Original Article

RegiSCAR DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms) Validation Scoring System and Japanese Consensus Group Criteria for Atypical Drug-Induced Hypersensitivity Syndrome (DiHS): A Comparative Analysis

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Abstract

Context: Drug reaction with eosinphilia and systemic symptoms (DRESS) and drug-induced hypersensitivity syndrome (DiHS) represent the same spectrum of a drug reaction. **Aims:** To compare the clinical profile of patients diagnosed as definite/probable DRESS by the Registry of Severe Cutaneous Adverse Reaction (RegiSCAR) scoring system and as atypical DiHS by Japanese consensus group criteria. **Settings and Design:** We did a retrospective study in a tertiary referral center. **Materials and Methods:** We included patients who satisfied the criteria for definite/probable DRESS and/or atypical DiHS and who received inpatient care in our department from January 2011 to December 2018. We compared the clinical and laboratory findings in patients diagnosed by the two criteria. **Statistical Analysis:** Pearson Chi-square test was used to compare the proportion of patients with severe reactions diagnosed by the RegiSCAR DRESS validation scoring system and the Japanese consensus group criteria. **Results:** Among the 390 case records reviewed, 138 patients could be classified as definite/probable DRESS and/or atypical DiHS. Japanese criteria did not diagnose atypical DiHS in 88/137 (64.2%) patients with definite/probable DRESS. RegiSCAR scoring system made a diagnosis of definite/probable DRESS in 49/50 (98%) patients with atypical DiHS. A total of 58/138 (42%) patients had a severe reaction. RegiSCAR scoring system diagnosed 57/58 (98.3%) patients with severe reaction as definite/probable DRESS. A total of 32/58 (55.2%) patients with severe reactions were diagnosed as atypical DiHS. The difference was statistically significant (<0.001). **Conclusion:** Japanese criteria for atypical DiHS showed reduced sensitivity to diagnose definite/probable DRESS, and this included more than 40% of patients with severe DRESS.

Keywords: *Atypical drug-induced hypersensitivity syndrome, drug reaction with eosinophilia and systemic symptoms, Japanese consensus group criteria, RegiSCAR DRESS validation scoring system, severe reaction*

Introduction

A combination of rash, lymphadenopathy, and multiorgan failure long after starting dilantin was reported as dilantin hypersensitivity syndrome. Later, it became clear that a similar reaction pattern was noted following other drugs as well.[1,2] Over the years, different names and diagnostic criteria were proposed for this severe drug reaction. A consensus meeting of the RegiSCAR group and Japanese investigators has recommended DiHS/DRESS among the many suggested names for the reaction.[3]

Japanese consensus group in 2006, laid down seven mandatory features for DiHS [Table 1].[4,5] Reactivation of human herpesvirus 6 (HHV 6) was one of the seven essential features. As this facility is not available in some centers, they suggested a modification with five essential features to diagnose atypical DiHS.[4,5]

A RegiSCAR DRESS validation scoring system based on the RegiSCAR study group criteria was subsequently proposed. This classified suspected cases as definite (score 6 and above), probable (score 4 and 5), possible (score 2 and 3), and no DRESS (score <2).[6,7] The scoring system did not consider HHV 6 reactivation to diagnose DRESS [Table 1].

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Table 1: RegiSCAR DRESS validation score for manifestations of atypical/typical DiHS

