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## An unusual case of ATT induced DRESS syndrome

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### Abstract

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a severe drug-induced hypersensitivity reaction characterized by skin rash, fever, blood abnormalities, and multiple organ involvement. The diagnosis of DRESS syndrome is often delayed because of its variable presentation. DRESS syndrome induced by antituberculosis drugs has rarely been reported. A 45-year-old female patient taking anti-tubercular drugs since 2 weeks presented to our hospital with extensive skin lesion with mucosal involvement. The case responded well to treatment with systemic corticosteroids and withdrawal of isoniazid with no recurrence of lesions and further follow-up.

**Keywords:** anti-tuberculosis treatment, drug rash with eosinophilia and systemic symptoms syndrome, adverse drug reaction, isoniazid

### Introduction

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, 1<sup>st</sup> described and named by Bocquet in 1996 [1], is a severe, idiosyncratic, multisystem life threatening reaction characterized by the clinical triad of fever, rash, and internal organ involvement. The mortality rate is estimated to be 8%, especially among patients with liver involvement, so early recognition is imperative [2]. Drugs commonly associated with the development of DRESS syndrome include anticonvulsants, long-acting sulfonamides, and anti-inflammatory medications; however, there are only a few reported cases implicating anti-tuberculosis medications [3, 4]. DRESS has a relatively long latency period (between 2 and 8 weeks), and symptoms may persist for up to 2 weeks after the discontinuation of the culprit drug. Early diagnosis and immediate withdrawal of the suspected drug is a key tenet of management of DRESS [5]. We report a rare case of DRESS syndrome following anti-tuberculosis treatment.

### Case History

A 45 year old female presented with productive cough and breathlessness of duration 4 years. She was diagnosed as microbiologically confirmed pulmonary tuberculosis case and was started on DOTS Category 1 (Rifampicin, Isoniazid, Pyrazinamide and Ethambutol) according to her body weight on 24.2.18 from her home district in Uttarakhand.

After 2 weeks, she developed skin rashes with erythema & exfoliation of fingers, lower limbs and back along with mucosal erosions on lips, redness of eyes and fever with chills. Rashes were present on more than 80% of her body surface area.

On admission, ATT was discontinued. Symptomatic treatment emollients and anti-histaminics were initiated. Haemogram showed eosinophilic leucocytosis with an AEC of 4620. Liver enzymes were raised (SGOT: 296, SGPT: 217) with a normal renal function tests. (Table 1) The clinical suspicion of DRESS syndrome in this patient was substantiated with RegiScar score of 5 (Table 2) which gives a definitive diagnosis of the syndrome. Within a week of cessation of ATT, skin condition showed improvement, itching and exfoliation subsided. Systemic steroids were started, ATT was sequentially introduced beginning with isoniazid 50mg, lesions worsened within 24 hours of re-introduction which was then stopped. Further reintroduction of pyrazinamide, ethambutol and rifampicin was done sequentially and over a period of 3 weeks which was successful and no worsening of skin lesion or eosinophilia was seen. Patient was discharged in stable clinical condition on rifampicin, pyrazinamide, ethambutol with steroids and anti-histaminics cover. No distressing respiratory complaints present.

On follow up after 2 weeks and then at 1 month, patient was tolerating, ATT with no complaints. Smear conversion was achieved at 2 months and maintained at 4, 6 and 9 months.

**Table 1:** Investigations

Date	TLC	DLC	AEC	SGPT	SGOT	Creat
11.3.18	11000	P49 L8 E42 M1	4620	217	296	0.6
14.3.18				86	40	0.5
16.3.18	8000	P60 L18 E20 M2	1600			
24.3.18	9600	P40 L14 E42 M4	4032			
17.4.18	13000	P60 L28 E11 M1	1430			

**Discussion**

Drug reaction with eosinophilia with systemic symptoms is a rare, drug induced hypersensitivity reaction that includes skin eruptions, hematological abnormalities like eosinophilia, atypical lymphocytes and internal organ involvement.

The incidence of drug reaction with eosinophilia and systemic symptoms (DRESS) is unknown. A prospective seven-year study in a West Indian general population estimated an annual incidence of 0.9/100,000 [6]. DRESS may occur in children [7], but most cases occur in adults without sex predilection [8].

