Probable Dress Syndrome: A Case of Drug Hypersensitivity in Young Man

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Abstract: Drug reaction with eosinophilia and systemic symptoms (DRESS) is one of drug hypersensitivity reaction. This condition shows a broad spectrum of clinical manifestations and severity. RegiSCAR scoring system is one of the diagnostic criteria exist for the diagnosis DRESS syndrome. The objective of this case report is to present a case of Probable DRESS syndrome without eosinophilia as one of Drug induced Severe Cutaneous Adverse Reactions (SCARs) in a young man. A 23 years old man admitted to hospital with generalized cutaneous rash and blood laboratory abnormality after consumed cefadroxyl, paracetamol and allopurinol for 2 weeks. Diagnosis Probable DRESS syndrome was made using RegiSCAR scoring system. Treatment with prolonged steroid systemic showed good clinical and laboratory result.

1 INTRODUCTION

Drug induced Severe Cutaneous Adverse Reactions (SCARs) include drug reaction with eosinophilia and systemic symptoms (DRESS), Acute Generalized Exanthematous Pustulosis (AGEP) and Stevens-Johnson Syndrome - Toxic Epidermal Necrolisis (SJS-TEN). DRESS syndrome is a rare case of drug reaction, comes with extensive rash, haemotology abnormalities and systemic involvement. This condition could be fatal with high mortality rate if it not handled immediately (Waseem et al, 2016; Choudhary et al, 2013).

Clinical manifestations in DRESS Syndrome is occuring about 2-8 weeks after introduction of the causative drug. Pruritic maculopapular and purpura cutaneous rash, with edema on fasial and extremities, fever and periferal lymphadenopathies are the usual symptoms of DRESS syndrome. Eosinophilia with atypical lymphocytes, elevated liver enzymes and the renal involvement were usually found in DRESS syndrome (Choudhary et al, 2013; Watanabe, 2018).

Making diagnosis for DRESS syndrome could be a challenging for the clinicians since the clinical manifestations are not immediately appeared after introduction of causative drugs (Choudhary et al, 2013). The diagnosis of DRESS syndrome is mainly clinical and clinician must consider the latency period and the diversity of signs and symptoms. Use of the term DRESS has been sometimes doubtful, because eosinophilia is not constantly found in clinical finding and the cutaneous and systemic signs are variable (Um et al, 2010). Making the right differential diagnosis of the type of SCARs is important since treatment, follow up and prognosis of different SCARs may not be the same (Casagrada et al, 2017). It is essential to consider this diagnosis since the life-threatening potential of DRESS syndrome is high and mortality is estimated as about10 percents (Choudhary et al 2013). The International study group investigating severe cutaneous reactions (SCAR) has developed RegiSCAR as one of diagnostic criteria for DRESS syndrome (Waseem et al, 2016).

The objective of this case report is to present a case of Probable DRESS syndrome without eosinophilia as one of Drug induced Severe Cutaneous Adverse Reactions (SCARs) in a young man.

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2 CASE

A 23 years-old man was admitted to hospital with three days history of generalized rash, starting on the face and then extending to the trunk and lower extremities. He also complained of swelling and erosion on the lips. From anamnesis there is history of fever 3 weeks before. He went to a clinic and doctor gave him antibiotic cefadroxyl and paracetamol. In addition he consumed allopurinol by himself. After 2 weeks consumed the medications, he realized had skin rash appeared on the face. He immediately stopped consumed all of the pills but rash still widespread to the trunk and ekstremities, and also he got swelling in his lips. On physical examination he presented fever of 390C with generalized erythema maculopapular rash, purpuric lesions on the trunk and lower extremities, edema and erosion on the lips. Lymphadenopathy was found on the coli region. Laboratory examination showed a slightly increased of Serum Glutamic Pyruvate Transaminase (SGPT) 33 µ/L (Normal value (NV) 5-31µ/L), blood ureum 62,2 mg/dl (NV 10-50 mg/dl) and the presence of lymphocyte athypical. According to RegiSCAR diagnosis criteria this patient's score of 5 that could be classified as Probable DRESS syndrome. Systemic corticosteroid therapy with methylprednisolone intravenous was started from the first day at a dose of 90mg (Body weight 85 kg) a day and gradually decrease over a week, and supportive local treatment for the skin and mucosal involvement. Any other medications were also stopped. Within a week we observed a significant improvement in clinical condition and laboratory result showed SGPT 14µ/L. We continued therapy with methylprednisolone oral and tappered off slowly for 2 weeks later.

