Annals of Medicine and Surgery 81 (2022) 104512

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Case Report

Management of drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome in a female Indonesian with pulmonary tuberculosis: A rare case report

Aghnia Permatasari, Gatot Soegiarto *

Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga – Dr. Soetomo General Academic, Surabaya, Indonesia

ARTICLE INFO

Keywords:
Anti-tuberculosis drug
DRESS
Pulmonary tuberculosis
Systemic steroid

ABSTRACT

Background: Anti-tuberculosis drugs (ATD) induced DRESS syndrome is rarely reported, and its diagnosis and management are very challenging.

Case presentation: A 33-year-old woman presented with fever, maculopapular rashes, hypereosinophilia, and hepatic involvement, which occurred 4 weeks after a fixed-dose combination of first-line ATD containing rifampicin, isoniazid, pyrazinamide, and ethambutol. The patient's condition improved after the withdrawal of the drugs and administration of systemic steroids. Furthermore, active pulmonary tuberculosis was treated with second-line ATD containing streptomycin, levofloxacin, and ethambutol with no adverse reaction.

Discussion: Early identification of the causal drug for ATD-induced DRESS syndrome is essential, and it helps to facilitate the treatment process. In some cases, the change from first-line ATD to second-line in pulmonary tuberculosis patients with the syndrome can be considered after recovery with strict follow-up. Furthermore, the administration of systemic corticosteroids for tuberculosis treatment is still debatable, but it had positive effects in this study.

Conclusion: Early recognition and withdrawal of all suspected drugs are crucial in managing DRESS because the delayed diagnosis can be life-threatening. The administration of systemic steroids is effective against DRESS in pulmonary tuberculosis infection.

1. Introduction

Drug reaction with eosinophilia and systemic symptoms (DRESS) is one of the drug-induced severe cutaneous adverse reactions (SCARs) [1,2]. Furthermore, it is a rare condition but can also be life-threatening. The prevalence of DRESS ranges from 1 in 1000–10,000 people, with a mortality rate of 10–20% [3,4]. It is characterized by fever, skin eruption, hematological abnormalities, and systemic organ involvement with a long latency period of 2–8 weeks. These symptoms are often experienced after the intake of the culprit drug [5,6], such as anticonvulsant, allopurinol, non-steroidal anti-inflammatory drugs (NSAIDs), and antibiotics [3,7].

Anti-tuberculosis drug (ATD)-induced DRESS syndrome is uncommon, but the diagnosis is often delayed because it is underestimated and underreported for a few years. The condition is also difficult to manage because it involves an early withdrawal of suspected drugs for an extended period while trying to identify the main causal drugs [3,8]. Patient therapy is often changed to less effective second-line treatment. This condition can cause TB disease progression, treatment failure, and acquired drug resistance. Clinicians often hesitate to use systemic corticosteroids for DRESS because of their potential immunosuppression effect [9]. Therefore, this case report summarizes the diagnosis and management of first-line ATD-induced DRESS in a patient with lung tuberculosis. We report based on SCARE 2020 guidelines [10].

2. Case presentation

A 33-years-old Javanese female complained of maculopapular rashes, which started in the abdominal area and spread over the entire body surface. The patient also complained of nausea, vomiting, cough, fever of 38.7 °C, and a month history of pulmonary tuberculosis prior to admission, with GeneXpert® MTB/RIF sputum showing *Mycobacterium*

* Corresponding author. Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga – Dr. Soetomo General Academic Hospital, Jl. Mayjend Prof. Dr. Moestopo No. 6-8, Airlangga, Gubeng, Surabaya, East Java, 60286, Indonesia.
E-mail address: gatot_soegiarto@fk.unair.ac.id (G. Soegiarto).

https://doi.org/10.1016/j.amsu.2022.104512
Received 25 June 2022; Received in revised form 21 August 2022; Accepted 21 August 2022
Available online 27 August 2022

tuberculosis. The patient also had a history of first-line ATD with a fixed-dose combination consisting of 150 mg rifampicin, 75 mg isoniazid, 400 mg pyrazinamide, and 275 mg ethambutol, 3 tablets per day for 4 weeks. The family history has pulmonary tuberculosis but no similar complaints with the patient.

