Clinical Challenge

A Novel Case of Pulmonary Nocardiosis with Secondary Hemophagocytic Lymphohistiocytosis

Teng Han1,2,1, Ying-Mei Liu1,2,3, Ting Yang1,2,3, Hua-Ping Dai1,2,3, Xiao-Lei Zhang1,2,3

1Center for Respiratory Diseases, China-Japan Friendship Hospital, Beijing 100029, China
2Department of Pulmonary and Critical Care Medicine, China-Japan Friendship Hospital, Beijing 100029, China
3National Clinical Research Center for Respiratory Diseases, Beijing 100029, China

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Pulmonary nocardiosis is an opportunistic infection, especially in immunocompromised patients. Hemophagocytic lymphohistiocytosis (HLH) is a rare but potentially fatal disease. We report a case of pulmonary nocardiosis with secondary HLH.

A 48-year-old Chinese male presented with skin rash, high-grade fevers, and arthralgia. He was diagnosed as adult-onset Still’s disease and treated with corticosteroids. The patient’s symptoms improved with no fever, and the leukocyte count and other inflammatory markers returned to normal after six weeks of treatment. However, two months later, his body temperature elevated again and he developed cough and yellow sputum. Chest computed tomography (CT) scan showed nodules with cavitation in the left lower lobe and bilateral multifocal ground-glass opacities [Figure 1a]. He was given imipenem and cilastatin sodium, vancomycin, and caspofungin with reduced dose of corticosteroid. Unfortunately, his symptoms and abnormalities on CT scan tended to get worse [Figure 1b]. Lung biopsy was performed with no diagnostic findings.

Then, the patient was admitted to our hospital with high-grade fever, significant short of breath, sputum production, conjunctival hemorrhage, purpura, yellow discoloration of the skin and sclera, tachycardia, and edema on the extremities. Laboratory examination showed mild anemia, agranulocytosis, thrombocytopenia, bilirubinemia, elevation of aminotransferase, hypertriglyceridemia, hypofibrinogenemia, and elevated ferritin. Cellular immunologic test showed marked reduction of CD4 to 9.6 × 10^9 cells/m³. Abdominal ultrasound showed splenomegaly. The patient was diagnosed with HLH according to the 2004 HLH diagnostic criteria. Percutaneous lung biopsy specimens and sputum sample both isolated Nocardia asiatica sp. nov [Figure 1c and 1d]. The patient was diagnosed as pulmonary nocardiosis and secondary HLH. Then, the issues turned to the treatment since the therapeutic strategies for pulmonary nocardiosis and HLH were contradictory. During the 1st week, the patient was treated with methylprednisolone sodium succinate and γ-globulin for HLH. Symptoms such as fever, hemorrhage, and yellow discoloration of the skin and sclera improved, as well as those laboratory abnormalities. Then, oral administration of trimethoprim/sulfamethoxazole (TMP/SMX) and intravenous administration of imipenem amikacin were added for pulmonary nocardiosis. With the continuous improvement of symptoms, the antibiotic therapy was switched to oral administration of TMP/SMX and minocycline. After eight weeks of treatment, the follow-up CT showed significant resolution of ground-glass infiltration and nodules [Figure 1e]. Then, the dosage of corticosteroid was tapped slowly.

The genus Nocardia is a group of environmental bacteria that usually manifest as an opportunistic infection in immunocompromised hosts. Host resistance to Nocardial infection depends on cell-mediated immunity. Patients with acquired immunodeficiency syndrome and those who receive...
treatments with corticosteroids or cytotoxic therapy are at a high risk for Nocardia infection.[1] A retrospective study showed that the most common risk factor for both pulmonary and disseminated nocardiosis was corticosteroid therapy.[2] Dose and duration of steroid treatment in nocardiosis patients receiving corticosteroids prior to diagnosis varied widely.

Nocardial infections range from minor cutaneous lesions to severe pulmonary or systemic nocardiosis, including central nervous system dissemination.[3] Pulmonary nocardiosis is the most common clinical presentation of infection because inhalation is the primary route of bacterial exposure. The clinical presentation of pulmonary nocardiosis is variable and nonspecific. Moreover, the chest radiologic manifestation can also be variable. Consolidations and large irregular nodules, often with cavity formation, are most common; nodules, masses, and interstitial patterns also occur. Since the clinical and radiologic manifestations are nonspecific, and the microbiological diagnosis is often difficult, pulmonary nocardiosis can be mistaken for other infections in some patients, such as tuberculosis, bacterial pneumonia, or malignancies.

In addition, the patient had a secondary HLH after pulmonary nocardiosis. HLH is an immune-mediated life-threatening disease. It is a rare disease and is divided into primary and secondary. Most causes of secondary HLH are viral, autoimmune, or neoplasia related.[4] Pulmonary nocardiosis has rarely been reported as a cause of HLH. Pulmonary nocardiosis shows a broad and variable clinical manifestation. Etiological diagnosis needs experienced clinical microbiology doctors. Etiological treatment is more important for a patient with infection-associated HLH.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understood that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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