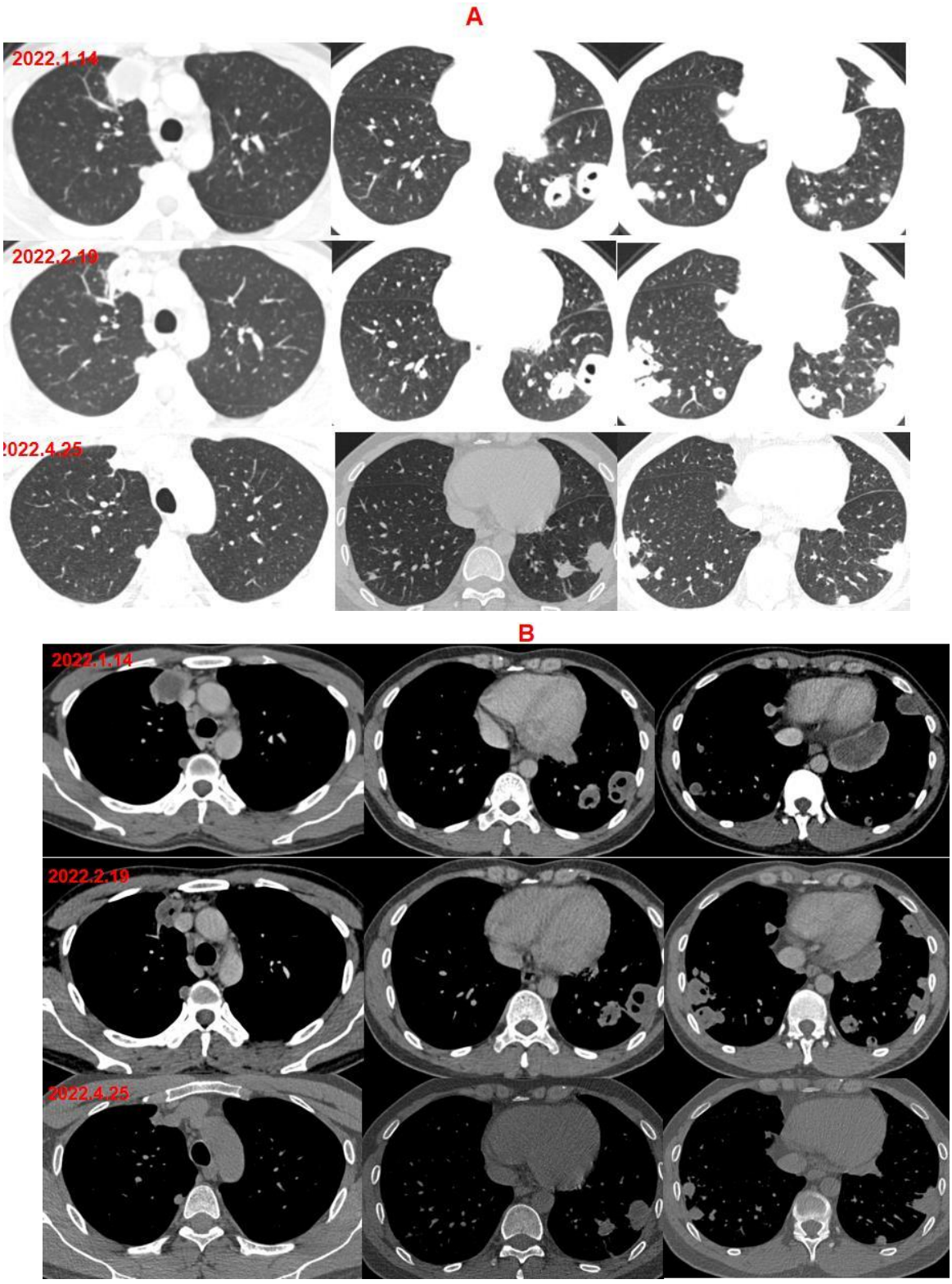

Figure 3: Comparison of chest CT before and after 3 months of treatment. A) Pulmonary window. B) Mediastinal window.

