

Myasthenia Gravis with Pulmonary Nocardia Pneumonia and Brain Abscess Misdiagnosed as Brain Metastasis from Lung Cancer

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Abstract

Pulmonary nocardiosis is a rare chronic suppurative granulomatous disease, which is easily misdiagnosed as lung cancer and other diseases. Early diagnosis is beneficial to the patient's rehabilitation. We herein report a case of myasthenia gravis in a 64-year-old female patient with a space-occupying lesion in the right lower lung. Her breast CT suggests high probability of lung cancer. Her head MRI indicates multiple nodules, considering metastases. Finally, the BAL RNA next generation sequencing (NGS) technology is used to confirm the pulmonary nocardiosis. The patient responded well to TMP/SMX treatment. The present study aims to investigate the clinical characteristics of the disease in order to improve the understanding of the disease, diagnosis and treatment.

Keywords: Nocardiosis; Lung; Procrystis; Cancer

Case Presentation

The patient, a 64-year-old woman, was admitted to hospital in 2019 due to dyspnea with chest pain for 1 month and having a fever for 9 days. She had a history of myasthenia gravis for 6 months previously, and was treated with corticosteroid and pyridostigmine bromide tablets for a long time. She has no smoking history, but has a history of hypertension for 10 years. She used to be admitted for treatment in other hospital before admitting to our hospital. The chest CT showed a tumor shadow in the inferior lobe of right lung. *Klebsiella pneumoniae* was detected in the sputum culture. Piperacillin and sulbactam, ceftriaxone tazobactam and moxifloxacin were given for anti-infection treatment. The body temperature dropped to normal, but the rest of the symptoms did not improve significantly. Therefore, the patient was transferred to our hospital. After admission, meropenem was given for anti-infection, atropine sulfate tablets and dipyridamole tablets and other symptomatic treatment for the improvement of myasthenia gravis, and high-dose immunoglobulin for the enhancement of immune function. Chest CT was completed and the results showed cavernous cluster and flake shadows in the right lower lung, considering peripheral lung cancer in the right lower lung with bilateral lung metastases and pulmonary lymphangitic carcinomatosis. Her brain MRI showed multiple nodules in the bilateral frontal parietal lobes, basal ganglia, cerebellar hemisphere and left temporal lobe, considering metastases (Figure 2a). In order to make clear diagnosis, bronchoscopy was completed. No obvious endobronchial lesions were discovered. Inflammatory swelling was found in the bronchial submucosa. Bronchial alveolar lavage (BAL) was performed in the right lower lobe of the bronchus. RNA next generation sequencing (NGS) was tested and indicated nocardia, pneumocystis and cytomegalovirus infection. No fungi, bacteria, acid-fast bacilli and cryptococcus were found after performing lumbar puncture and sampling cerebrospinal fluid for examination. Taking into account the patient's history of myasthenia gravis, we gave the patient a sufficient dose of TMP/SMX (1.2/0.8g ,q6h), ganciclovir and imipenem/cystatins for combined treatment. As symptoms improved, the patient continued the oral administration of TMP/SMX. Chest CT was performed 9 months after TMP/SMX treatment and the results revealed that the lesions in the right lower lung were significantly absorbed (Figure 1b). Brain MRI showed significant reduction and absorption of nodules (Figure 2b).

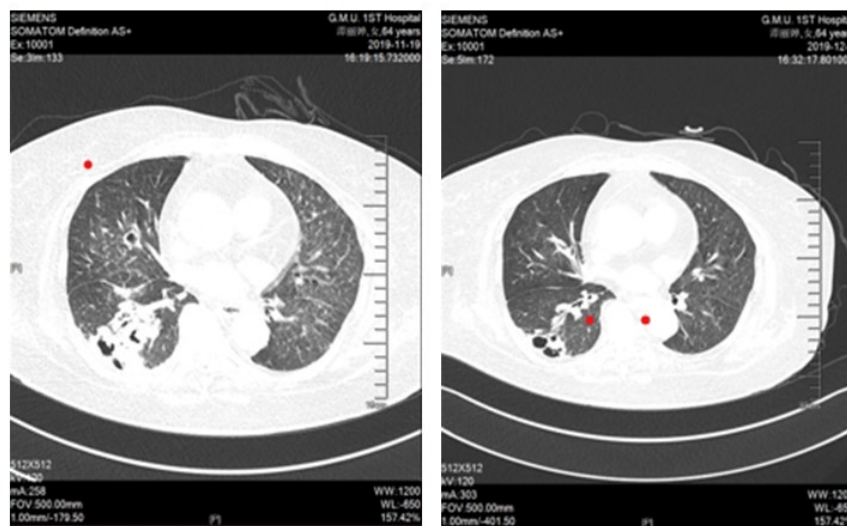


Figure 1 A

Figure 1 B

Figure 1: A Chest CT scan shows 5*6 cm consolidation shadow of right lower lung. B The chest CT show this lesion resolved after half a month of treatment.