Parameter considered by Japanese consensus group criteria	The possible manifestations (for each parameter) that can satisfy a diagnosis of DiHS	†Point on RegiSCAR DRESS validation scoring system for features of atypical/ typical DiHS	Minimum and maximum points that can be obtained by a patient with atypical/typical DiHS on RegiSCAR DRESS validation scoring system	
			Minimum	Maximum
Latent period between onset of drug intake and appearance of symptoms	More than 3 weeks	0	0	0
Duration of clinical symptoms after withdrawal of the offending drug	Prolonged clinical symptoms after withdrawal of the offending drug	0	0	0
Fever	Fever	0	0	0
Maculopapular rash	1. Maculopapular rash involving >50% of body surface area and does not satisfy features of rash suggestive of DRESS	+1 point for generalized maculopapular rash and -1 point for rash not showing 2/4 features suggestive of DRESS. Net score 0	0	+2
	2. Maculopapular rash and two of the four features among facial edema, rash resolving with psoriasiform desquamation, infiltrated skin lesions, and purpuric lesions on areas other than legs.	+1 point for generalized maculopapular rash and +1 point for rash showing 2/4 features suggestive of DRESS. Net score 2		
Internal organ involvement	1. One internal organ involvement	+1	+1	+2
	2. Two or more internal organ involvement	+2		
Hematological criteria	1. Leukocytosis >11,000 cells/mm^3	0	0	+3
	2. >5% atypical lymphocytes in peripheral smear	+1		
	3. Absolute eosinophil count >1500 cells/mm^3	+2		
	4. 1+2	+1		
	5. 1+3	+2		
	6. 2+3	+3		
	7. 1+2+3	+3		
*Cervical/generalized lymphadenopathy	1. Cervical lymphadenopathy	0	0	+1
	2. Generalized lymphadenopathy	+1		
*Human herpesvirus-6 reactivation	Human herpesvirus-6 reactivation	0	0	0
Total score	Atypical DiHS		1	7
	Typical DiHS		1	8

RegiSCAR: Registry of severe cutaneous adverse reactions; DRESS: drug reaction with eosinophilia and systemic symptoms; DiHS: drug-induced hypersensitivity syndrome. *Features are not considered for diagnosing atypical DiHS. †If at least three out of the four tests were performed and found negative (antinuclear antibody, infection with hepatitis A, B, and C viruses, infection due to Mycoplasma/Chlamydia, blood culture), one more point will be added on RegiSCAR scoring system

Though there exists a consensus on terminology, the criteria that define definite/probable DRESS and atypical DiHS show differences in the parameters assessed and the importance assigned to the individual parameter [Table 1]. Fever, maculopapular rash, and persistence of clinical symptoms after discontinuation of the offending drug are mandatory to diagnose typical/atypical DiHS. RegiSCAR scoring system does not assign any positive points for these three features. Instead, the absence of fever and resolution before 15 days are given one negative point each. The scoring system defined rash suggestive of DRESS as a rash with two of the four features (facial edema, resolution with psoriasiform desquamation, infiltrated skin lesions, and purpuric lesions involving areas other than legs). One point is given to rash suggestive of DRESS. When the rash does not show two of the four features, one negative point is awarded.[4-7] Typical and atypical DiHS are not differentiated by the scoring system as the additional features (cervical/generalized lymphadenopathy and HHV-6 reactivation) for typical DiHS, may not always earn any extra points.[4-7] Scoring system

assigns one point only if lymphadenopathy of more than 1 cm in size affects two anatomical regions. A patient who satisfies the criteria for atypical DiHS can get a score anywhere from 1 to 7 (no DRESS- definite DRESS) on the RegiSCAR scoring system [Table 1] by virtue of the manifestations assessed by the Japanese criteria. A patient with typical DiHS may obtain a score of 1–8 (no DRESS- definite DRESS).

Different studies/case reports have adopted different criteria to define their study population.[8-11] Shiohara *et al*.[3] suggested that DRESS/DiHS could be part of the same spectrum with DRESS including clinically milder forms of DiHS as well, as a diagnosis of definite DRESS does not require all the essential features for typical/atypical DiHS. Ushigome *et al*.[12] suggested that DRESS validation score may be used when HHV-6 evaluation is unavailable as they found the diagnosis of DiHS was consistent with that of definite or probable DRESS after analyzing 30 cases of DiHS. But there is a dearth of studies that have assessed the comparability of the two criteria from the country. Moreover, we did not come across any previous studies that assessed the comparability of the RegiSCAR scoring system and Japanese criteria for atypical DiHS.

