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Tuberculosis Infection in HIV-Positive Patient: A Case Report

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Abstract: ***Introduction: Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) are a lethal combination, these two diseases accelerate disease progression one another. These infections affect each other in all aspects of the disease, from pathogenesis, epidemiology, clinical manifestations, treatment and prevention. This article aims to report a case of TB and HIV co-infection and its management. Case illustration: A twenty-eight-year-old male came with chief complaint shortness of breath. The patient also had a history of fever, cough, night sweats, weight loss, and malaise for one month. Laboratory examinations revealed leukocytosis, reactive anti-HIV immunoserology, gene Xpert MTB/RIF assay detected Mycobacterium tuberculosis in the specimen and showed no rifampicin (RIF) resistance. The chest x-ray obtained was active lung TB with secondary infection. The patient was diagnosed with active pulmonary TB and HIV. This patient was treated with Anti-tuberculosis drug 1st category. Discussion: Most common manifestation of TB-HIV co-infections are fever, weight loss, and cough Physical examination sometimes do not show signs that are specific to TB patients. It is recommended to screen TB in HIV patients because TB co-infection is common in HIV Patients. TB infection can be diagnosed by using sputum examination or GeneXPERT MTB/RIF. ARV administration is given at least 2 weeks after Anti Tuberculosis Drugs to prevent IRIS (Immune Reconstitution Inflammatory Syndrome).***

Keyword: Tuberculosis, HIV, Anti-Retroviral Therapy

1.Introduction

Tuberculosis (TB) is an infection disease caused by Mycobacterium tuberculosis. One-third of people in the world were thought to be infected with M. tuberculosis, but only 10-20% of them will develop into active TB, whereas the rest are still asymptomatic. Tuberculosis is one of the top 10 causes of death in the world. In 2016, 10.4 million people suffer from tuberculosis, and 1.7 million died as a result of the disease. India occupies the first position as a country with highest death because of tuberculosis in the world, followed by Indonesia in second place, then China, Philippines, Pakistan, Nigeria, and South Africa. The number of TB cases in Indonesia in 2016 was 298,128 cases.[1]

Tuberculosis and HIV are a lethal combination, these two diseases accelerate disease progression one another. These infections affect each other in all aspects of the disease, from pathogenesis, epidemiology, clinical manifestations, treatment, prevention, and even can affect bigger issues such as social, economic, and political. HIV-positive people are estimated to be 21-34 times more prone to active TB compared to HIV-negative people. Tuberculosis is also a leading cause of death in HIV-positive patients. In 2016, 40% of HIV deaths were caused by TB. Indonesia found as many as 360,565 cases of tuberculosis, with 14% of them also known to suffer from HIV-positive.[2]

Highly active antiretroviral therapy (HAART) significantly reduces the incidence of opportunistic infections and death in patients with advanced HIV and simultaneously includes patients with TB-HIV co-infection. The improvement in immunity associated with HAART administration is not only a positive response that reflects the success of therapy but can also lead to immunopathological reactions and clinical deterioration at the time of initiation. Some patients with TB-HIV co-infection experience worsening both clinically and radiologically. This condition is known as immune reconstitution inflammatory syndrome (IRIS).[3,4] This article aims to report a case of twenty-eight-year-old male with TB and HIV co-infection and its management.

2.Case Illustration

A twenty-eight-year-old Asian male came to Emergency Room (ER) with a chief complaint of shortness of breath. The patient also had a history of fever, cough, night sweats, weight loss, and malaise for one month. The fever was intermittent; the temperature was not measured by the patient because he didn't have a thermometer. Fever only appeared at night. The patient took an antipyretic but the fever only improved temporarily. The cough was filled with phlegm and had gotten worse in the last few days. The patient also had a weight loss of 6 kg in the last 3 months and diarrhea 3 times since yesterday.

The patient had a history of anxiety disorders for two years and already seeking treatment from a psychiatrist. The history of treatments was Clozapine 1x25 mg, trihexyphenidyl 3x2 mg, and trifluoperazine 2x5 mg. The patient had no history of chronic disease and allergies. Blood pressure of the patient was 95/60 mmHg, pulse 115 bpm, Respiration rate 30 times per minute, temperature 36.9 C, SpO2 90% on room air and 95% on nasal cannula 4 liters per minute. Physical examination showed symmetrical inspection during inspiration and expiration, normal fremitus palpation, sonor percussion, and vesicular auscultation. Other physical examinations were within normal limits.