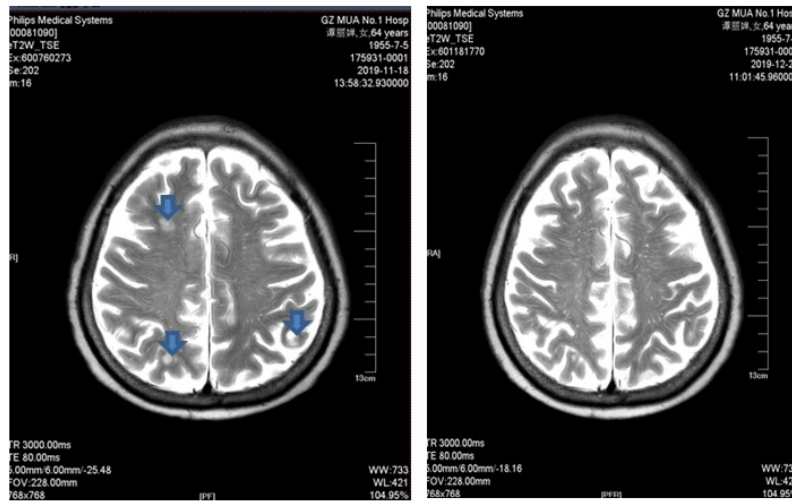


Figure 2 A

Figure 2 B

Figure 2: A The brain MRI show the nodules in brain. B The brain MRI showed significant reduction and absorption of the nodules after a month treatment.

Discussion

Nocardia, a type of gram-positive aerobic bacteria, is branched and rod-shaped, with acid fast staining positive. It is classified into actinomycetes which generally survive in soil and rot [1]. There are many kinds of nocardia, which are clinically significant for human beings, including novel nocardia complex, traverse nocardia complex, Far's nocardia complex and nocardia asteroides, etc. [2]. Pulmonary nocardiosis is acute, subacute or chronic infectious disease usually caused by nocardia asteroides infection. It often occurs in people with low immunity, mainly in patients [3] lacking T cell-mediated immunity. In addition, people exposed to livestock may also infect the nocardia [4]. Therefore, the most susceptible patients include those with solid organ transplantation, hematopoietic stem cell transplantation, tumors, chronic lung diseases (e.g. pulmonary alveolar proteinosis), systemic lupus erythematosus, human immunodeficiency virus (HIV) infection, those taking long-term corticosteroids and those undergoing a malignant process [5]. This patient has a history of myasthenia gravis previously and orally taken long-term hormones. These are risk factors for the disease. However, one third of nocardia may also occur in people with normal immune function [6].

Nocardia is not a common colonizing bacterium in human body. It can infect the man through the respiratory tract, skin and other parts of the body. In addition to the infection in the respiratory tract, skin and other parts of the body, nocardia in severe patients can be disseminated through blood to form migratory lesions (mainly abscess) mainly in the brain, liver and kidneys. The brain abscess caused by nocardia accounts for 1%-2% of all brain abscesses, with mortality as high as 31% [7]. This patient has suffered from nocardiosis with brain metastases, which is clinically rare. There is no specific clinical manifestation in pulmonary nocardiosis which can be characterized by acute infection, subacute infection or chronic infection. Its clinical symptoms often include fever, cough, dyspnea or chest pain, which can be complex and diverse due to lung lesions such as lung cavities and abscesses, pleural effusion or pulmonary edema. Some studies have shown that the nocardiosis involving various parts has no specific [8] clinical manifestations. The main manifestations of this patient consist of dyspnea, chest pain and fever.

Imaging findings of pulmonary nocardiosis may show irregular nodules, cavities, diffuse alveolar pulmonary infiltration, pulmonary abscesses or pleural effusion. Literature statistics reveals about one third of pyothorax [9] and one third of cavities [10] appear in patients with nocardiosis. It is easily misdiagnosed as lung cancer and tuberculosis, etc. However, some studies have shown that the imaging manifestations of pulmonary nocardiosis have certain characteristics, namely, the initial images of pa-