In this retrospective analysis, we have compared the clinical profile and laboratory parameters of patients diagnosed with probable/definite DRESS by the RegiSCAR DRESS validation scoring system and as atypical DiHS by the Japanese consensus group criteria. We also tried to find out whether the patients diagnosed by the RegiSCAR scoring system and the Japanese consensus group criteria represent the same spectrum of disease with the latter diagnosing severe forms of the reaction.

Materials and Methods

With institutional ethics committee approval, we reviewed the case records of consecutive patients who were diagnosed as probable adverse cutaneous drug reactions by the World Health Organization causality assessment (drug re-challenge was not performed) from January 2011 to December 2018. We applied the RegiSCAR scoring system and the Japanese consensus group criteria to this cohort.[4-7] We included patients with a RegiSCAR score of 4 or more (definite/probable DRESS) and/or patients who satisfied the Japanese consensus group criteria for atypical DiHS. We excluded case records with insufficient data.

We collected data regarding age, gender, offending drug, the time interval between the onset of drug intake and the appearance of initial symptoms (latent period) of drug reaction, clinical findings, total leukocyte count, absolute eosinophil count, percentage of atypical lymphocytes in the peripheral smear, liver and renal function tests, and other laboratory investigation results in each patient using a pre-set proforma.

We defined severe reaction in the study participants (definite/probable DRESS and/or atypical DiHS). The patients with signs of severity (transaminases >5 times above normal, renal/cardiac involvement, pneumonia, hemophagocytosis) or life-threatening signs (hemophagocytosis with bone marrow failure, encephalitis, severe hepatitis, renal failure, respiratory failure) as defined by the French Society of Dermatology or patients who had a fatal outcome due to the drug reaction were considered to have a severe reaction.[13]

The data were entered in Microsoft Excel and analyzed using SPSS Inc IBM company version 18 Chicago, SPSS Inc. (United States of America). We compared the proportion of severe reaction observed in definite/probable DRESS and atypical DiHS using the Pearson Chi-square test. A *P* value of less than 0.05 was considered statistically significant.

Results

We reviewed the case records of 413 patients who required inpatient care for an adverse cutaneous drug reaction. We excluded 23 cases sheets with insufficient data.

A total of 138 (138/390, 35.4%) patients who had either a score of four or more on the RegiSCAR scoring system and/or who satisfied the Japanese criteria for atypical DiHS constituted the study population. The study participants included 80 females and 58 males with a female to male ratio of 1.4:1. The age of the study participants ranged 2–77 years (mean age 39. 9 ±+18.9 years).

RegiSCAR DRESS validation scoring system diagnosed 137/390 (35.1%) cases as DRESS {53/390 (13.6%), and 84/390 (21.5%) patients were definite and probable DRESS, respectively}. Fifty patients (12.8%) were atypical DiHS. Among the 50 cases of atypical DiHS, 29 (58%) had a score of 6 or more on the RegiSCAR DRESS validation scoring system (definite DRESS), 49 (98%) had a score of 4 or more (definite/probable DRESS), and 1 patient (2%) had a score of 2 (possible DRESS). A total of 29/53 patients (54.7%) with definite DRESS and 49/137 (35.8%) patients with definite/probable DRESS satisfied the Japanese criteria for atypical DiHS. The concordance between Japanese criteria and RegiSCAR scoring system was 77.2% when DRESS was diagnosed for a score of 4 or more (definite/probable DRESS). When DRESS was diagnosed for a score of 6 or more (definite DRESS), the concordance was 88.5% [Table 2].

The latent period, clinical profile, and investigation results documented among the study participants are shown in Table 3.

