Anti-Tuberculosis Therapy after DRESS: Case Report

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ABSTRACT

Introduction. Anti-tuberculosis-induced DRESS (drug reaction with eosinophilia and systemic symptoms) is uncommon, and usually delayed in diagnosis. The patient has minor complain and the clinical presentation involves the side effect on their heart and skin. Antituberculosis-related DRESS may have been present, but it has been underdiagnosed and underreported for several years. Management including discontinuation of the suspected drugs and changing it with second line treatment become less effective. Identifying the causative drug in DRESS is very difficult, especially in antituberculosis drugs.
Case. A 34-year-old woman complains of having itch and redness throughout the body and fever. Two months before hospitalization, the patient was diagnosed with tuberculosis based on GeneXpert examination. Patients were given anti-tuberculosis drug therapy (OAT) which was 4 fixed drug combinations (FDC). Two weeks after taking the drugs, complains appeared. After 3 weeks the drug was stopped and in the next 1 week the patient's condition got worse, with itching and redness of the whole body accompanied by fever. Patients received treatment for 13 days with 125 mg/24-hour methylprednisolone therapy gradually reduced with OAT therapy levofloxacin 500 mg/24 hours and streptomycin 1 gram/24-hour IM (intramuscular).
Conclusion. DRESS triggered by OAT was very rare and underreported. The choice of therapy after DRESS needed to be well considered, because it increased the risk for a DRESS to return with more severe manifestations when re-administering the same drug. The management in tuberculosis patients with a history of DRESS was given with second-line OAT with treatment options based on the clinician's experience.

Keywords: DRESS (drug reaction with eosinophilia and systemic symptoms), anti-tuberculosis drugs (OAT), second-line therapy

Abstrak

***Pendahuluan**. Kejadian sindroma DRESS (*drug reaction with eosinophilia and systemic symptoms*) yang diinduksi oleh obat anti-tuberkulosis jarang terjadi dan diagnosisnya sering terlambat. Tampilan klinis penderita baru dapat dikenali karena efek samping hati dan kulit yang terjadi. Mengidentifikasi obat penyebab pada DRESS sangat sulit terutama pada obat anti-tuberkulosis. Manajemen dalam menghentikan obat yang dicurigai dan mengganti pengobatan menjadi lini kedua kurang efektif. Laporan kasus ini menjelaskan kejadian DRESS yang diinduksi anti-tuberkulosis, penanganan, dan pemilihan pengobatan anti-tuberkulosis pada pasien.*
***Kasus.** Seorang perempuan usia 34 tahun dengan keluhan demam disertai gatal dan kemerahan seluruh badan. Dua bulan sebelum masuk rumah sakit pasien didiagnosis menderita tuberkulosis berdasarkan pemeriksaan genexpert. Pasien diberikan terapi obat anti tuberkulosis (OAT) yaitu 4* fixed drug combination *(FDC), kemudian setelah 2 minggu pasien mengeluh gatal. Setelah 3 minggu terapi obat kemudian dihentikan dan 1 minggu setelah dihentikan obat, kondisi pasien bertambah berat yaitu gatal dan kemerahan seluruh tubuh disertai demam. Pasien mendapat perawatan selama 13 hari dengan terapi methylprednisolon 125 mg/24 jam diturunkan bertahap dengan terapi OAT levofloxacin 500 mg/24 jam dan streptomycin 1 gram/24 jam IM (intramuscular).*
***Kesimpulan**. DRESS yang dipicu oleh karena OAT kejadiannya sangat jarang dan sering tidak terlaporkan. Pemilihan terapi setelah DRESS perlu dipikirkan dengan baik, karena sangat berisiko untuk terjadinya DRESS kembali dengan*

manifestasi yang lebih berat bila memberikan obat yang sama. Pemilihan terapi pada pasien tuberkulosis dengan riwayat DRESS dapat diberikan dengan OAT lini kedua dengan pilihan terapi berdasarkan pengalaman klinisi.

