Case Report

DRESS syndrome due to anti-TB drugs: A complex case with successful re-desensitization of group A drugs

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Abstract

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare, life-threatening adverse reaction caused by certain medications. Clinical findings usually include rash, fever, lymphadenopathy, and eosinophilia, and in some cases, they may affect major organs. This reaction caused by antituberculosis (TB) medication poses a public health risk due to treatment discontinuation, adherence, or success in cure. We present a 23-year-old female patient who developed DRESS syndrome as a result of group A anti-TB drugs (ATDs), an exceedingly rare occurrence. The patient's medication was successfully retrieved using a re-desensitization protocol.

Keywords: Antituberculosis medication, desensitization, drug hypersensitivity syndrome, tuberculosis

Introduction

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe, infrequent hypersensitivity reaction caused by certain drugs, primarily anticonvulsants, allopurinol, and antibiotics.[1] Its incidence is variable and is described between 1:1000 and 1:10,000 exposures to the drug, with a mortality rate of up to 20%.[2] DRESS syndrome usually presents between two and eight weeks and is characterized by rash, fever, lymphadenopathy, eosinophilia, and, rarely, involvement of major organs.[3]

The causation of DRESS syndrome by anti-TB drugs (ATDs) is an infrequent occurrence, and approximately 95% of cases are caused by first-line drugs, including isoniazid (INH), rifampicin (RIF), ethambutol (MEB), and pyrazinamide (PZA).[4] The literature discusses the mandatory withdrawal of the causative drug, but in the context of tuberculosis (TB), desensitization methods are available for recovery from ATD. This has the potential to improve the cure rate, reduce costs, and shorten the treatment time.[4,5] Therefore, the patient would benefit and could continue to receive regular monitoring and treatment under the supervision of the primary care physician.[6]

We describe an unusual case of DRESS syndrome caused by two group A drugs, linezolid (LZD) and levofloxacin (LFX). Furthermore, we outline the desensitization procedure used to reintroduce these drugs.

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Case History

We present a 23-year-old female patient from the Peruvian Coast with a history of pulmonary TB. Figure 1 displays the chronology of the disease. The patient was diagnosed with TB sensitive to RIF and INH by GeneXpert and started treatment with first-line drugs. After 26 days, the patient developed fever, pruritus, and redness on her torso, which subsequently spread to her limbs. As a result, the patient was hospitalized for DRESS syndrome (October until December 6, 2022). During hospitalization, first-line ATDs were suspended and an induction regimen was initiated by escalating dosages of "group A" (LZD and LFX) and "group D" (amikacin (AMK)) medications over 2 to 7 days. However, this approach was found to be ineffective as the DRESS syndrome persisted. As a result, she was referred to our hospital, where she was admitted to the pulmonology department.

During the patient's hospitalization, his vital signs were within normal limits upon admission. His skin has only a few crusty lesions. Chest and lungs: The chest has adequate amplexation and normal lung sounds without wheezing or rales. In the laboratory examination, the hemoglobin levels were 14.7 g/dL, while the leukocyte count was 9260 mm^3, and eosinophils and lymphocytes were 560 mm^3 and 2232 mm^3, respectively. Blood tests for liver enzymes were within the normal range. A chest computed tomography (CT) scan revealed cavitated and cystic nodular lesions, as well as the presence of tree in bud in the S1 and S2 segments of the right hemithorax [Figure 2].

The patient underwent rapid desensitization in an attempt to recover from RIF and INH. Unfortunately, this led to a diffuse cutaneous reaction, resulting in a generalized maculopapular rash [Figure 3], followed by desquamation and alterations in her laboratory profile, which included an elevation in eosinophils (3450 mm3) and serum IgE levels (>6000 IU/l). Consequently, it was decided to discontinue both medications. Five days after the adverse event, a slow desensitization protocol was initiated for the group A drugs to which the patient had prior exposure: moxifloxacin (MFX) and LZD, with increasing doses administered over a 7-day period [Table 1]. The patient was observed until February 21 and was eventually discharged with MFX, LZD, cycloserine (CS), and clofazimine (CFZ). During the patient's monthly follow-up visits, she demonstrated excellent adherence to the treatment regimen, and no further skin reactions or hypersensitivities were observed.