Four (4/137, 2.9%) and two patients (2/137, 1.5%) diagnosed as definite/probable DRESS did not manifest fever and rash, respectively.[9]

Ninety study participants (90/138, 65.2%) had the involvement of internal organs. Eighty seven (87/138, 63%) patients had hepatic involvement

Table 2: Concordance between the diagnosis by RegiSCAR DRESS validation scoring system and Japanese consensus group criteria

Study participants	Definite DRESS (*n*=53)		Definite/probable DRESS (*n*=137)	
	No	Yes	No	Yes
Japanese criteria for atypical DiHS *n*=50				
No	316	24	252	88
Yes	21	29	1	49
Concordance between the criteria	88.5%		77.2%	

RegiSCAR: Registry of severe cutaneous adverse reactions; DRESS: Drug reaction with eosinophilia and systemic symptoms; DiHS: Drug-induced hypersensitivity syndrome

Table 3: Latent period, precipitating drug and clinical features in patients with definite DRESS, definite/probable DRESS and atypical DiHS

Clinical features		RegiSCAR DRESS validation score 6 or more Definite DRESS *n*=53	RegiSCAR score DRESS validation 4 or more Definite/ probable DRESS *n*=137	Atypical DiHS *n*=50
Offending drug n (% of total)	Anticonvulsants	36 (67.9%)	82 (59.9%)	37 (74%)
	Antibiotics	3 (5.7%)	22 (16.1%)	0 (0%)
	Sulfasalazine	6 (11.3%)	9 (6.6%)	6 (12%)
	Dapsone	0 (0%)	5 (3.6%)	3 (6%)
	Isoniazide	1 (1.9%)	4 (2.9%)	0 (0%)
	Allopurinol	3 (5.7%)	4 (2.9%)	2 (4%)
	Others	4 (7.5%)	11 (8%)	2 (4%)
Latent period	3 weeks or less	18 (34%)	56 (40.9%)	0 (0%)
	More than 3 weeks	35 (66%)	81 (59.1%)	50 (100%)
Rash suggestive of DRESS		49 (92.5%)	131 (95.6%)	48 (96%)
Morphology of predominant rash	Maculopapular	47 (88.7%)	115 (83.9%)	50 (100%)
	Erythroderma	2 (3.8%)	10 (7.3%)	0 (0%)
	Others	3 (5.7%)	10 (7.3%)	0 (0%)
Lymphadenopathy	No	34 (64.2%)	102 (74.5%)	38 (76%)
	1 cm size involving 2 or more sites	18 (34%)	35 (25.5%)	12 (24%)
Internal organ involvement	No	0 (0%)	37 (27%)	0 (0%)
	One organ	45 (84.9%)	91 (66.4%)	43 (86%)
	Two or more organs	8 (15.1%)	9 (6.6%)	7 (14%)
Absolute eosinophil count	0-699 cells/mm^3	6 (11.3%)	27 (19.7%)	13 (26%)
	700-1499 cells/mm^3	21 (39.6%)	53 (38.7%)	24 (48%)
	1500 cells/mm^3 or above	26 (49.1%)	57 (41.6%)	13 (26%)
Atypical lymphocytes in peripheral smear	Nil	20 (37.7%)	74 (54%)	18 (36%)
	0%-5%	20 (37.7%)	40 (29.2%)	16 (32%)
	more than 5%	13 (24.5%)	23 (16.8%)	16 (32%)
Total leukocyte count	11,000 cells/mm^3 or below	13 (24.5%)	40 (29.2%)	9 (18%)
	Above 11,000 cells/mm^3	40 (75.5%)	97 (70.8%)	41 (82%)
Time taken for resolution	<15 days	0 (0%)	0 (0%)	0 (0%)
	15 days or more	53 (100%)	137 (100%)	50 (100%)
Severe reaction		36 (67.9%)	57 (41.6%)	32 (64%)

DRESS: Drug reaction with eosinophilia and systemic symptoms; DiHS: Drug-induced hypersensitivity syndrome

{isolated rise in liver transaminases (68/138, 49.3%), isolated hyperbilirubinemia (2/138, 1.4%), or combination of both (17/138, 12.3%)}. We found hyperbilirubinemia in eight of the 50 cases (8/50, 16%) of atypical DiHS and 11 of the 88 (12.5%) cases that were not atypical DiHS. The difference was not significant. Fourteen patients (14/138, 10.1%) had elevated liver transaminases in the range of 81–100 IU/mL, and six of them had definite DRESS (6/53, 11.3%). Seven patients (7/138, 5.1%) had pneumonitis, six developed nephritis (6/138, 4.3%), and four (4/138, 2.9%) had hepatosplenomegaly.