Discussion

GPA is known as Wegener's granuloma formerly which is a rare and unknown etiology necrotizing granulomatous vasculitis, it mainly affects the upper and lower respiratory tract and kidney. Lesions involving arterioles, venules, capillaries, occasionally involving large arteries. Pathology is characterized by necrotizing granulomatous inflammation of the vascular wall. It usually begins with focal granulomatous inflammation of nasal mucosa and lung tissues and progresses to diffuse necrotizing granulomatous inflammation of blood vessels. Anti-Neutrophil Cytoplasmic Antibodies (ANCA) contains GPA, Microscopic Polyangiitis (MPA), Eosinophilic Granulomatosis Polyangiitis (EGPA) **[7].** ANCA incidence is about 20/100000 in Europe and North America. It is predominantly male and can occur at any age, with a high incidence between 40-50 years of age, of which GPA is the most common. In the European population, 24-157/100000 is affected, without sex difference, and the age of onset is 45-65 years, with the highest incidence in Sweden and the United Kingdom, where the median survival after GPA diagnosis is 0-4 months before alkanating **[8].** The histological feature of GPA is involvement of small and medium vessels, beginning with granuloma formation of neutrophils **[8].** 75% of GPA patients were positive for C-ANCA and anti-protease 3-ANCA (PR3-ANCA), while 60% of MPA patients were mainly positive for anti-myeloperoxidase-ANCA (MPO-ANCA) **[9].** GPA patients, their first clinical manifestation are mainly in the lung and kidney **[10,11]** 25-80% of cases will involve the lung, and lung manifestations include cough, hemoptysis, dyspnea, pleurisy chest pain, etc. At 15-20% of cases also have pleural effusion **[11,12].** At 40-70% of patients with chest CT will shows pulmonary nodules, which are often multiple, polymorphic and variable. And it can also display ground glass and consolidation shadows, halo signs, anti-halo signs. There are larger than 2 cm cavities in 50% of nodules, thick or thin walls. Enhanced CT scan showed low to moderate enhancement in the center of the nodules and obvious enhancement at the edges **[13].** Due to atypical imaging, GPA is usually hard to distinguish from infectious diseases, such as tuberculosis, aspergillus, cryptococcosis, parasitic infections and non-infectious diseases, such as lung cancer, lymphoma, pulmonary sarcoidosis, allergic pneumonia, silicosis, and coal miner's lung. However, this patient had occurred the symptoms of chest pain, headache, cough, expectoration, nasal bleeding and decreased hearing during the course of the disease. Brain CT showed bilateral maxillary sinus and ethmoid sinus mucosa thickening and right mastoid inflammation. Enhanced chest CT examination at admission showed mass in the upper lobe of right lung accompanied by lung metastases and mediastinal lymph node enlargement, low to moderate enhancement in the center of the nodules and obvious enhancement at the edges.

Laboratory examination showed antineutrophil cytoplasmic antibody results showed cANCA (1:10) positive (+), anti-PR3 positive (++). The second time lung biopsy pathological finding revealed chronic inflammation of lung tissue with significant proliferation of local fibrous tissue, focal aggregation of neutrophils could be seen in fibrous tissues, small vascular inflammatory changes were considered, and focal fibrinoid necrosis and focal atypical granuloma formation were observed. According to American College of Rheumatology GPA classification criteria in 1990 **(Table 1) [4],** this patient was in line with ①②and ④And ACR/EULARGPA classification criteria of in 2017 **(Table 2) [5]** who had a score of 14, so GPA was diagnosed.

Table 1: American College of Rheumatology published GPA classification criteria in 1990 **[4].**

1900 American College of Rheumatology GPA classification criteria	
①Inflammation of the nose or mouth	Painful or painless oral ulcers, purulent or bloody nasal secretions
②Abnormal chest X-ray	Pulmonary nodules, fixed infiltrating lesions or cavities
③Abnormal urinary sediment	Microscopic hematuria (RBC>5/high magnification, or red cell tube type)
④Pathological granulomatous inflammatory changes	Granulomatous inflammation is formed by neutrophil infiltration in the artery wall or around the artery, or outside the blood vessel (artery or arteriole)
Notes: patients with 2 or more criteria were diagnosed as GPA, with a sensitivity or specificity of 88.2% or 92%, respectively	

Table 2: ACR/EULAR published GPA classification criteria in 2017 **[5].**

2017 Granulomatous polyvasculitis classification Criteria (ACR/EULAR)	
Clinical criteria	**Score**
(1) The bloody nasal discharge, ulcer, nasal scab or sinus-nasal congestion/obstruction	3
(2) Nasal polyps	-4
(3) hearing loss or decline	1
(4) Cartilage involvement	2
(5) Red eyes or sore eyes	1
Laboratory examinations	
(1) C-ANCA or PR3-ANCA antibody positive	5
(2) Eosinophil count≥1×109/L	-3
(3)Imaging showed nodules, masses or voids	2
(4) Granuloma was observed on lung biopsy	3
Notes: patients with the sum of the above 9 scores≥5 points can be classified as GPA	