Kata kunci: *DRESS* (Drug reaction with eosinophilia and systemic symptoms)*, obat anti tuberkulosis (OAT), terapi lini kedua*

Introduction

Drug Reaction Eosinophilia Systemic Syndrome (DRESS) is a rare and life-threatening drug reaction with a mortality rate of 2% to 10%.[1] A retrospective study reported 13.1% of sequelae of DRESS including autoimmune diseases and infections. Drugs that often lead to DRESS are anti-epileptic drugs, allopurinol, and antibiotics such as sulfonamides or minocycline. Although DRESS-induced anti-tuberculosis drugs are uncommon, the diagnosis is often late. The patients are only recognized for their side effects on liver and skin independently, so DRESS related to antituberculosis drugs may have occurred, but have been underdiagnosed and not reported for several years. Management to stop the drugs that are suspected and changing to second-line treatment becomes less effective. Identifying the causative drug in DRESS is very difficult, especially in antituberculosis drugs.[3]

Cases

A 34-year-old woman presented with itching and redness all over her body and had a fever. Two months before entering the hospital, the patient had been diagnosed with tuberculosis based on the GeneXpert examination. The patient was given anti-tuberculosis drug therapy (OAT) which is 4 fixed drug combinations (FDC) of rifampicin, isoniazid, pyrazinamide, and ethambutol. After 3 weeks, the drug therapy was then stopped and 1 week after the drug was stopped, the patient's condition got worse namely itching and redness of the whole body accompanied by fever. Patients received treatment for 13 days with 125 mg / 24-hour methylprednisolone therapy gradually reduced with OAT therapy levofloxacin 500 mg / 24 hours and streptomycin 1 gram / 24-hour IM (intramuscular).

Physical examination revealed compos mentis condition, tachycardia, fever, icteric sclera in both eyes, and maculopapular rash on the face, the abdomen, and the back (Figure 1). There was no mucous membrane involvement in the patient. Examination of both lung fields was normal. Abdominal examination showed palpable hepatomegaly 3 fingers under the arcus costa with a blunt edge surface with no bumps and soft consistency. Blood tests showed that eosinophil increased by 10% with eosinophil counts of 2351, mild thrombocytopenia (142.000), accompanied by an increase in the transaminase enzymes (SGOT 1124, SGPT 1297), and an increase in total bilirubin (5.54).

An assessment for DRESS was performed on this patient by using the RegiSCAR score, a score of 5 was obtained in this patient with a probable DRESS interpretation.

The patient was treated for 13 days and received initial dose of 125 mg / 24-hour methylprednisolone therapy. On the third day of therapy, the patient's skin condition got better, then the dose of methylprednisolone was gradually reduced. Patients get SNMC 2 ampoules / 24-hour later gradually reduced until the 10th day of care. Evaluation of laboratory examination showed that eosinophils significantly improved to 0.8% on the second day and 0%

on the day the patient discharged. Liver function examination was also improved with SGOT 489, SGPT 960 on the fourth day of treatment, and SGOT 59, SGPT 170, total bilirubin 2.39 at the day of the discharge.