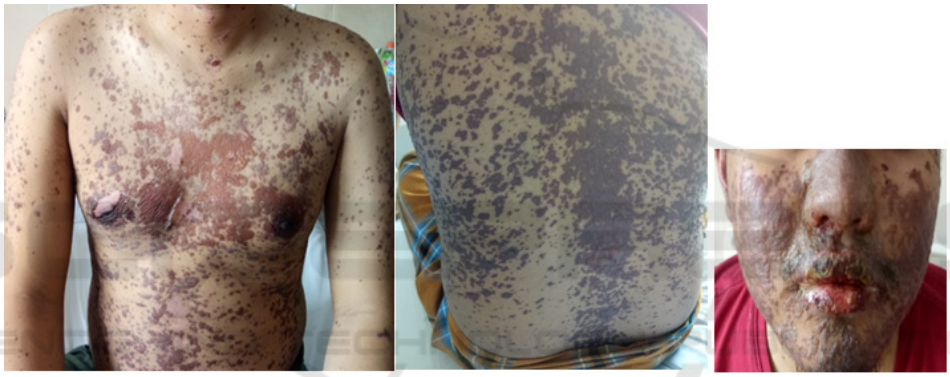

Figure 1. Cutaneous rash found on the trunk and face of the patient on 1st day

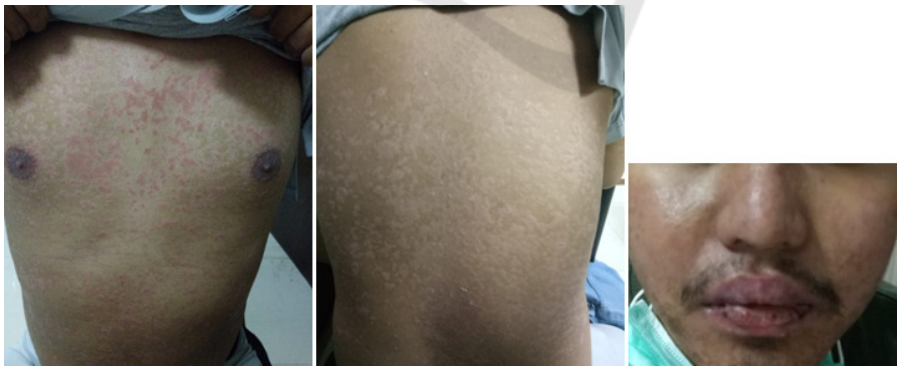

Figure 2. Clinical improvement after 3 weeks followed up

3 DISCUSSION

Drug reaction with eosinophilia and systemic symptoms (DRESS) was first defined in 1996 by Bocquet et al, present with extensive rash, fever, lymphadenopathy, hematologic abnormalities and organ involvement(Waseem et al, 2016). Use of the term DRESS has been inconsistent, since eosinophilia is not a constant clinical finding. Some literature use Drug-induced hypersensitivity syndrome (DIHS)/DRESS to include both the DIHS and DRESS syndrome. DHIS/DRESS was first

described by Chaiken et al in 1950. The most common clinical presentation of DHIS/DRESS are cutaneous eruption, fever and enlarged lymph nodes[4].

RegiSCAR scoring system is one of the most used diagnostic criteria exist for diagnosis of DRESS syndrome.This RegiSCAR was developed by an international study group investigating severe cutaneous reactions (SCAR).

Table 1. RegiSCAR diagnosis score for DRESS[1]

Features	no	Yes	Unknown
Fever (≥ 38,5^{0}C)	-1	1	-1
Enlarged lymph nodes (≥2 sites, ≥1cm)	0	1	0
Athypical lymphocytes	0	1	0
Eosinophilia:			
700-1499 or 10%-19,9%	0	1	0
≥ 1500 or ≥ 20%	0	2	0
Skin rash :			
Extent >50%	0	1	0
At least 2: edema, infiltration, purpura, scalling	-1	1	0
Biopsy suggesting DRESS	-1	0	0
Internal organ involvement:			
one	0	1	0
Two or more	0	2	0
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.			

According to RegiSCAR criteria this patient was diagnosed with Probable DRESS syndrome with score 5 for the presence of fever, athypical lymphocyte, extent skin rash >50% with purpuric lesions, facial edema and scalling with liver and renal involvement.