Discussion

DRESS syndrome due to ATD has been increasingly reported, despite its low incidence.[7] First-line ATDs account for over 75% of cases, and up to 48.1% of cases are attributable to two or more drugs.[8,9] This is consistent with what was reported in our patient, which was caused by RIF, INH, AMK, LFX, and LZD. Group A ATDs, such as quinolones and LZD, that have caused DRESS syndrome are exceedingly infrequent. According to Sharifzadeh *et al.*,[10] less than 2% of cases involve these drugs. Only one case report of LZD-triggering DRESS syndrome is described in the literature.[11] We believe that our patient is an exceptional case due to the rare hypersensitivity developed to the two drugs, which are the least uncommon in DRESS syndrome. Furthermore, the patient had no identifiable risk factors, such as autoimmune or infectious diseases.[12] What can be noted is the patient's eosinophilia (3450 mm^3) and elevated IgE value, which is in line with the extensive skin lesions. However, it is not a reliable predictor of more severe adverse events, as only severe skin reactions and mild liver dysfunction have been reported.[7,13]

The authors attribute this unusual occurrence to the genetic polymorphism of the patient's anti-TB and multiple genetic variants of their human leukocyte antigen (HLA), similar to raltegravir (HLA-B*53) or vancomycin (HLA-A*32:01).[14,15] For this reason, it is recommended to perform HLA typing in patients with DRESS syndrome as it notably decreases the occurrence of hypersensitivity-related adverse events.[16] In the context of TB, it is particularly vital as dropout rates of 4 to 10% have been reported solely due to skin reactions.[13,17]

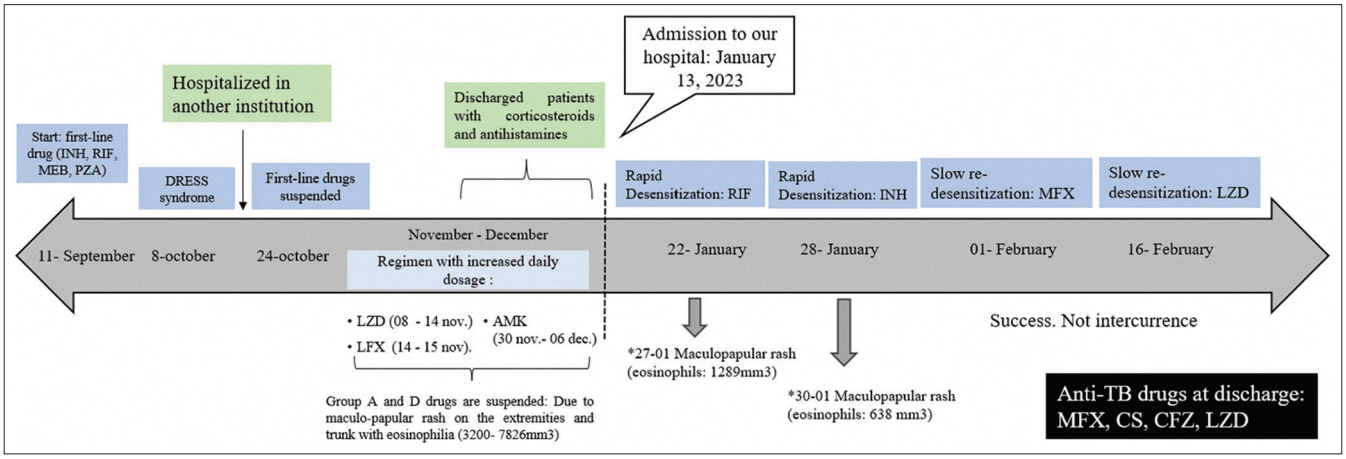

Figure 1: Timeline of anti-TB drug regimens used in the patient with DRESS syndrome

