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A Case of Mycobacterium Tuberculosis Associated Immune Reconstitution Inflammatory Syndrome after Diagnosis and Treatment of AIDS with Multiple

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Marneffei; Antituberculosis; Gene-Xpert

1. Abstract

Acquired immune deficiency syndrome (AIDS) is a serious infectious disease caused by human immunodeficiency virus (HIV), which damages the immune system and leads to various opportunistic infections, such as mycobacterium tuberculosis infection and cyanobacteria Marneffei infection. Patients with AIDS who are infected with Mycobacterium tuberculosis (MSTB) have been initiated with antiretroviral therapy (ART). immune reconstruction inflammatory syndrome (IRIS) may occur, leading to worsening of the condition. An AIDS patient with mycobacterium

tuberculosis infection and cyanobacteria Marneffei infection was reported. Tb-related IRIS appeared 2 weeks after ART initiation. The patient's condition improved after the diagnosis of IRIS and the treatment with glucocorticoid. Since AIDS patients with concurrent mycobacterium infection and cyanobacteria Marneffei infection are rarely seen clinically, attention should be paid to the interaction between antituberculosis drugs, antifungal drugs and antiretrovirals during treatment.

2. Case Summary

A 36-year-old male patient was admitted to the hospital on September 7, 2019 due to "fever and cough for more than 2 months". Previous diagnosis of AIDS, no ART. Since July 2019, the patient has developed fever without obvious causes, with a maximum body temperature of 39℃, accompanied by paroxysmal cough, a small amount of white phlegm, obvious night sweats, and pinprick pain in the left chest. Chest CT: Multiple lesions in both lungs and high density lesions in the upper lobe of the right lung were detected by sputum smear for acid-fast bacilli (+) and sputum Gene-Xpert (MTB)RIF3+. The patient still had fever after anti-tuberculosis treatment with isoniazid, rifampicin, ethambutol, and pyrazinamide for 1 week. The patient was detected in sputum culture, blood culture and bone marrow culture. The fever was relieved after antifungal treatment with amphotericin B. ART was given after 3 weeks of antituberculosis treatment and 2 weeks of antifungal treatment. In order to reduce drug interaction, itraconazole capsules were changed as antifungal drugs, and the antituberculosis regimen was adjusted to isoniazid, rifambutin, ethambutol, and pyrazinamide. After 2 weeks of ART, the patient developed fever again, with more infectious lesions in the lungs on CT and a small amount of pleural effusion. No abnormalities were found in routine and biochemical examination of pleural effusion, negative pleural effusion culture, negative bone marrow culture, and negative acid-fast bacilli on sputum smear. The patient was diagnosed as tuberculous IRIS, and the fever was relieved after treatment with prednisone acetate. Pulmonary CT showed improvement in absorption of both pulmonary lesions.

Introduction of the Disease The chief complaint: Fever and cough for over 2 months.

History of present disease: No history of hypertension or coronary heart disease.

Past History: Previous diagnosis of AIDS, no ART.

Personal and family history: Personal and family history was non-contributory. His wife is not infected with HIV.

Laboratory examinations:

Cyanobacteria marneffei were detected in sputum smear with acid-fast bacilli (+), Gene-Xpert(MTB)RIF 3+, sputum culture,

blood culture and bone marrow culture. CD4 count was 7cells/ul, HIV-RNA250000copies/ml.

2.1. Imaging examinations

The patient underwent three lung CT examinations during hospitalization: ① On admission, lung CT showed multiple lesions in both lungs and high-density lesions in the upper lobe of the right lung (Figure 1).

② After 2 weeks of ART treatment, pulmonary CT showed more infectious lesions in both lungs and a small amount of pleural effusion (Figure 2). ③ The absorption of lung lesions on CT was improved after treatment with Jandasone (Figure 3).