The physical examination revealed the presence of icteric sclera, lymph node enlargement, and maculopapular rash >50% of the body surface area, as shown in Fig. 1. Chest X-ray showed bilateral infiltrates in the lower lung lobes (Fig. 2). Laboratory examination showed anemia (Hb level of 10.9 g/dL) and leukocytosis (WBC of 16.27 $\times$ 10^3/mm^3). The patient also had hyper-eosinophilia with 1960/μL of eosinophil and thrombocytopenia with a platelet count of 106,000/L. Furthermore, atypical lymphocytes were also detected on the peripheral blood smear. The liver test results were abnormal with AST, ALT, albumin, direct and total bilirubin of 1145 U/L, 1474 U/L, 2.63 mg/dL, 3.21 mg/dL, and 3.76 mg/dL, respectively. Prolonged activated prothrombin time of 41.2s was also observed, along with elevated C-reactive protein of 87 mg/L. The progress of the laboratory results is presented in Table 1. Serological tests for viral infections, autoantibodies, and blood culture were negative. The clinical and laboratory findings fulfil the criteria for diagnosing definite DRESS syndrome according to the European Registry of Cutaneous Adverse Reaction (RegiSCAR), scoring 6.

The administration of ATD was temporarily stopped, and the patient was given intravenous methylprednisolone of 62.5 mg/day or 1.5 mg/kg/day for 7 days, along with 0.25% desoximetasone cream for skin rash. It was then followed by oral corticosteroid therapy at decreasing dose of 3 $\times$ 16 mg. On the fifth day, the clinical and laboratory findings and rash improved. Hence, the second-line ATD consisted of 750 mg streptomycin, 750 mg levofloxacin, and 800 mg ethambutol. The patient was discharged on the 8th day, and the skin lesions were gradually resolved. The pulmonary team advised continuing using tuberculosis treatment by replacing first-line ATD with second-line. There was improvement during the outpatient treatment, and no adverse reaction was observed, as shown in Fig. 2.

3. Discussion

Diagnosis of DRESS in the patient was established based on signs and symptoms, including maculopapular rash, fever of >38 °C, transaminase elevation, leukocytosis, atypical lymphocytes, eosinophilia, and lymphadenopathy at multiple sites after 4 weeks of tuberculosis treatment. Medicines most commonly associated with DRESS syndrome are anticonvulsants, antibiotics (particularly β-lactams), and allopurinol. Other medications that are known to be associated with DRESS include non-steroidal anti-inflammatory drugs, captopril, stabilizers, and antiretrovirals [11]. Furthermore, the diagnosis of definite DRESS syndrome is made when the RegiSCAR score >5 [9,12]. Management of ATD-induced DRESS syndrome includes early recognition, withdrawal of the offending drug(s), supportive treatment, and administration of corticosteroids [13,14]. Early identification of the causal drugs is essential to shorten the duration of treatment interruption. However, when tuberculosis treatment is needed immediately, specifically in severe conditions, 2-3 second-line ATD can be administered to minimize the impact of treatment interruption while awaiting drug re-challenge after recovery with strict follow-up [14,15].

In Indonesia, tuberculosis is an endemic disease and a significant health problem. Hence, it is essential to cure the affected patients and prevent their transmission, which helps to lower the incidence and prevalence rate [16,17]. Furthermore, the disease is more complicated when it occurs along with ATD-related DRESS syndrome because its management must consider the risk of acute liver failure associated with DRESS cases [18]. The patient in this study experienced signs and

