

Efficacy of add-on therapy with intravenous immunoglobulin in steroid hyporesponsive DRESS syndrome

Da Woon Sim, Jieun Yu, Young-Il Koh 

First published: 18 November 2021

<https://doi-org.bibliosan.clas.cineca.it/10.1111/cts.13201>

Funding information:

This work was supported by the Chonnam National University Hospital Biomedical Research Institute (Grant number: BCRI21033).

Abstract

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare, potentially life-threatening, delayed, drug-induced hypersensitivity reaction. Immediate withdrawal of the culprit drug and administration of systemic corticosteroids is the most widely accepted treatment. However, it is difficult to manage patients with DRESS syndrome who are not responsive to systemic steroids. We studied the efficacy of intravenous immunoglobulins (IVIGs) in patients with DRESS syndrome unresponsive to systemic steroids. We retrospectively reviewed patients with DRESS syndrome who received IVIG in addition to systemic steroids during 2012–2017 and compared the clinical features and course of DRESS syndrome, before and after IVIG treatment. Eighteen DRESS patients (9 men) were included. The most frequent offending drugs were dapsone in five patients, followed by vancomycin in three patients, and carbamazepine in three patients. Rash, fever, lymphadenopathy, atypical lymphocytes, and hepatic involvement were common clinical findings. IVIG treatment was added within a median time of 7 days from the commencement of systemic steroid therapy. After IVIG treatment (total dosage: 1–2 g/kg), the fever resolved within a median time of 1 day (range, 0–3) and liver enzymes improved substantially within a median time of 13 days (range, 0–27). No severe adverse reactions related to IVIG therapy were observed in this study; however, there was one case of mortality. The addition of IVIG in DRESS syndrome in cases refractory to systemic steroid treatment may be helpful in hastening recovery. However, comparative studies using a placebo group are needed.

Study Highlights

WHAT IS THE CURRENT KNOWLEDGE ON THE TOPIC?

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a severe delayed drug reaction. The main treatment is administration of systemic steroids. However, treatment of steroid hyporesponsive adults is unclear.

WHAT QUESTION DID THIS STUDY ADDRESS?

We studied the efficacy of intravenous immunoglobulins (IVIGs) in patients with DRESS syndrome unresponsive to systemic steroids.

WHAT DOES THIS STUDY ADD TO OUR KNOWLEDGE?

We describe cases of adults with steroid hyporesponsive DRESS syndrome who were successfully treated with add-on IVIG therapy with systemic steroids with minimal side effects.

HOW MIGHT THIS CHANGE CLINICAL PHARMACOLOGY OR TRANSLATIONAL SCIENCE?

Our results show the benefits of IVIG add-on treatment with systemic steroids in steroid hyporesponsive DRESS syndrome, and suggest pretreatment medication may result in fewer side effects.

INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare, potentially life-threatening, delayed, drug-induced hypersensitivity reaction.¹ Clinical manifestations include skin eruptions, fever, malaise, lymphadenopathy, hepatic dysfunction, renal impairment, and pneumonitis.¹

The reactivation of herpesviruses has also been shown to play a role in the pathogenesis of DRESS syndrome, especially the human herpesvirus.² Unlike other drug allergies, its clinical course is characterized by relapses or flares despite withdrawal of the culprit drug.¹ Prompt withdrawal of the culprit drug is the mainstay of treatment for DRESS syndrome.¹ In addition, most patients have visceral organ involvement and are treated with corticosteroids.¹ However, the current treatment for steroid hyporesponsive DRESS syndrome has not been evaluated in randomized trials.³

Pediatric case reports have demonstrated the beneficial effects of intravenous immunoglobulin (IVIG) treatment for steroid-resistant DRESS syndrome.^{4, 5} Marcus et al.

reported nine pediatric cases of severe DRESS syndrome that were treated successfully with IVIG in addition to systemic corticosteroids, with mild side effects, such as transient hyponatremia and transient fever.⁶

Some adult patients with DRESS syndrome have also been administered IVIG in addition to systemic corticosteroids for steroid hyporesponsive DRESS syndrome.^{3, 5, 7, 8} However, IVIG treatment in adults with DRESS syndrome is controversial; in a study of six patients with DRESS syndrome treated with IVIG, five experienced severe adverse effects.⁹

The aim of the present study was to describe a series of adult patients who were diagnosed with DRESS syndrome, hyporesponsive to systemic steroids, and successfully treated with IVIG.

METHODS

Patients

This was a retrospective study of all adult patients with DRESS syndrome admitted to Chonnam National University Hospital from January 2012 to December 2017, who were administered IVIG in addition to systemic corticosteroids after withdrawal of the culprit drug. The study protocol was approved by the institutional review boards of Chonnam National University College of Medicine (CNUH-2017-134). The requirement for informed consent was waived due to the retrospective nature of the study.

Diagnostic criteria for DRESS syndrome

The diagnosis of DRESS syndrome was based on the Registry of Severe Cutaneous Adverse Reaction (RegiSCAR) score.¹⁰ The RegiSCAR score system requires that patients fulfill at least three of the following seven criteria: skin rash, fever, enlarged lymph nodes, internal organ involvement, lymphocytosis or lymphocytopenia, eosinophilia, and thrombocytopenia.¹⁰ Based on the RegiSCAR scores, patients were classified as follows: those who fulfilled less than two criteria were excluded, those who fulfilled two to three criteria were possible cases, those who fulfilled four to five criteria were probable cases, and those who fulfilled greater than five criteria were definite cases.