Seventeen (17/53, 32.1%) cases of definite DRESS, showed all except one feature of atypical DiHS {11 patients (11/53, 20.8%) had a latent period of fewer than 3 weeks, four did not show maculopapular rash (4/53, 7.5%), and two (2/53, 3.8%) had liver transaminases in the range of 81–100 IU/mL}. When definite and probable DRESS

considered together, 43 out of the 88 (48.9%) patients that were not atypical DiHS, showed all except one feature of the latter {eighteen (18/88, 20.5%) had a latent period of fewer than 3 weeks, fifteen (15/88, 17%) did not show internal organ involvement, four (4/88, 4.5%) showed elevated transaminases which weres in the range of 81–100 IU/mL, four did not show maculopapular rash (4/88, 4.5%), and two (2/88, 2.3%) failed to satisfy the hematological criteria}.

All the patients received systemic corticosteroids (0.5 mg–1 mg/kg body weight prednisolone or its equivalent) after the withdrawal of the offending drug. The duration of treatment with systemic corticosteroids ranged 25–154 days (mean 39.6+_17.3 days). Two patients (2/138, 1.5%) had a fatal outcome. One could be classified as both definite DRESS and atypical DiHS, whereas the other was probable DRESS and atypical DiHS.

Fifty eight (58/138, 42%) patients could be classified as severe reaction [Table 4]. RegiSCAR scoring system diagnosed 57/58 (98.3%) patients with severe reaction as definite/probable DRESS. A total of 32/58 (55.2%) severe cases could be diagnosed as atypical DiHS [Tables 3 and 4]. The difference was significant (*P*-value <0.001).

Discussion

In this retrospective analysis of 138 patients, we found that the Japanese criteria diagnosed less number of cases. A total of 48.9% of the 88 cases of probable/definite DRESS that did not satisfy the Japanese consensus group criteria showed four out of the five essential features for atypical DiHS.[4,5] One-fifth of these 88 patients were not diagnosed as atypical DiHS, only because of a latent period of 3 weeks or less. Soria *et al*.[8] have suggested that a shorter latent period should not be against a diagnosis of DRESS in patients who satisfy the other features. We found a latent period of 3 weeks or less in 34% ofthe patients with definite DRESS [Table 3]. The Japanese criteria failed to diagnose several patients with comparable features by also insisting on the presence of maculopapular rash and by defining elevation of liver transaminases as >100 IU/mL as the cutoff, instead of more than two times the upper limit as adopted by the RegiSCAR scoring system.[4-7]

We adopted atypical DiHS instead of typical DiHS as the inclusion criteria due to the lack of facility to test for HHV 6 reactivation. This is unlikely to have an effect on the sensitivity of Japanese criteria to diagnose DRESS, as diagnosis of typical DiHS requires all the five features of atypical DiHS in addition to cervical/generalized lymphadenopathy and HHV 6 reactivation. Previous authors proposed the criteria for atypical DiHS as they noted that those who satisfied the criteria for atypical DiHS, on most occasions, satisfied the additional criteria for typical DiHS as well.[14] We did not include patients with possible DRESS in the analysis as Cacoub *et al*.[15] in a literature search of 172 cases reported that possible DRESS differed from definite/probable DRESS. Others also noted that DiHS was comparable to definite/probable DRESS.[12] Previous authors have considered typical and atypical DiHS as definite and probable DiHS, respectively.[3] A total of 49/50 (98%) cases of atypical DiHS in the study, showing a RegiSCAR score of 4 or more was also supportive of these findings. The clinical and laboratory findings in definite/probable DRESS in the study showed varying combinations of symptoms similar to those observed in atypical DiHS [Table 3]. We did not find the RegiSCAR score of 4 or more to be less specific than the Japanese criteria to diagnose DRESS/DiHS. On the contrary, we observed the Japanese criteria missed many cases with comparable features by insisting on certain essential features.