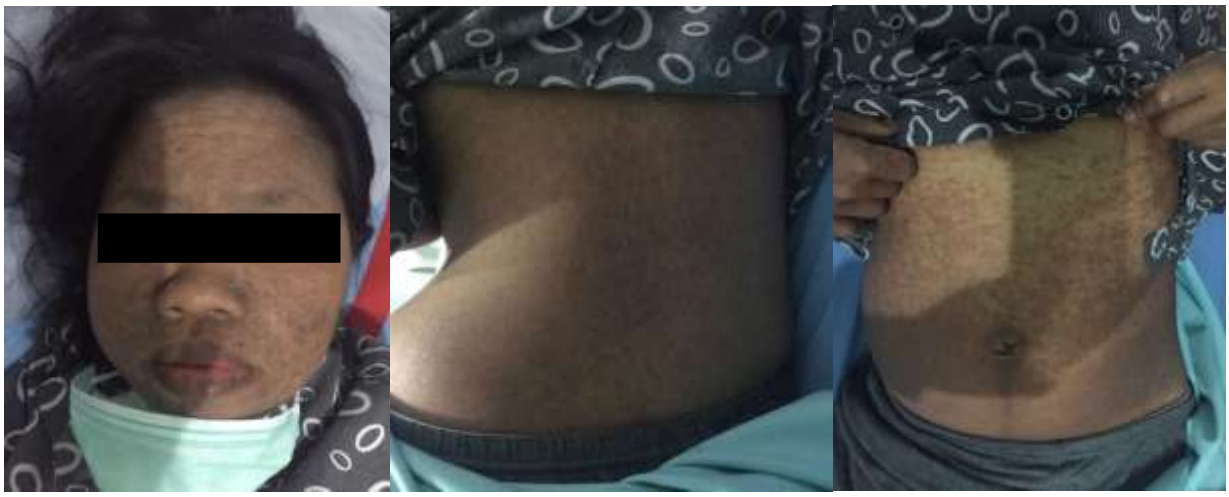

Figure 1. Maculopapular rash on the abdomen and the back

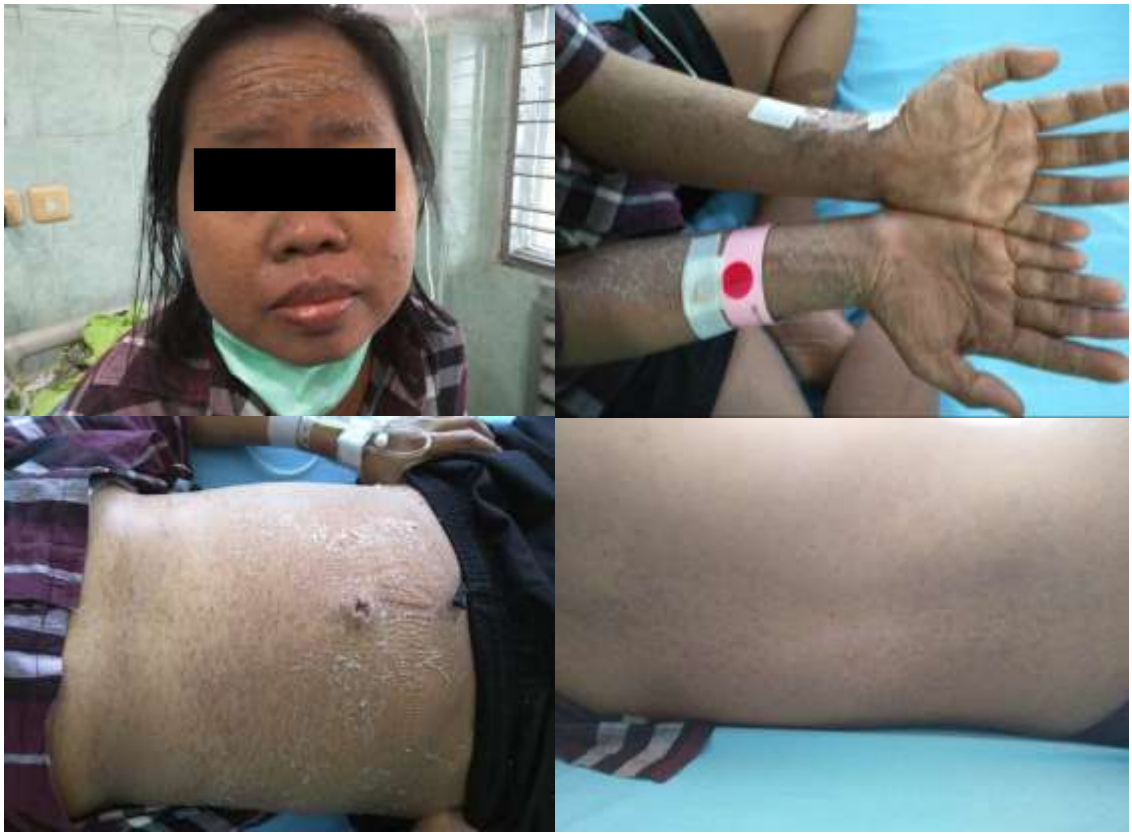

Figure 2. Skin appearance on the sixth day of treatment

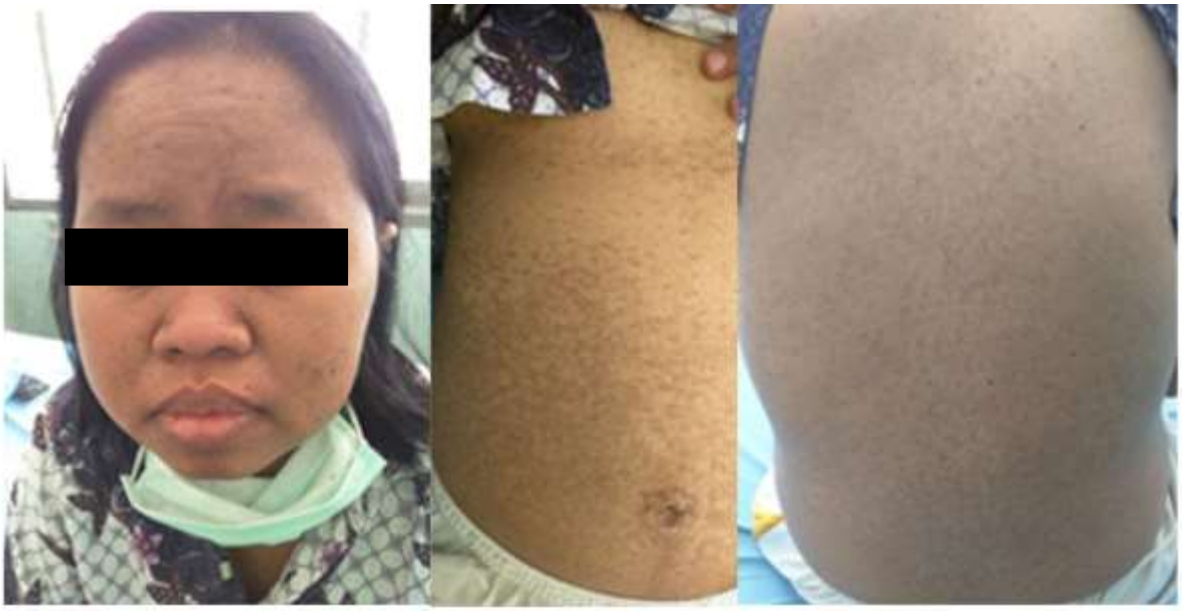

Figure 3. Skin appearance at discharge

This patient was planned to be given second line OAT with levofloxacin, streptomycin and ethambutol. Before taking the medicine, the patient underwent skin prick and intradermal test. Ethambutol showed positive result in both of the skin prick and intradermal tests, so the patient was only given levofloxacin 500 mg/24-hour and streptomycin 1 g/24-hour (intramuscular injection) as the second line OAT.

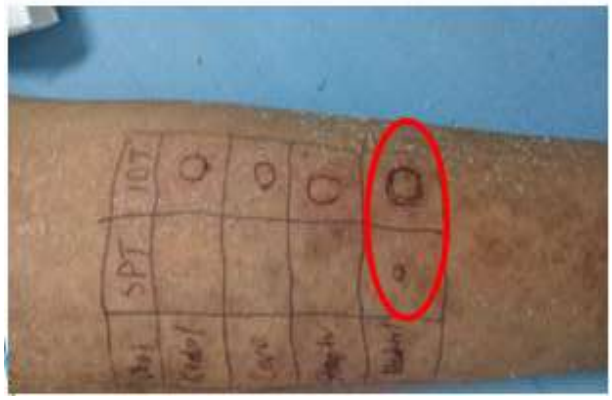

Figure 4. Skin prick and intradermal test showed positive results on ethambutol

Discussion

Drug Reaction Eosinophilia Systemic Syndrome (DRESS) is a rare and life-threatening drug reaction, with a mortality rate of 2% to 10%.1 A retrospective study reported 13.1% of DRESS sequelae including autoimmune diseases and infections. The drugs that often trigger DRESS are antiepileptic drugs, allopurinol, and antibiotics such as sulfonamides or minocycline. Although DRESS-induced anti-tuberculosis drugs are not common, the diagnosis is often late. Indeed, because they are well and are recognized for their side effects on liver and skin independently,

DRESS related to antituberculosis drugs may have occurred, but have been underdiagnosed and not reported for several years.