From the results of laboratory examinations, white blood cell count 8.62 x 103/mm3, normal liver function test,

normal kidney function test, reactive anti-HIV immunoserology, gene Xpert MTB/RIF assay detected Mycobacterium tuberculosis in the specimen and showed no rifampicin (RIF) resistance. The chest x-ray obtained was active lung TB with secondary infection. The patient was diagnosed with active pulmonary TB, HIV stage IV and Pneumonia CAP. The patient received nebulization Salbutamol and Ipratropium bromide (Combivent) every 6 hours, levofloxacin 750 mg once a day IV, paracetamol 1000 mg thrice a day IV, vitamin C 1 gr once a day IV, vitamin D 5000 IU once a day per oral, Anti-tuberculosis drug 1st category (Isoniazid 75 mg, Rifampicin 150 mg, Ethambutol 275 mg, Pyrazinamide 400 mg) 4 tablets a day. The patient was admitted for one week and the symptoms were relieved.

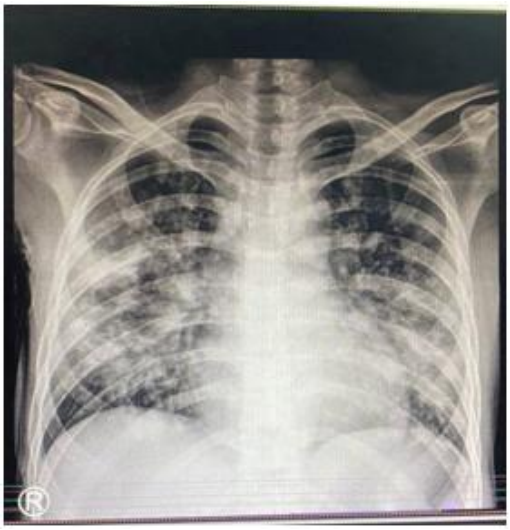

Figure 1: Chest X-ray of the patient revealed fibroinfiltrate in right parahilar with multiple cavities in right lung.

3.Discussion

Tuberculosis (TB) is an airborne infectious disease caused by Mycobacterium tuberculosis. These bacteria are straight rod-shaped bacteria with a size of about 0.4 x 3 that do not produce spores and are obligate aerobic. These bacteria are also known as bacteria that are resistant to acid conditions. Mycobacterium tuberculosis is found in droplets with a diameter of 1-10 in the air. The disease is transmitted from people who have been infected with M. tuberculosis through coughing, sneezing or talking. Droplets containing these mycobacteria can be in the air for several hours which will then be inhaled by healthy people and enter the respiratory system.[5]

When symptoms first manifested, fever, weight loss, and cough were the most prevalent. Study revealed in 25.28% of the patients, neurological involvement was clinically evident for an average of one week before the diagnosis. The majority of patients with neurological symptoms had headaches and sensorium changes. Oral candidiasis was the most prevalent opportunistic infection after tuberculosis. ESR levels were elevated in 64.36% and anemia was found in 45.97% patients.[6]

Physical examination sometimes does not show signs that are specific to TB patients. The usual investigation used to detect TB is a chest X-ray. This chest X-ray examination can show pulmonary infiltrates. However, the gold standard for diagnosing TB is to culture the patient's sputum.[5] The procedure for establishing a diagnosis in TB patients coinfected with HIV/AIDS is basically no different from patients without HIV/AIDS infection. It is necessary to pay attention to the risk factors for HIV/AIDS transmission to determine the cause and to identify the possibility of other infections. Molecular Rapid Test is very necessary in this patient's case because it is known that HIV/AIDS is one of the risk criteria for MDR TB.[7]

The treatment for TB coinfected with HIV/AIDS is in principle no different from patients without HIV/AIDS. ARV administration is given 2-8 weeks after anti Tuberculosis Drugs. If the CD4 value is less than 50 cells/mm3, then ARV administration can be started in the first 2 weeks after initial Anti Tuberculosis Drugs administration with monitoring, while in TB meningitis ARV administration is given after the intensive phase is complete. In the administration of antiretroviral drugs, it is necessary to pay attention to drug interactions, overlapping side effects of drugs, immune-reconstitution inflammatory syndrome (IRIS), and medication adherence problems.[8-10]

HIV-positive patients receive the same general treatment for tuberculosis as HIV-negative patients, but there are a few more factors to take into account. The combination of isoniazid, rifampicin, ethambutol, and pyrazinamide for 2 months, followed by 4 months of isoniazid and rifampicin, is the recommended regimen for drug-susceptible disease. The clinical trials that support this regimen were carried out decades ago in HIV-negative patients, but numerous studies have shown efficacy in people with HIV.[3]