We adopted signs of severity or life-threatening signs put forth by the French dermatology association or a fatal outcome due to the drug reaction to define severe reaction.[13] We did not consider the duration of treatment to define disease severity as the initial dose of systemic steroids was not uniform in all the patients (varied from 0.5 to 1 mg/kg body weight). As systemic steroids were tapered and withdrawn, a high initial dose itself could prolong the duration of treatment.

We tried to assess whether atypical DiHS represented severe DRESS. We found that atypical DiHS failed to diagnose more than 40% of study participants with a severe reaction. Among the features considered to diagnose typical DiHS, only human herpesvirus (HHV)-6 reactivation, is well known for its association with severe DRESS.[3,14] Diagnostic definition of typical/atypical DiHS is not consistent with the signs of severity/life-threatening signs put forth by the French Society of Dermatology or the parameters identified as markers of disease severity

Table 4: Clinical manifestations in definite/probable DRESS and/or atypical DiHS with severe disease

Clinical manifestations in study participants with severe disease (*n*=58)	Patients with severe reaction who satisfied the criteria for definite/probable DRESS (*n*=57)	Patients with severe reactions who satisfied the criteria for atypical DiHS (*n*=32)
Liver transaminases >5 times the upper limit of normal and/or hyperbilirubinemia (*n*=55)	54 (98.2%)	28 (50.9%)
Renal involvement (*n*=6)	6 (100%)	4 (66.7%)
Pneumonia (*n*=7)	7 (100%)	4 (57.1%)
Fatal outcome (*n*=2)	2 (100%)	2 (100%)

DRESS: Drug reaction with eosinophilia and systemic symptoms; DiHS: Drug-induced hypersensitivity syndrome

in DiHS/DRESS (age >75 years, >_7 days drug exposure after the onset of the disease, exposure to allopurinol, treatment with pulse steroids, erythematous rashes involving >70% of body surface area, erosive lesions affecting >10 body surface area, persistent fever, loss of appetite, elevated serum creatinine, alanine transaminase >_400 IU/L, and elevated C-reactive protein).[13,16] The literature suggests erythema multiforme (EM) lesion as a feature of severe DRESS.[17] Japanese criteria may miss patients who manifest EM by insisting on the presence of a maculopapular rash. We did not observe any significant difference in frequency of hyperbilirubinemia (which is considered as a feature of severe hepatotoxicity) in patients with atypical DiHS (16%) in comparison to those who were not atypical DiHS (12.5%).[18] Moreover, the criteria for DiHS has not considered cytomegalovirus (CMV) reactivation which is known to cause fatal complications in DiHS.[3]

The lone case of atypical DiHS that was not diagnosed as definite/probable DRESS had fever, maculopapular rash, liver function derangement, and leucocytosis above 11,000 cells/mm^3. The patient was diagnosed as possible DRESS as one point each was added for generalized maculopapular rash, organ involvement, and for adequate investigations; and one negative point was given for not having two of the four features (facial edema, rash resolving with psoriasiform desquamation, infiltrated lesions, purpuric lesions on areas other than legs) needed for rash suggestive of DRESS. Whether assigning a positive point for fever (seen in 70%–100% cases of DRESS) would improve the sensitivity of the scoring system to diagnose DRESS needs analysis in multicenter studies.[14]

Limitation: retrospective study design and lack of information on HHV 6 reactivation were the major limitations.

In summary, we found that Japanese criteria failed to diagnose a significant proportion of DRESS cases which included severe forms as well. We suggest that diagnosis of DRESS/DiHS should be based on the RegiSCAR scoring system and that reactivation of human herpesviruses (not only HHV 6 but also CMV, Epstein–Barr virus, and HHV 7) may better serve as prognostic indicator.

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Conflicts of interest

There are no conflicts of interest.