The onset of symptoms in DRESS syndrome is often delayed. It may took 2-8 weeks after introduction of triggering drug. Fever and rash were the most common symptoms. Lymphadenopathy in more than one sites is common and may occur in 75% cases (Choudhary et al, 2013; Corneli et al,2017). In this case, cutaneous rash appeared after 2 weeks consumed cefadroxyl, paracetamol and allopurinol. There was also fever and lymphadenopathy found only at coli region.

Systemic organ involvement was common in DRESS syndrome and liver is the most common organ involved. Liver failure is the most common cause of death. Renal abnormalities may occur in 11% patients, and commonly associated with allopurinol (Lens et al, 2010;Alexander et al,2013). In this case there was slightly elevated of SGPT and blood ureum that considered as the involvement of liver and renal organ.

Hematologic abnormalities in DRESS syndrome present with leukocytosis or leucopenia, eosinophilia or atypical lymphocytes. In this case there was no eosinophilia but we found the presence of atypical lymphocyte. The presence of atypical lymphocyte was found in 67% cases reported by the RegiSCAR study group, while eosinophilia was demonstrated by 95% cases (Watanabe, 2018; Corneli et al,2017). Studies about atypical lymphocyte found that this reactive lymphocyte have been associated with viral infection and plays an important role in the immune response (Cho.2017)

In this case there were some clinical entities share same features with Stevens-Johnson syndrome (SJS), the erosion of lip mucosal that usually found in SJS, and eosinophil count still in normal range. But, the delayed onset and the presence of fever and atypical lymphocyte could be directing our diagnosis to DRESS syndrome.

Some medicines had implicated in triggering DRESS syndrome, there were anticonvulsants (phenytoin,carbamazepine), antidepressants (desipramine, amitriptiline), sulpha drugs,NSAIDS, antibiotics (minocycline,linezolide, doxycycline, piperacilin-tazobactam), antivirals (abacavir, telaprevir, zalcitabine), ACE inhibitors (enalapril), Beta blockers (atenolol) and also allopurinol (Waseem et al, 2016). In this case we could not identified the causal drug with certainty, since our

patient consumed cefadroxyl (2nd generation of sephalosporin), paracetamol and allopurinol in the same time period. Literatures have been reported sefalosporine and allopurinol as potential trigger drugs in DRESS syndrome (Corneli et al,2017;Kim et al,2014).

The pathophysiology of DRESS is still unclear. It is hypothesized by a complex mechanism. Genetic factor might be plays a role in the incidence of drug hypersensitivity, including DRESS syndrome. Genetic deficiency of detoxifying enzymes needed to drug metabolism, and some Human Leucocyte Antigen (HLA) have been reported associated with drug hypersensitivity (Choudhary et al, 2013; Watanabe, 2018). Reactivation of Human Herpes Virus 6 (HHV-6), Epstein-Barr virus and cytomegalovirus have been suggested had a close relationship with DRESS syndrome[1,6]. However, the exactly mechanism for this viral reactivation theory is still unclear, is it direct effect of the defect in drugs metabolism or effect of the "cytokine storm" that could be found in viral reactivation (Waseem et al, 2016;(Cho et al,2017)

Systemic steroids have been used in the management of drug hypersensitivity cases, including DRESS Syndrome. In some cases of DRESS syndrome, relapses have been occured after withdrawal or tappering off. Dosage, duration of treatment and situations where steroids should be used are not clearly defined. Some authors suggest the use of corticosteroid systemic at a dose equivalent to 1 mg/kg/day of prednisone in case with sign severity including liver or renal involvement, pneumonia, or cardiac involvement. The use of systemic steroids for a prolonged period with a gradual decrease is important in DRESS syndrome to avoid relapses (Silva-Feistner et al,2017). In this case, we gave methylprednisolone intravenous at 90 mg starting dose and tappering off over a week, then continued with slow tappering off oral methylprednisolon. Our patient showed good improvement and there was no relapses after 2 weeks followed up.

4 CONCLUSION

We report here a case of Probable DRESS syndrome in a 28 years old man, probably due to cefadroxyl and/or allopurinol, which was diagnosed by RegiSCAR validation scores. Our patient showed good clinical result with steroid systemic therapy in a slowly tappering off within 3 weeks.

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