tients are mostly nodules, lumps or consolidation. With the progression of the disease, the consolidation, nodules or lumps will partially appear necrosis and form cavities [11]. When suspicious images of the brain are not consistent with clinical and imaging findings, a brain MRI scan is the preferred radiological method [12] for the diagnosis of suspected nocardia abscesses. The brain metastases usually show low spontaneous signals and high ADC on the MR diffusion sequence, while the brain abscess lesions show high diffusion signals and low ADC [13] on the MR diffusion sequence. In this case, the imaging findings of the patient not only show cavities in the lung, the brain MR but also suggests the presence of metastases. It is easily misdiagnosed as peripheral lung cancer in the right lower lung with brain metastases. Because of lack of specificity in clinical and imaging findings, it is easy to be confused with lung cancer complicated with brain metastasis. Lumbar puncture is not helpful in the diagnosis of nocardiosis. Usually, the lymphocytes are increased while the protein and glucose are decreased in the cerebrospinal fluid, and few pathogens can be found [14]. In this case, except for a small amount of red blood cells (due to puncture injury) in the cerebrospinal fluid, the remaining indexes such as protein, glucose, bacteria and fungi are generally abnormal. It is difficult to identify brain metastases and brain abscesses through cerebrospinal fluid. On the one hand, the head CT enhancement scan of this patient indicates that the intracranial lesion is an annular enhancement lesion (brain metastases are generally homogeneous enhancement lesions) and the head MR enhancement scan suggests an abnormally enhanced lesion. The patient has no history of tumors. Her five items of tumor markers are normal and the lung tissue biopsy results show the absence of tumor cells. On the other hand, the patient's immunity is low, and the test results of NGS alveolar lavage fluid suggest the nocardia infection. In the case of low immunity, the probability of nocardia spreading to the brain through blood may increase. Therefore, the patient is diagnosed with pulmonary nocardiosis with metastatic brain abscess rather than lung cancer with brain metastasis.

Clinically, the basic assessment when considering nocardiosis should include bacterial culture at the site of infection, skin biopsy, purulent secretion, sputum, deep abscess or pleural effusion, as well as the brush biopsy of alveolar lavage fluid under bronchoscope. Once the nocardia was found in these specimens above, it can be confirmed. Nocardia grows slowly. Therefore, enough growth time up to 3-5 days shall be left when suspected. It is worth mentioning that we may also use NGS technology to identify pathogens with the progress of science and technology. This patient is diagnosed with nocardia infection by BAL NGS test. Moreover, the lesions are well absorbed and the treatment is effective after targeting nocardia.

At present, nocardia is generally sensitive to sulfonamides. Some scholars believe that sulfonamides may slow down the occurrence of nocardia infection events [15]. Moreover, it is sensitive to linezolid and imipenem but resistant to moxifloxacin, ceftriaxone, clarithromycin, and fully resistant to erythromycin [16]. The treatment generally lasts at least 6 months and should continue for at least another month [17, 18] after the symptoms of infection have disappeared by using antibiotics. In the case complicated with brain abscesses, the antibiotics selected should have good diffusivity in the brain, such as compound sinomine or ceftriaxone [6]. Within one year after stopping using antibiotics, the patient shall be closely followed up in order to monitor the recurrence, as well as imaging findings and laboratory tests. Some studies reveal the treatment effect of brain surgery on pulmonary nocardiosis combined with brain metastases. This experiment shows that if the length of the abscess is less than 2 cm, the treatment generally only chooses antibiotics. If the patient's symptoms deteriorate or the treatment is not satisfactory within one month, the positional aspiration should be performed for decompression and diagnosis. Any brain abscess with a long axis of more than 2.5 cm will be preferred for surgical treatment [17].

Conclusion

To sum up, pulmonary nocardiosis mostly occurs in population with chronic pulmonary underlying diseases or low immune function. Its clinical and imaging manifestations are poorly specific. The diagnosis needs to rely on etiological tests, as well as NGS techniques if necessary. Sulfonamides are the first choice of treatment for pulmonary nocardiosis, and the combined treatment is even effective. The prognosis of pulmonary nocardiosis is associated with the patient's age, basic condition and infec-

tion sites, etc. For example, the recovery rate of nocardiosis patients involving the skin and soft tissue is almost 100%, that of patients with pleural or lung tissue involvement is about 90%, and that of patients with brain abscesses is about 50% [19]. The recovery rate of pulmonary nocardiosis is about 90% [20] under early diagnosis and early treatment. Especially in most immunosuppressive patients, the early treatment can improve the prognosis [21, 22] of most patients.

Availability of Data and Materials

The data that support the findings of this study are openly available.

Author Contributions

Conceived and designed the article: M.Z., Y.W, and P.R. Collect case information: X.H,X.W. Contributed to writing manuscript: M.Z., Y.W,X.Y. All the authors approved the submission of the manuscript for publication.

Competing Financial Interests

The authors declare no competing financial interests.

Declaration of Competing Interest

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