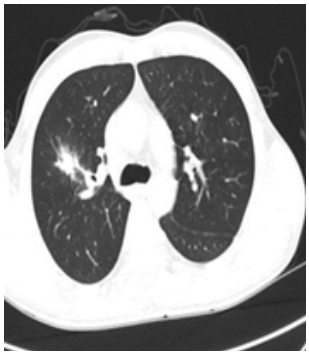

Figure 1: Lung CT on admission.

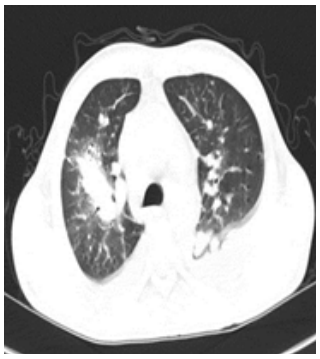

Figure 2: Pulmonary CT at diagnosis of TB-associated IRIS.

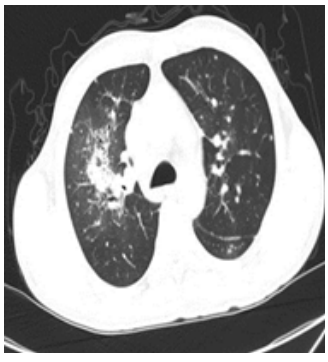

Figure 3: Lung CT after prednisone treatment.

3. Final Diagnosis

1. AIDS with multiple infections (Mycobacterium tuberculosis infection, cyanobacteria marneffei infection); 2. Tuberculosis associated immune reconstitution inflammatory syndrome.

3.1. Treatment

The patient was given anti-tuberculosis treatment with isoniazid, rifampicin, ethambutol, and pyrazinamide for 1 week after sputum smear examination for acid-fast bacilli (+), and sputum GeneXpert (MTB)RIF 3+. The patient's fever did not relieve. The sputum culture, blood culture and bone marrow culture were tested for cyanobacteria marneffiae. Due to immune dysfunction, ART was given. In order to reduce the interaction between antiviral drugs, antituberculosis drugs and antifungal drugs, the ART regimen was tenofovir (TDF) + lamivudine (3TC) + dotiravir (DTG). The antituberculosis drugs were adjusted to isoniazid, rifambutin, ethambutol and pyrazinamide, and the antifungal drugs were adjusted to itraconazole. After 2 weeks of comprehensive treatment, the patient developed fever again, lung CT and bilateral pulmonary infectious lesions increased compared to before, accompanied with a small amount of pleural effusion, routine and biochemical examination of pleural effusion showed no evidence, pleural effusion culture was negative, bone marrow culture was negative, sputum smear was negative acid-fast bacilli, inflammation indicators were normal, etiological tests showed no evidence of other opportunistic infection, and the patient was diagnosed as tuberculous related IRIS. After treatment with prednisone, the fever was relieved, and reexamination of CT showed improvement in absorption of pulmonary lesions.

3.2. Outcome and Follow-Up

The fever was relieved, lung CT lesion absorption improved, HIV-RNA was less than 50copies/ml, and CD4 count increased to 120cells/ul.

4. Discussion

AIDS is a serious infectiousdisease caused by human immunodeficiency virus (HIV), leading to a variety of opportunistic infections, tuberculosis, Marneffei infection is a common opportunistic infection of AIDS patients and one of the main causes of death, early diagnosis and anti-tuberculosis, anti-fungal treatment, Early antiretroviral therapy (ART) is the key to improve their survival rate [1]. Tuberculosis associated immune reconstructive inflammatory syndrome (TB-IRIS) is a complex complication [2], which mostly occurs after ART treatment, and its main mechanism is abnormal inflammatory reaction after immune activation. At present, the main views on the treatment of HIV-associated TB-IRIS are as follows [3]: (1) Strengthen anti-tuberculosis therapy, continue ART therapy, and optimize antiviral therapy according to drug interactions. In this case, the patient received ART, anti-tuberculosis and anti-fungal therapy at the same time, and the etiological treatment has been optimized and comprehensive as far as possible, but drug interaction cannot be avoided. Rifambutin can reduce itraconazole concentration by 70%, potentially inhibiting rifambutin metabolism. It is necessary to monitor itraconazole concentration and adjust corresponding dose, and monitor rifambutin toxicity. However, the AUC of rifambutin and dotilavir did not change significantly, and the plasma trough concentration decreased by 30%. The dosages of rifambutin and dotilavir did not need to be

