International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 7; Issue 10(C); October 2018; Page No. 15878-15880
DOI: http://dx.doi.org/10.24327/ijcar.2018.15880.2912

Research Article

DRUG RASH WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS SYNDROME DUE TO ANTI-TB MEDICATION

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A R T I C L E I N F O

Article History:

Received 4th July, 2018
Received in revised form 25th August, 2018
Accepted 18th September, 2018
Published online 28th October, 2018

Key words:

DRESS, RIPE (Rifampin, Isoniazid, Pyrazinamide, and Ethambutol), SGOT, SGPT, Eosinophils.

A B S T R A C T

Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is a severe, idiosyncratic, multi-system reaction. This syndrome clinically characterized by fever, morbiliform eruption, pleural effusion, lymphadenopathy, cardiac & gastrointestinal disorders, renal and liver dysfunctions, hematological abnormalities**.** We report a case of DRESS syndrome from anti-TB therapy. A 58-year-old male with pulmonary TB presented with diffuse pruritic skin eruption, 6 weeks after starting Rifampin, Isoniazid, Pyrazinamide, and Ethambutol (RIPE) therapy. Physical exam was significant for diffuse, exfoliative erythematous macules with target lesions involving the entire skin surface, without mucosal involvement. Laboratory data was significant for SGOT, SGPT and eosinophil. RIPE therapy was discontinued and patient was started on topical corticosteroids, oral acyclovir drug. After skin biopsy patient was put on systemic corticosteroid. Patient was discharged on day 16 with oral prednisolone and second line TB therapy. After 1 month the rashes disappeared completely and eosinophils returned to normal levels.

INTRODUCTION

Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is a severe, idiosyncratic, multi-system reaction. The calculable incidence of this syndrome ranges from 1 in 1000 to 1 in 10,000 drug exposures. The onset of symptoms is commonly delayed, occurring 2-6 weeks after drug initiation. The clinical image of DRESS includes fever, morbiliform eruption, pleural effusion lymphadenopathy, cardiac and gastrointestinal disorders, renal and liver dysfunctions, hematological abnormalities such as eosinophilia and atypical lymphocytosis. The mortality of DRESS syndrome is approximately 10%. DRESS syndrome may occur in children, but most cases occur in adults**.** The most commonly implicated drugs are anticonvulsants, sulphonamides and anti-inflammatory medications. We report a case of DRESS syndrome due to anti-tubercular drug therapy.(1,2)

Case Report

A 58 -year-old man was diagnosed with pulmonary tuberculosis (TB) 2 months back & was put on anti-tubercular treatment; rifampin: 150mg, isoniazid: 75mg, ethambutol: 275mg, and pyrazinamide: 400mg once a day.

Then he presented to the clinic with diffuse skin eruption since past 15 days. Patient initially developed a pruritic rash & scaling that began on his face and eventually covered >90% of his body. Exfoliation of skin which was moderate, sticky& redness of skin were noted all over his body since 15 days. At some places the exfoliation left behind raw areas with oozing of watery fluid which was foul Smelling. Cutaneous examination revealed multiple dark coloured raised lesions all over his body, erythematous macular rash on face, Superficial Erosions with Crust Formation and serous exudates over per orbital region of the face and diffuse scaling over scalpnot extending beyond the hairline. Oral cavity examination showed hyperpigmented patch presented over palate. Similar patches were present on palms and soles. Inguinal lymph nodes were enlarged bilaterally. There was no conjunctival involvement.

Then patient was admitted to the skin ward of tertiary care teaching hospital. All four TB medications were immediately discontinued because of possible suspicion of allergic reaction. On admission, the laboratory findings showed significant increase in eosinophil count, SGPT and SGOT. Table 1.

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Table 1 Laboratory Investigation

Test	Day 1	Day 6	Day 14
Hemoglobin (g/dl)	10	11.4	11.5
WBC (/mm3)	8400	11000	10600
Neutrophils (%)	59	56	58
Absolute eosinophil count (%)	16	12	8.2
Platelets (/mm3)	174000	392000	370000
SGPT (U/L)	218	237	45
SGOT (U/L)	149	94	40
Alkaline Phosphate	236	169	161
Total Protein	6.8	7.5	6.9
Serum bilirubin (mg/dl)	0.9	0.9	1
Blood urea	25	18	NA

SGOT: Serum glutamic oxaloacetic transaminase,
SGPT: Serum glutamic pyruvic transaminase

Patient was started on topical steroid cream twice a day for erythema multiforme and oral Acyclovir in a dose of 400 mg TDS. Skin biopsy reported erythroderma with eosinophilic infiltration. He was then put on oral prednisolone 40 mg OD and later was discharged on day 16 with oral prednisolone and second line TB therapy. After 2 weeks of follow up there was regression in rashes and after 1 month the rashes disappeared completely. The eosinophils returned to normal levels on repeated laboratory tests.