References

1. Kumari R, Timshina DK, Thappa DM. Drug hypersensitivity syndrome. Indian J Dermatol Venereol Leprol 2011;77:7-15.
2. Kumar M, Mandal PK, Dolai TK, Bhattacharya M. Imatinib causing drug rash with eosinophilia and systemic symptoms: A rare cutaneous reaction. Indian Dermatol Online J 2014;5(Suppl S2):120-2.
3. Shiohara T, Mizukawa Y. Drug induced hypersensitivity syndrome (DiHS)/drug reaction with eosinophilia and systemic symptoms (DRESS): An update in 2019. Allergol Int 2019;68:301-8.
4. Shiohara T, Iijima M, Ikezawa Z, Hashimoto K. The diagnosis of a DRESS syndrome has been sufficiently established based on typical clinical features and viral reactivation. Br J Dermatol 2007;156:1083-4.
5. Shiohara T, Inaoka M, Kano Y. Drug-induced hypersensitivity syndrome (DIHS): A reaction induced by a complex interplay among herpesviruses and antiviral and antidrug immune responses. Allergol Int 2006;55:1–8.
6. Kardaun SH, Sidoroff A, Valeyrie-Allanore L, Halevy S, Davidovici BB, Mockenhaupt M, *et al*. Variability in the clinical pattern of cutaneous side-effects of drugs with systemic symptoms: Does a DRESS syndrome really exist? Br J Dermatol 2007;56:609-11.
7. Chen YC, Chang CY, Cho YT, Chiu HC, Chu CY. Reply to: ''Using a diagnostic score when reporting the long-term sequelae of the drug reaction with eosinophilia and systemic symptoms''. J Am Acad Dermatol 2013;69:1060-2.
8. Soria A, Bernier C, Veyrac G, Barbaud A, Puymirat E, Milpied B, *et al*. Drug reaction with eosinophilia and systemic symptoms (DRESS) may occur within two weeks of drug exposure: A retrospective study, J Am Acad Dermatol 2019;82:606-11.
9. Sasidharanpillai S, Chathoth AT, Khader A, Reena Mariyath OK, Riyaz N, Binitha MP, *et al*. Predictors of disease severity in drug reaction with eosinophilia and systemic symptoms. Indian J Dermatol Venereol Leprol 2019;85:266-75.
10. Ang CC, Wang YS, Yousuf EM, Tay YK. Retrospective analysis of drug induced hypersensitivity syndrome: A study of 27 patients. J Am Acad Dermatol 2010;63:219-27.
11. Ebrahimpour S, Mohammadi M, Ghollami K. Drug reaction with eosinophilia and systemic symptoms with teicoplanin: A case report. Drug Saf 2017;4:1.
12. Ushigome Y, Kano Y, Hirahara K, Shiohara T. Human herpesvirus 6 reactivation in drug-induced hypersensitivity syndrome and DRESS validation score. Am J Med 2012;125:e9-10.
13. Descamps V, Ben-Said B, Sassolas B, Truchetet F, Avenel-Audran M, Giardin P, *et al*. Management of drug reaction with eosinophilia and systemic symptoms (DRESS). Ann Dermatol Venereol 2010;13711:703-8.
14. Shiohara T, Kano Y, Takahashi R. Current concepts on the diagnosis and pathogenesis of drug-induced hypersensitivity syndrome. JMAJ 2009;52:347–52.
15. Cacoub P, Musette P, Descamps V, Meyer O, Spiers C, Finzi L, *et al*. The DRESS syndrome: A literature review. Am J Med; 2011;124:588-97.
16. Mizukawa Y, Hirahara K, Kano Y, Shiohara T. Drug-induced hypersensitivity syndrome (DiHS)/drug reaction with eosinophilia and systemic symptoms (DRESS) severity score: A useful tool for assessing disease severity and predicting fatal cytomegalovirus disease. J Am Acad Dermatol 2019;80:670-8.
17. Walsh S, Diaz-Cano S, Higgins E, Morris-Jones R, Bashir S, Bernal W, *et al*. Drug reaction with eosinophilia and systemic symptoms: Is cutaneous phenotype a prognostic marker for outcome? A review of clinicopathological features of 27 cases. Br J Dermatol 2013;168:391-401.
18. Temple R. Hy's law: Predicting serious hepatotoxicity. Pharmacoepidemiol Drug Saf 2006;15:241-3.