Anti-tubercular therapy causing Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome

Puneet Saxena[1], Deepak Chadha[2], Rishika Goyal[2]

Abstract

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is an idiosyncratic drug reaction following a characteristic long latency period. It is previously known as drug induced delayed multiorgan hypersensitivity syndrome (DIDMOHS) or drug induced hypersensitivity (DIHS). The syndrome is manifested by wide range of clinical symptomatology that hold a potential to be life threatening but still is under recognised. The major drugs that cause DRESS syndrome are anticonvulsants, followed by sulfonamides and many anti-inflammatory drugs.

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Correspondence to:
Dr Puneet Saxena,
Senior Professor and Unit Head
Department of Medicine
S.M.S. Medical college and Hospital
Jaipur
India

Email:
puneetsaxena96@yahoo.co.in

Introduction

Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) syndrome is distinct from other drug reactions because of presence of wide array of clinical features like presence of fever with skin involvement/cutaneous eruptions with internal organ involvement in the form of hepatitis, nephritis, pneumonitis and or carditis along with haematological alterations like leucocytosis with predominant eosinophilia and or presence of atypical lymphocytes with lymphadenopathy.[1,2,3] The features appear after a latency of weeks to months following drug exposure. The mortality rate associated with DRESS syndrome is around 8-10%, usually seen in patients with liver involvement.[4]

Case report

A 27 year old male with a diagnosis of pulmonary tuberculosis made one month prior and currently on antituberculosis treatment (rifampicin 450 mg, isoniazid 300 mg, pyrazinamide 750 mg twice a day and ethambutol 600 mg twice a day) presented to the emergency department with high grade fever associated with skin lesions from the past three to four days. They began as maculopapular eruptions initially on the dorsum of hands and shins of both legs and eventually spread to involve whole of the body surface but excluding the palms, soles and the face [Figure 1]. The rashes were confluent over the trunks, maintaining their discrete margins and are non tender but erythematous, dry and scaly in nature. There was no mucus membrane or genital involvement. The rashes showed desquamative changes over the trunk and extremities in the days after admission.

On examination the patient was febrile with marked yellowing of sclera, palms and soles and of mucus membranes. There was no obvious organomegaly. On ausculatation air entry was absent on the right side suggestive of pleural effusion. The pertinent laboratory investigations revealed leucocytosis with predominant eosinophilia associated with dearranged liver and kidney functions with coagulopathy in the form of dearranged PT-INR [Table 1].

Table 1 Laboratory parameters of our patient

Parameters	Day 1	Day 5	Day 14
Hemoglobin (g/dl)	13	12	14
TLC (/mm3)	32,000	23,000	11,000
Platelets (/mm3)	74,000	93,000	1,67,000
Absolute eosinophill count (/mm3)	2850	3020	202
Serum bilirubin (mg/dl)	17	13.8	3.2
SGOT (U/L)	4659	236	220
SGPT (U/L)	3201	2272	106
International normalized ratio (INR)	2.3	2.1	1.3
Blood urea	147	98	23
Serum creatinine	4.2	3.02	0.97

[1]Senior Professor, and Unit Head, Department of Medicine, S.M.S. Medical college and Hospital, Jaipur, India; [2]Junior Resident, Department of Medicine, S.M.S. Medical college and Hospital, Jaipur, India

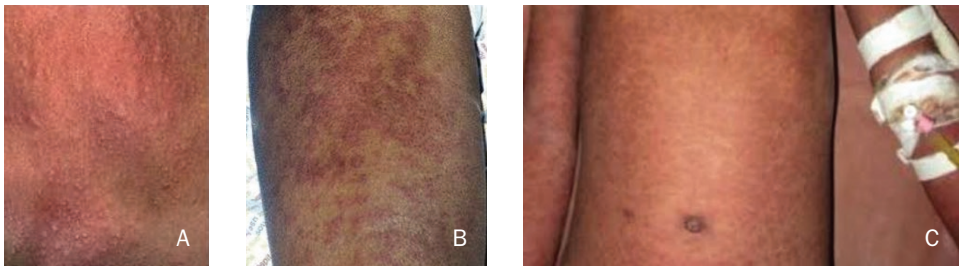

Figure 1 Rashes seen in our patient (A, B and C)

Chest X-ray revealed right upper lobe cavitatory lesion along with right side moderate pleural effusion that was further corroborated by ultrasonography. A diagnosis of possible drug reaction with multiorgan dysfunction was made on the clinical grounds. The ATT was completely stopped and broad spectrum IV antibiotics were initiated. The cultures of blood and urine were sterile and serum procalcitonin was in control range. The punch biopsy from the skin lesions was suggestive of drug reaction in the form of perivascular and periadnexal infiltrates of eosinophills associated with admixture of atypical lymphocytes. In context of skin changes with predominant eosinophilia and multiorgan dysfunction, the diagnosis of DRESS syndrome was finally made. The patient was put on steroids and was monitored closely for a period of 10-15 days and then was initiated on modified ATT. After two weeks, the leucocytosis along with dearranged liver and renal functions were restored to normal and most of the rashes disappeared.

Discussion

DRESS syndrome is an immune mediated idiosyncratic reaction following a drug use. It was first described in 1960s as hypersensitivity reaction to anticonvulsant (phenytoin) and so was named as anticonvulsant hypersensitivity syndrome that further evolved to be named as drug induced hypersensitivity (DIH) or drug induced delayed multiorgan hypersensitivity syndrome (DIDMOHS) and is currently referred to as drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome.[5] It is still under recognized despite its life threatening potential because it is easily confused with infectious, rheumatologic or neoplastic conditions. The diagnosis of DRESS syndrome involves following criteria:

1. widespred skin eruptions
2. fever
3. haematological abnormalities like eosinophilia > 1500/m m3, presence of atypical lymphocytes
4. systemic involvement like hepatitis, pneumonitis, nephritis, and or carditis

A skin biopsy is not a mandatory requirement for diagnosing DRESS syndrome.[4]

Genetic predisposition as being evident from positive family history along with defective drug detoxification and toxic metabolites accumulation triggers an immune mediated response that plays a role in the pathogenesis of the syndrome. The drugs most frequently seen in association with DRESS syndrome are anticonvulsants, antiinflammatory and antibiotics. [Table 2]

Table 2 Drugs implicated in DRESS syndrome

Anti convulsants	Phenytoin Carbamazepine Phenobarbitone Lamotrigine
Anti inflammatory	NSAIDS
Antibiotics	Sulfonamides Cotrimoxazole Pencillins Minocycline Nitrofurantoin
Anti retroviral agents	Abacavir Nevirapine
Others	Dapsone Allopurinol

Discontinuation of the offending drug is the only reliable treatment option available; however there are no reliable randomized controlled trials available for the usage of glucocorticoids in the treatment of DRESS syndrome.[6]

Conclusion

A possibility of DRESS though rare should always be borne in mind while encountering skin eruptions with eosinophilia and multiorgan dysfunction in the context of any newly started drug. It is essential to discontinue the offending agent.

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