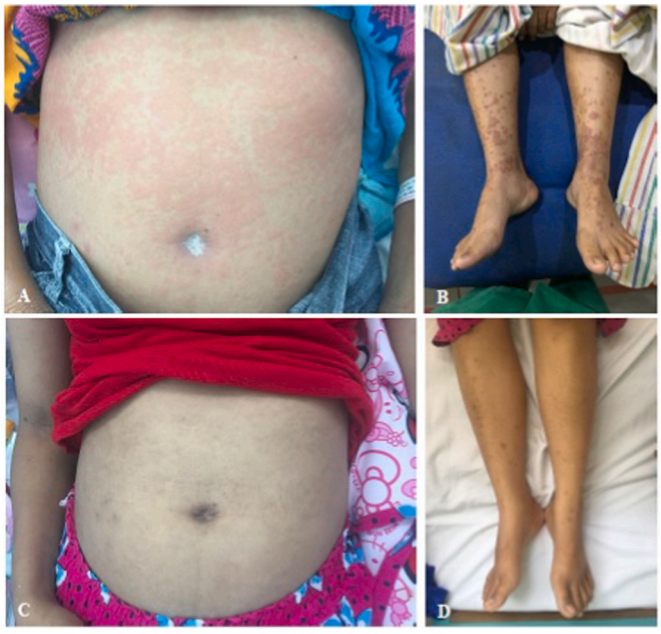

Fig. 1. The diffuse maculopapular rash was observed on the abdomen and lower extremities at admission (A, B) and resolution of skin rash when discharged (C, D).

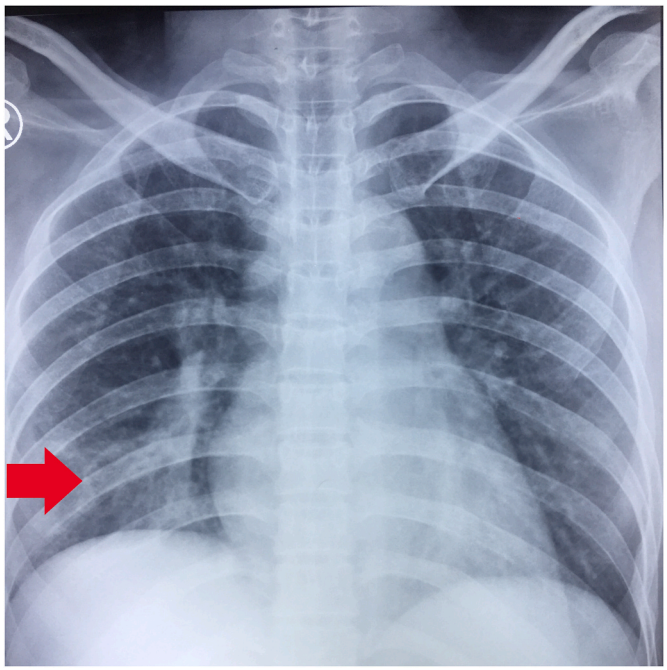

Fig. 2. Chest X-ray anterior-posterior showed infiltrate in right inferior lobe of the lung.

Table 1
Laboratory results of the patient.

Variable	Day 1	Day 2	Day 5	Day 8
Hb (g/dL)	10.9	10.5	10.0	10.3
WBC (cell count/uL)	16,270	18,930	15,420	12,340
Eosinophil (cell count/uL)	1960	2710	1880	400
PLT (cell count/uL)	106,000	173,000	200,000	248,000
AST (U/L)	1145	-	141	58
ALT (U/L)	1474	-	640	394
Direct Bilirubin (mg/dL)	3.21	-	-	1.1
Total Bilirubin (mg/dL)	3.76	-	-	1.58

Note: Hb, hemoglobin; WBC, white blood cells; PLT, platelet; ALT, alanine transaminase; AST, aspartate transaminase.

symptoms of liver disorders, such as icteric sclera, the elevation of AST, ALT, direct and total bilirubin of 1.145 U/L, 1474 U/L, 3.21 mg/dL, and 3.76mg/dL, respectively. This is consistent with a previous study that 75–94% of people with DRESS experienced liver disorders [14,19]. The ATD was temporarily stopped, and systemic steroids were administered at a dose >1 mg/kg/day. The dosage was lowered after 6–8 weeks and maintained for 2–3 months to prevent relapse [20,21]. Although systemic corticosteroid use is still debatable, its administration in the patient did not worsen pulmonary tuberculosis. The clinical and laboratory examination also showed improvement with a good prognosis. The administration of second-line ATD was then resumed for the patient.