Antituberculosis-related DRESS occurs at recommended doses, which are not recommended dose-dependent effects. In most cases, other triggering drugs that are known to cause DRESS are associated with antituberculosis drugs. Vancomycin was suspected with antituberculosis drugs in 21 cases and allopurinol in 7 cases. Considering chronological criteria (time to first start symptoms after introduction of antituberculosis drugs, gradual improvement after cessation of both allopurinol and antituberculosis drugs) and absence of evaluation drug allergies, the role of antituberculosis drugs cannot be ruled out. In addition, in 1 case, after the initial diagnosis of allopurinol induced DRESS, reintroduction of the antituberculosis drug 2 months after the acute phase induced recurrence of DRESS.

A reintroduction of anesthetic drugs is an absolute contraindication after a diagnosis of DRESS. However, due to the nature and severity of tuberculosis infection, the lack of adequate therapeutic alternatives, and the balance of risks/benefits, the reintroduction of antituberculosis drugs can be justified. The reintroduction of antituberculosis drugs caused recurrence of clinical symptoms in 7 of 13 patients. Three of them developed a recurrence with DRESS criteria (skin lesions, eosinophilia, and visceral involvement). Further investigation to identify the suspected drugs and to observe intradermal tests with delayed readings can be done carefully by a trained team in DRESS management to help doctors optimize line treatment the second is tuberculosis infection.

Conclusion

DRESS triggered by OAT was very rare and often underreported. The choice of therapy after DRESS needed to be well considered, because it increased the risk for a DRESS to return with more severe manifestations when re-administering the same drug. The management in tuberculosis patients with a history of DRESS is given the second-line OAT with treatment options based on the clinician's experience.

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