TB drugs in HIV patients are as effective as in TB patients without HIV. In TB HIV co-infection, hepatitis infection is often found so that side effects of drugs that are hepatotoxic are easy to occur. The dose of Anti Tuberculosis Drugs is recommended in fixed-dose combinations (FDC). In 1st line of ARV treatment, Efavirenz (EFV) is a good NNRTI group used for antiretroviral therapy in people living with HIV in Anti TuberculosisDrugs therapy. Efavirenz is recommended because it has a lighter interaction with rifampin than nevirapine. The 2nd lineHIV treatment uses a drug combination containing Lopinavir/Ritonavir (LPV/r), which has a very strong interaction with rifampin because rifampin activates enzymes that increase LPV/r metabolism thereby lowering plasma LPV/r levels lower than the minimum inhibitory concentration (MIC). In these conditions, the option is to replace rifampin with streptomycin. If rifampin is still to be used with LPV/r, especially in tuberculous meningitis, it is recommended to increase the dose of LPV/r to 2 times the normal dose. Both drugs are hepatotoxic, so it is necessary to monitor liver function more intensively. If people living with HIV

have chronic liver disorders, the combination is not recommended.[11]

Cotrimoxazole is given to all HIV TB patients regardless of CD4 cell count as prevention of other opportunistic infections. In people living with HIV/AIDS without TB, prophylactic cotrimoxazole is recommended for patients with CD4 values <200 cells/mm3. Cotrimoxazole administration in HIV patients can reduce mortality.[11]

Tuberculosis Prevention Treatment is given as part of efforts to prevent the occurrence of active TB in people living with HIV. TB preventive treatment is given to people living with HIV who have no proven TB and have no contraindications to drug choices. There are several choices of regimens for TB prevention according to WHO recommendations:

1. Preventive Treatment with INH (PP INH) for 6 months, with a dose of INH 300 mg/day for 6 months with B6 at a dose of 25 mg/day.
2. Preventive Treatment using Rifapentine and INH, once weekly for 12 weeks (12 doses), may be used as an alternative. The dose used is INH 15 mg/BW for age > 12 years with a maximum dose of 900 mg and a dose of Rifapentine 900 mg for age > 12 years and BW > 50 Kg (for BW 32-50 kg = 750 mg)[11]

Studies have shown that extending tuberculosis therapy to 9–12 months reduces the chance of relapsing in HIV-positive individuals who are not on ART, although there is no survival benefit. There is debate about whether those with HIV are more likely to relapse than those without the virus. Although some have argued for a lengthier course of treatment, this suggestion has not been included in worldwide standards. Instead of intermittent dosage regimens, which are linked to a higher risk of treatment failure, relapse, and the development of rifampicin resistance, persons with HIV should receive daily treatment for tuberculosis. In HIV-negative individuals with tuberculosis, higher dosages of rifampicin (up to 50mg/kg per day) are being investigated to see if this would allow therapy to be shortened. Higher doses would need to be tested in HIV-positive individuals whether effective and safe in these patients due to potential for special safety and drug-drug interaction issues.[3,8]

ART need to be delayed in TB-HIV patients to prevent IRIS. The concept of IRIS as a result of immunological changes or improvements is widely accepted. Several studies have shown steady improvement in CD4 cell counts in patients with advanced HIV who have received HAART for more than 3-4 years. The phenomenon of IRIS-TB occurs because of increased inflammation in the tissues that can exacerbate TB symptoms or stimulate reactivation of latent TB. This increased inflammatory response may be due to an excessive increase in the number of antigens as a result of the innate or humoral response in IRIS-TB which includes: restoration of effector function of CD4+ T cells in granulomas that can kill MTB and release antigens, dysregulation of type 2 cytokine response (interleukin 12,4,5,13) into type 1 cytokines (interferon [IFN]-g, IL-2), and/or increased migration and activation of T cells at the site of infection. Previously, the body's immune response to MTB in HIV infection.[1]

IRIS is predisposed by a CD4 count 50 cells/mm3, greater CD4 counts on antiretroviral therapy (ART), higher pre-ART and lower on-ART HIV viral loads, severity of TB disease, particularly a high pathogen burden, and a shorter time between the start of TB and HIV therapies than 30 days. The emphasis is very much on not delaying treatment. However, despite the low current prevalence, insufficient early treatment or drop out in medication may increase the risk of multi drug resistance (MDR) TB development. MDR-TB continues to be a concern due to its prolonged duration and complex treatment as well as its increased risk of transmission among contacts and higher mortality rates in patients who simultaneously have HIV.[2,9,10]

4.Conclusion

Most common manifestation of TB-HIV co-infections are fever, weight loss, and cough Physical examination sometimes do not show signs that are specific to TB patients. It is recommended to screen TB in HIV patients because TB co-infection is common in HIV Patients. TB infection can be diagnosed by using sputum examination or GeneXPERT MTB/RIF. ARV administration is given at least 2 weeks after Anti Tuberculosis Drugs to prevent IRIS.

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