4. Conclusion

A 33-years-old Javanese female complained of maculopapular rashes on the whole body after using first-line ATD for 4 weeks. The laboratory finding showed eosinophilia, atypical lymphocyte, and elevated liver enzyme. The RegiSCAR criteria obtained a score of 6, indicating DRESS occurrence. The first-line ATD was discontinued, while the patient received systemic steroid and supportive therapy. Subsequently, active tuberculosis was treated with second-line anti-tuberculosis drugs, consisting of streptomycin, levofloxacin, and ethambutol. The follow-up checkup showed the absence of clinical worsening.

Abbreviations

ALT = alanin aminotransferase; AST = aspartat aminotransferase; ATD = Anti-tuberculosis drug; DRESS = drug reaction with eosinophilia and systemic symptoms; Hb = hemoglobin, MTB = mycobacterium tuberculosis; RIF = rifampicin; SCARs = severe cutaneous adverse reactions; WBC = white blood cell.

Ethical approval

Not applicable.

Sources of funding

None.

Author contribution

All authors contributed to data analysis, drafting and revising the paper, giving final approval of the version to be published, and agreeing to be accountable for all aspects of the work.

Registration of Research Studies

1. Name of the registry: -.
2. Unique Identifying number or registration ID: -.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): -.

Guarantor

Gatot Soegiarto is the person in charge of the publication of our manuscript.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

Aghnia Permatasari and Gatot Soegiarto declare that they have no conflict of interest.

Acknowledgement

The authors thank the manuscript's editor, "Fis Citra Ariyanto".