DISCUSSION

The Drug Reaction with Eosinophilia and Systemic Symptom (DRESS) is a severe adverse drug-induced reaction. The diagnosis may be troublesome due to nonspecific clinical features. The syndrome usually mimics infectious, neoplastic, or rheumatologic conditions. Mortality rate is around 10-20%. Liver failure is the commonest cause of death.(1,3,4)The exact pathogenesis of DRESS syndrome is unknown. DRESS Syndrome is diagnosed using RegiSCAR diagnosis score. RegiSCAR program was developed by an international study group investigating severe cutaneous reactions (SCAR).(2,5)

RegiSCAR Diagnosis Score for DRESS

Features	No	Yes	Unknown
Fever (≥ 38.5°C)	-1	0	-1
Enlarged lymph nodes (≥2 sites, ≥1 cm)	0	1	0
Atypical lymphocytes	0	1	0
Eosinophilia	0		0
700-1499 or 10%-19.9%		1	
≥1500 or ≥20%		2	
Skin rash	0		0
Extent >50%	0	1	0
At least 2: edema, infiltration, purpura, scaling	-1	1	0
Biopsy suggesting DRESS	-1	0	0
Internal Organ Involvement	0		0
One		1	
Two or more		2	
Resolution in more than 15 days	-1	0	-1
At least 3 biological inv done and negative to exclude alternative diagnosis	0	1	0
Final score: <2 = no; 2-3 = possible; 4-5 = probable; >5 = definite			

Figure 2 RegiSCAR Diagnosis Score For DRESS (2,5)

This patient was classified as a definitive DRESScase according to the RegiSCAR scoring system. Typically, DRESS syndrome has a latency period usually 2-6 weeks after drug initiation. A retrospective study showed that the average time interval for drug reaction to appear was 20.7 days (range, 3-76 days).(6) In this case, anti TB treatment was started 6 weeks before the appearance of rash. The pathophysiology of DRESS syndrome is unclear. The pathological process could probably be drug-induced hypersensitivity caused by abnormalities in production and detoxification of its active metabolites. In this case the patient had history of drug intake for tuberculosis for last 2 months and it may be the cause of DRESS. A genetic predisposition may additionally exist, as proved by an increased risk in patients with a family history of DRESS syndrome. The syndrome is also associated with epoxide hydrolase deficiency, which results in accumulation of harmful metabolites, called arene oxides that may trigger an immunologic response. Association between human herpes virus 6 infection and the development of DRESS syndrome has been suggested in susceptible patients.(3,7,8) In this case human herpes virus was negative. The recovery from this condition has been reported to be slow, lasting many weeks to months; recurrences have also been reported.(9) Glucocorticoids stay the most widely used agents for treatment of DRESS syndrome and can result in clinical improvement. No randomized controlled trials of corticosteroids in the treatment of DRESS syndrome are available. Relapse can occur throughout the tapering of glucocorticoids.(10) Successful use of IV immune globulin in nevirapine induced DRESS syndrome has been reported.(7) In this patient, use of glucocorticoids helped to prevent progression of disease.

CONCLUSION

DRESS syndrome may be a serious drug reaction with high mortality due to systemic involvement. Early diagnosis, discontinue of the causative medication and avoid re-exposure is aappropriate management. Despite the fact that guidelines for appropriate management do not exist, steroids are routinely used in its management. Use of other modalities like N Acetyl Cysteine, plasmapheresis and rituximab has also been reported.

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How to cite this article:

Ashish Gupta *et al* (2018) 'Drug rash with Eosinophilia and Systemic Symptoms Syndrome Due to anti-tb Medication', *International Journal of Current Advanced Research,* 07(10), pp. 15878-15880.
DOI: http://dx.doi.org/10.24327/ijcar.2018.15880.2912

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