It is suspected in a patient who have received a new drug treatment in previous 2 to 6 weeks and presented with signs and symptoms of skin eruptions, fever and facial oedema and enlarged lymph nodes. In addition to meeting these criteria, DRESS syndrome is a diagnosis of exclusion. All these signs and symptoms were present in our patient. The clinical suspicion was substantiated by history of ATT initiation 2 weeks back with eosinophilia, hepatitis with RegiScar score (Table 2) of 5 which gives a definitive diagnosis of DRESS syndrome.

Severe bacterial and viral infections, malignancies, and autoimmune diseases should be ruled out before arriving at a definitive diagnosis [9]. DRESS may be associated with pulmonary manifestations like changes in chest X-ray and CT. This should be differentiated from pulmonary infection [10].

Other severe cutaneous drug eruptions (Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), Acute generalized exanthematous pustulosis (AGEP), Hyper eosinophilic syndrome), viral or bacterial infections, hypereosinophilic syndrome, Angio immunoblastic T cell lymphoma, lymphoma, Sézary syndrome, Acute cutaneous lupus erythematosus and autoimmune connective tissue disease may present with skin eruption, fever, and systemic symptoms and mimic DRESS [11, 12].

Identification and prompt withdrawal of the offending drug is the mainstay of treatment for patients with drug reaction with eosinophilia and systemic symptoms. Those with exfoliative dermatitis require fluid, electrolyte, and nutritional support. Additional measures include a warm and humid environment and gentle skin care with warm baths/wet dressings and emollients. For symptomatic relief of pruritus and skin inflammation, high or super high potency topical corticosteroid are recommended rather than systemic corticosteroids. Topical corticosteroids for symptomatic treatment of pruritus in patients with DRESS have not been evaluated in a randomized trial and their use is based upon clinical experience in other pruritic inflammatory skin conditions. In some case series, complete recovery is reported in patients without severe organ involvement treated with only supportive care including topical corticosteroid [13, 14, 15]. Few reports of rapid resolution of DRESS with organ involvement with a short course of oral cyclosporine [16, 17]. Intravenous immunoglobulins (IVIG) have been reported as beneficial in a few patients with DRESS and detrimental in others [18, 19]. Most patients with DRESS recover completely in weeks to months after drug withdrawal. Patients who recover from DRESS may have an increased risk of reaction to structurally unrelated drugs [20]. The risk appears to be higher in the first few months following DRESS occurrence. Retrospective studies have reported a mortality rate for DRESS of 5 to 10 percent [21]. The main causes of death are acute liver failure, multiorgan failure, fulminant myocarditis, or hemophagocytosis [22, 23, 24].

**Table 2:** Registry of Severe Cutaneous Adverse Reactions: Regi Scar Score. Scoring system for classifying drug reactions with eosinophilia and systemic symptoms (DRESS)

Item	Present	Absent
Fever 38.5 °C (101.3°F)	0	-1
Enlarged lymph nodes (>1 an size, at least two sites)	1	0
Eosinophilia: 2700 or 210 percent (leucopenia)	1	2
Atypical lymphocytes	1	0
Rash 250 percent of body surface area	1	0
Rash suggestive (22 of facial edema, purpura, infiltration, desquamation)	1	0
Skin biopsy suggesting alternative diagnosis	-1	0
Organ involvement: one	1	2
two or more		0
Disease duration >15 days	0	-2
Investigation for alternative cause (blood cultures, ANA, serology for Hepatitis viruses, mycoplasma, Chlamydia) 23 done and negative	1	0

Source: UpToDate.com

Total score <2: excluded; 2-3: possible; 4-5: probable; 26: definite.

Adapted from: Kardaun SH, Sidoroff A, Valeyrie-Allanore L, et al Variability in the clinical pattern of cutaneous side-effects of drugs with systemic symptoms: Does a DRESS syndrome really exist? *Erl Dennatol* 2007; 156:609.



**Fig 1:** Mucosal & Skin lesions seen in DRESS syndrome and resolution after cessation of offending drug.



**Fig 2:** Severe skin lesions of extremities seen in DRESS syndrome and resolution after cessation of offending drug.

**Conclusion**

ATT induced DRESS syndrome is not widely studied and might be largely under-diagnosed and can be mistaken as other drug reaction. Reliable diagnostic criteria and management guidelines should be constituted owing to high mortality rate of 10% [25]. One of the major issues is the management of smear positive patients who develop due to important anti tubercular drug like INH.

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