References

[1] Anggraeni S. Damayanti, C.R. Sp, M. Hutomo, H. Sukanto, Severe cutaneous adverse drug reaction, Berkala Ilmu Kesehatan Kulit dan Kelamin 29 (2) (2017) 151–157, https://doi.org/10.20473/bikk.V29.2.2017.151-157.
[2] Damayanti, M.A. Umborowati, S. Anggraeni, C.R.S. Prakoeswa, M. Hutomo, H. Sukanto, Clinicoepidemiological profile of severe cutaneous adverse drug reaction: a retrospective study, Berkala Ilmu Kesehatan Kulit dan Kelamin 31 (1) (2019) 1–6, https://doi.org/10.20473/bikk.V31.1.2019.1-6.
[3] M. Allouchery, S. Logerot, J. Cottin, P. Pralong, C. Villier, B. Ben Saïd, Antituberculosis drug-associated DRESS: a case series, J. Allergy Clin. Immunol. Pract. 6 (4) (2018) 1373–1380, https://doi.org/10.1016/j.jaip.2017.11.021.
[4] P.T. Taweesedt, C.W. Nordstrom, J. Stoeckel, I. Dumic, Pulmonary manifestations of drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome: a systematic review, BioMed Res. Int. 2019 (2019), 7863815, https://doi.org/10.1155/2019/7863815.
[5] S.A. Walsh, D. Creamer, Drug reaction with eosinophilia and systemic symptoms (DRESS): a clinical update and review of current thinking, Clin. Exp. Dermatol. 36 (1) (2011) 6–11, https://doi.org/10.1111/j.1365-2230.2010.03967.x.
[6] L. Carneiro-Leão, I. Gomes, C. Freitas, E.S.M. Costa, R. Viseu, J. Cernadas, Multiple drug hypersensitivity syndrome to antituberculosis drugs: a case report, J. Invest. Allergol. Clin. Immunol. 30 (1) (2020) 70–71, https://doi.org/10.18176/jiaci.0446.
[7] P.R. Criado, R.F. Criado, J.M. Avancini, C.G. Santi, Drug reaction with eosinophilia and systemic symptoms (DRESS)/drug-induced hypersensitivity syndrome (DIHS): a review of current concepts, An. Bras. Dermatol. 87 (3) (2012) 435–449, https://doi.org/10.1590/s0365-05962012000300013.
[8] Q. Kizilbash, A. Vasquez, B. Seaworth, Strategies for successful treatment of active tuberculosis in the setting of DRESS on RIPE, Open Forum Infect. Dis. 5 (4) (2018) ofy062, https://doi.org/10.1093/ofid/ofy062.
[9] H. Kwas, E. Guermazi, I. Khouaja, A. Khattab, I. Zendah, H. Ghédira, Drug rash with eosinophilia and systemic symptoms (DRESS) induced by antituberculous treatment, La Tunisie medicale 94 (12) (2016) 900.
[10] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) guidelines, Int. J. Surg. 84 (2020) 226–230, https://doi.org/10.1016/j.ijsu.2020.10.034.
[11] J. Intarasupht, A. Kanchanomai, W. Leelasattakul, T. Chantrarat, A. Nakakes, W. Tiyanon, Prevalence, risk factors, and mortality outcome in the drug reaction with eosinophilia and systemic symptoms patients with cardiac involvement, Int. J. Dermatol. 57 (10) (2018) 1187–1191, https://doi.org/10.1111/ijd.14174.
[12] V. Descamps, S. Ranger-Rogez, DRESS syndrome, Joint Bone Spine 81 (1) (2014) 15–21, https://doi.org/10.1016/j.jbspin.2013.05.002.
[13] S.A. Martínez-Cabriales, F. Rodríguez-Bolaños, N.H. Shear, Drug reaction with eosinophilia and systemic symptoms (DReSS): how far have we come? Am. J. Clin. Dermatol. 20 (2) (2019) 217–236, https://doi.org/10.1007/s40257-018-00416-4.
[14] R. Cabañas, E. Ramírez, E. Sendagorta, R. Alamar, R. Barranco, N. Blanca-López, et al., Spanish guidelines for diagnosis, management, treatment, and prevention of DRESS syndrome, J. Invest. Allergol. Clin. Immunol. 30 (4) (2020) 229–253, https://doi.org/10.18176/jiaci.0480.
[15] A. Kapur, H.S. Rehan, Drug reaction with eosinophilia and systemic symptoms syndrome associated with ethambutol use: a case report, Curr. Drug Saf. 14 (3) (2019) 249–251, https://doi.org/10.2174/1574886314666190307150757.
[16] A. Fauzi, A. Permatasari, Disseminated tuberculosis with symptoms of decreased consciousness: a rare case in Indonesian male, Ann. Med. Surg. 73 (2012), 103209, https://doi.org/10.1016/j.amsu.2021.103209, 2022.
[17] W. Wijaksono, W. Koesoemoprodjo, Hemorrhagic pleural effusion in Indonesian male with pulmonary tuberculosis: a rare case, Int. J. Surg. Case Rep. 91 (2022), 106800, https://doi.org/10.1016/j.ijscr.2022.106800.
[18] P. Ichai, F. Saliba, F. Antoun, D. Azoulay, M. Sebagh, T.M. Antonini, et al., Acute liver failure due to antitubercular therapy: strategy for antitubercular treatment before and after liver transplantation, Liver Transplant. 16 (10) (2010) 1136–1146, https://doi.org/10.1002/lt.22125.

[19] Y.T. Cho, C.W. Yang, C.Y. Chu, Drug reaction with eosinophilia and systemic symptoms (DRESS): an interplay among drugs, viruses, and immune system, Int. J. Mol. Sci. 18 (6) (2017), https://doi.org/10.3390/ijms18061243.
[20] J.Y. Lee, S.Y. Lee, J.E. Hahm, J.W. Ha, C.W. Kim, S.S. Kim, Clinical features of drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome: a study of 25 patients in Korea, Int. J. Dermatol. 56 (9) (2017) 944–951, https://doi.org/10.1111/ijd.13667.
[21] T. Shiohara, Y. Mizukawa, Drug-induced hypersensitivity syndrome (DiHS)/drug reaction with eosinophilia and systemic symptoms (DRESS): an update in 2019, Allergol. Int. : official journal of the Japanese Society of Allergology 68 (3) (2019) 301–308, https://doi.org/10.1016/j.alit.2019.03.006.