adjusted. Dotenavir and itraconazole were used at the same time without dose adjustment. (2) Glucocorticoid for moderate to severe patients, short-term (4-8weeks) treatment with glucocorticoid [4] (prednisone 1.5mg/kg for 2 weeks, 0.75mg/kg for 2 weeks or equivalent dose of hormone) can reduce clinical symptoms and mortality.

This paper reports a case of tuberculosis immune reestablishment inflammatory syndrome (TB-IRIS) after treatment of AIDS complicated with Mycobacterium tuberculosis infection and cyanobacteria Marneffei infection. The patient developed TB-related clinical manifestations before starting anti-retroviral therapy and was diagnosed with tuberculosis, but the disease continued to progress during the course of anti-tuberculosis treatment. The patient was diagnosed as AIDS with multiple infections. The anti-fungal treatment of amphotericin B for 2 weeks relieved the fever, and the anti-tuberculosis and anti-fungal treatments were effective. ART should be started as early as possible in HIV/AIDS patients with tuberculosis, and it is recommended to start ART as early as possible within 2 weeks after anti-tuberculosis treatment [5]. ART regimen containing dotiravir has been recommended for HIV / AIDS patients with tuberculosis [6]. It should be noted that when dotiravir is combined with rifampicin, the dose of dotilavir needs to be increased (50mg, twice a day) [7], while rifambutin has a weak induction effect on aminotransferase. Patients with HIV infection /AIDS complicated with tuberculosis who are treated with dotilavir or latilavir can be considered to use rifambutin instead of rifampicin without dose adjustment.

The patient in this case had the following characteristics: (1) Prior to initiation of ART treatment, he was infected with two pathogens, with high HIV load and low CD4 count. (2) Fever occurred 2 weeks after ART treatment, lung CT indicated a significant increase in lesions, sputum culture, blood culture and bone marrow culture were negative again, indicating that the infection was well controlled by C. marneffei, inflammation indicators CRP and PCT were normal, etiological tests showed no other evidence of opportunistic infection, and the patient was diagnosed as TB-related immune reconstructive inflammatory response syndrome. After treatment with prednisone, the fever was relieved, and reexamination of lung CT showed improvement in absorption of both pulmonary lesions. (3) After treatment, the patients' fever was relieved, lung CT lesion absorption improved, HIV-RNA was less than 50copies/ml, and CD4 count was higher than ART. According to the above characteristics, this case is consistent with the TB-related immune reestablishment inflammatory response syndrome. In short, since AIDS patients are both susceptible to tuberculosis and Marnefee cyanobacteriasis, and IRIS is prone to appear after ART, attention should be paid to early detection and treatment of patients with IRIS. This case emphasizes the importance of screening for tuberculosis infection and fungal infection before starting antiretroviral therapy, which provides certain reference experience for the treatment of TB-related IRIS after the treatment of AIDS with multiple infections.

5. Conclusion

We report a case of tuberculosis related IRIS after treatment of AIDS complicated with multiple infections. The patient's condition improved after treatment with glucocorticoid after diagnosis of IRIS. In the treatment of AIDS patients with concurrent mycobacterium infection and cyanobacteria marneferi infection, attention should be paid to the interaction between anti-tuberculosis drugs, anti-fungal drugs and anti-retroviral drugs, and early detection and treatment should be achieved for patients with IRIS, which emphasizes the importance of screening for tuberculosis infection and fungal infection before starting anti-retroviral therapy.

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