Table 1: Example of a successful "re-desensitization" protocol with linezolid

Start day	Time	Dose	Laboratory control**	Preparation
1	8:00 am	0.1mg	Hemogram and liver profile	For example, prepare 0.1 mg of LZD.
	8:00 pm	0.5mg		Dilute a linezolid tablet in 60cc of water
2	08:00 am	8mg		a) 600 mg–60 cc, therefore
	16:00 pm	16mg		b) 10 mg in 1 cc; we will add 9cc of water
3	8:00 am	100mg	Hemogram and liver profile	c) 10mg–10cc of water, therefore
	14:00 pm	100mg		d) 0.1 mg is 0.1 cc (use a 1 cc syringe)
	20:00 pm	100mg		
4	8:00 am	200mg		To get 8 mg of LZD.
	21:00 pm	300mg		Dilute a tablet in 60 cc of water
5	8:00 am	200mg	Hemogram and liver profile	a) 600 mg–60 cc, therefore
	22:00 pm	400mg		b) 10 mg in 1cc
6	8:00 am	600mg		c) 8 mg will be 0.8 cc (use 1cc syringe)
7	8:00a m	600mg*	Hemogram and liver profile	

*Adjust to the required dose, in the case of linezolid 10–20 mg/kg/day or only a 600mg dose once a day. **Before starting the medication

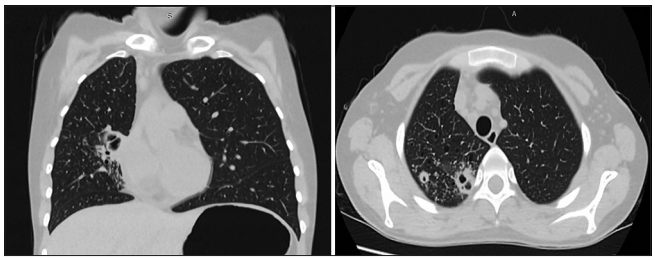

Figure 2: Chest tomography with signs of tuberculosis activity

Desensitization is a rarely used method to recover ATD due to the possibility of failure.[18] However, the literature reports varying success rates ranging from 70% to 100%, which may be influenced by the type of protocol employed (fast or slow desensitization).[19,20] It should be noted that the patient had prior exposure to LFX and LZD. Therefore, resensitization was attempted as desensitization to RIF and INH was unsuccessful. A comparable case was published by Buhari, G. *et al.*,[21] who achieved positive results (82%) upon readministration of the ATD. Furthermore, we did not encounter any significant adverse events or identify clinical predictors that would contradict the process of re-desensitization.[22] We believe these findings are important in preventing reliance on expert opinion when reintroducing ATDs that cause DRESS syndrome. Clearly, this must be performed by assessing the risks and benefits of each patient, and the decision will ultimately be made by the treating physician in an objective manner.

Finally, after the ATD is recovered, we suggest that the patient continue treatment under the primary care physician's supervision, aiming to ensure more frequent periodic evaluations to detect possible late hypersensitivity until the end of treatment. Likewise, in primary care centers, greater efforts should be made to timely identify a DRESS syndrome due to ATD to be referred to a more specialized care center.

Conclusion

We report the first documented case of DRESS syndrome caused by two group A ATD. It is possible to recover drugs through a resensitization protocol, which has a high success rate. The primary care physician should have adequate skills for the identification and follow-up of TB patients who have developed DRESS syndrome.

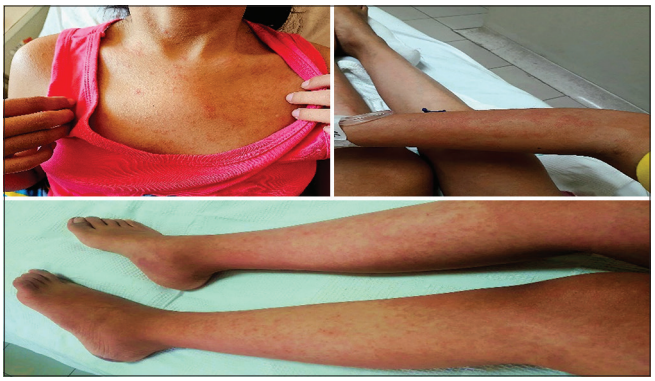

Figure 3: Urticarial-like maculopapular lesions on the trunk and extremities

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given consent for their images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and that every effort will be made to conceal his or her identity.

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Conflicts of interest

There are no conflicts of interest.

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