GPA therapy is associated with disease status. Laboratory examinations of the patient's Erythrocyte Sedimentation Rate (ESR) was 89 mm/h, which increased significantly. Combined with the patient's cough, headache, hearing loss, and imaging examination results, the disease was in the active stage **[6].** 2021 Guidelines for the management of antineutrophil cytoplasmic antibody associated vasculitis in rheumatology/Vasculitis, the disease status of GPA can be divided into: 1. Active Period: New, persistent or worsening clinical signs and/or symptoms attributable to GPA and unrelated to prior injury. 2. Serious diseases: Vasculitis that threatens life or organs (for example: alveolar hemorrhage, glomerulonephritis, central nervous system vasculitis, multiple mononeuritis, heart involvement, mesenteric ischemia, limb/finger ischemia). 3. Non-serious diseases: Vasculitis without life-threatening or organ manifestations (for example, naso-sinusitis, asthma, mild systemic symptoms, skin diseases without complications, mild inflammatory arthritis). 4. Remission: No clinical signs or symptoms attributable to GPA during or without immunosuppressive therapy. 5. Intractable disease: Persistent active disease persists despite appropriate immunosuppressive therapy. 6. Relapse: Active disease recurrence after remission. Hormone therapy for GPA is fundamental; the drugs that need to be combined with immunosuppressants or biological agents include methotrexate, azathioprine, cyclophosphamide, rituximab, mycophanolate and leflunomide, etc. According to the 2017 ACR/EULAR assessment, ≥15 points

were considered to be active. The patient's Erythrocyte Sedimentation Rate (ESR) increased significantly to 89 mm/h, despite a score of 14, combined with the patient's clinical symptoms was considered to be active. The patient's body weight is 60 kg, steroid dose of 60 mg/day and cyclophosphamide dosage of 1200 mg/month were recommended in accordance with the guidelines. However, in the first time pathological results indicated that was inclined to mycobacteriosis, and ESR was high, although PPD, T-SPOT tests were negative, sputum and brush tests showed no mycobacterium tuberculosis, the patient suffered from repeated high fever during the course of the disease, and the re-examination of infection indicators increased. After moxifloxacin anti-infective treatment one week, fever symptoms persisted, but the possibility of mycobacterium tuberculosis (NTM) infection was not excluded. Therefore, he were treated 30mg prednisone acetate by mouth everyday and 500mg cyclophosphamide by intravenous infusion over ninety minutes every half-month, After one month treatment, the patient's clinical symptoms almost disappeared, but repeated chest CT scan results showed that there were multiple space-occupying lesions in both lungs, some of which were enlarged and formed multiple voids, and some of which were smaller than before. Considering the poor efficacy, so multi-disciplinary discussion was invited to adjust the diagnosis and treatment plan. Acer etiology sequencing (NGS) is recommended for the second lung biopsy, and NGS results were negative again, then tuberculosis infection was not considered. So it was recommended to adjust the prednisone acetate dose to 60mg/day at 1mg/kg and cyclophosphamide was recommended to be adjusted to 1200 mg/month at 20 mg/kg. After two month treatment, no abnormality was found in serum ANCA, chest CT suggested lung nodules and mass, mediastinal lymph node shrinkage. The patient's clinical symptoms were improved and his condition was stable, CT imaging suggested that the absorption of the lesion was well. The treatment was effective, who had been regularly followed up.

Conclusion

GPA is a rare and unknown etiology ILD. Although the clinical symptoms and imaging manifestations are not characteristic, the imaging manifestations may be multiple, polymorphic, changeable and accompanied by cavities, so it is difficult to distinguish and easily misdiagnosed clinically. The diagnosis was wrong, the treatment was not timely, and the survival was very short. Medical history inquiry is not detailed, can also cause misdiagnosis and missed judgment, delay diagnosis and treatment. According to the vasculitis guideline management recommendations, different disease states and different degrees of severity lead to different treatment plans. Without sufficient amount and sufficient course of treatment, standardized treatment results in unsatisfactory treatment effects. Therefore, once the diagnosis is clear and relevant factors are excluded, a full dose of treatment plan is required. At the same time, GPA is prone to relapse, and without treatment, the survival rate is low. Therefore, correct diagnosis, standardized treatment and follow-up are essential.

Author Contributions

Songjun Shao and Yu Tan contributed equally to this work.

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Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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