Laboratory data and imaging study

Complete blood cell counts with differential counts; presence of atypical lymphocytosis on peripheral blood smears (PBS); C-reactive protein (CRP) levels; erythrocyte sedimentation rates (ESR); liver function parameters like aspartate aminotransferase (AST), alanine aminotransferase (ALT), and total bilirubin; renal function parameters, including blood urea, nitrogen, and creatinine; and coagulation profiles including D-dimer, fibrin degradation product (FDP), lactate dehydrogenase (LDH), and ferritin levels were collected. Serological tests for autoimmune antibodies and viral antibodies, such as cytomegalovirus, Epstein-Barr

virus, and HIV were performed to exclude the potential for underlying diseases. Serum human herpesvirus-6 (HHV-6) DNA was assayed by polymerase chain reaction, because its reactivation may play a role in DRESS syndrome.²

In addition to physical examinations and laboratory tests to determine the involvement of enlarged lymph nodes and internal organs, computed tomography (CT) images of the chest, abdomen, and neck were collected.

Identification of culprit drugs

Two physicians reviewed the medication histories using Naranjo's scale to identify the culprit drugs,¹¹ which were classified as possible, probable, or certain to induce DRESS syndrome.

Statistical analyses

Statistical analyses were performed using SPSS version 20.0 (IBM Corp.). Continuous data are presented as median (range) and categorical data are presented as absolute and relative frequencies. Wilcoxon signed-rank test was used to compare two related samples regarding therapeutic effects before and after IVIG injection. Statistical significance was set at $p < 0.05$.

RESULTS

Clinical manifestations of the study subjects

Eighteen patients were included in this study: nine men and nine women. The median age at presentation was 54 years (range, 18–83). The clinical presentations and laboratory findings are summarized in Table [S1](#). The median RegiSCAR score was 7 (range, 4–9). Seventeen (94%) subjects were classified as having definite and one (6%) as having probable DRESS syndrome.

All patients presented with fever (median 38.8°C) and maculopapular rash. Four patients had oral mucosal involvement. Sixteen patients presented with lymphadenopathy, most commonly in the axillary area. Six patients had facial edema.

Offending drugs

Patients were exposed to different potential culprit drugs, including dapsone (5), carbamazepine (3), vancomycin (3), and others (Table [S1](#)). The median Naranjo scale score for the evaluation of causality was four (range, 2–8). The median time between drug exposure and symptom onset was 28 days (range, 8–92).

Laboratory and radiologic findings

Fifteen patients had peripheral eosinophilia, and atypical lymphocytosis on PBS was marked in 14 patients (Table [S1](#)). No patient lacked both peripheral eosinophilia and atypical

lymphocytes in the PBS simultaneously. Four patients showed renal function abnormalities. All patients had elevated liver enzymes, and half had hyperbilirubinemia. Patients showed increased inflammatory indicators, such as ESR (7), CRP (18), FDP (17), and D-dimer (17). All patients had elevated LDH, and all but one had elevated ferritin. Of the 17 patients tested for HHV-6 infection, three tested positive. Many patients had abnormal chest and abdomen CT findings: hepatomegaly (1), hepatosplenomegaly (2), splenic infarction (3), pleural effusion (4), pericardial effusion (1), and splenomegaly (2).

Hospital course and response to IVIG treatment

All 18 patients were administered IVIG as add-on therapy to systemic steroid treatment. Their hospital course and response to DRESS syndrome are summarized in Table 1 and Figure 1. Withdrawal of the culprit drug was initiated as soon as the diagnosis was made by an allergist for all but one patient (no. 18), who had vancomycin-loaded bone cement; we recommended removal because the possible culprit drug was vancomycin. However, she refused surgery, her DRESS syndrome worsened despite intensive treatment, and she subsequently died. All patients had severe disease and were initially treated with systemic corticosteroids (dose range 1.0 mg–2.0 mg/kg), but because there was no improvement (such as fever, rash, and laboratory findings), IVIG treatment was added within a median time of 6.5 days from the commencement of corticosteroid administration. Sixteen patients received an IVIG dose of 2 g/kg, and two received 1.5 g/kg.

TABLE 1. Clinical responses to add-on intravenous immunoglobulin with systemic steroids

Patient no.	Steroid doses (mg/kg/day)	Duration of steroid use before IVIG (days)	IVIG dose (g/kg)	Duration of steroid use after IVIG (days)	Time to defervescence after IVIG start (days)	Time to ALT normalization after IVIG start (days)
1	2	11	2	49	0	15
2	2	11	2	91	1	13
3	1	14	2	79	0	13
4	1	2	2	16	0	9
5	1	3	2	67	3	4
6	1	10	2	3	0	0
7	1	11	1.5	36	1	14
8	2	4	2	7	0	7
9	2	8	2	131	1	13

Patient no.	Steroid doses (mg/kg/day)	Duration of steroid use before IVIG (days)	IVIG dose (g/kg)	Duration of steroid use after IVIG (days)	Time to defervescence after IVIG start (days)	Time to ALT normalization after IVIG start (days)
10	1.5	5	2	5	2	2

Abbreviations: ALT, alanine aminotransferase; IVIG, intravenous immunoglobulin.

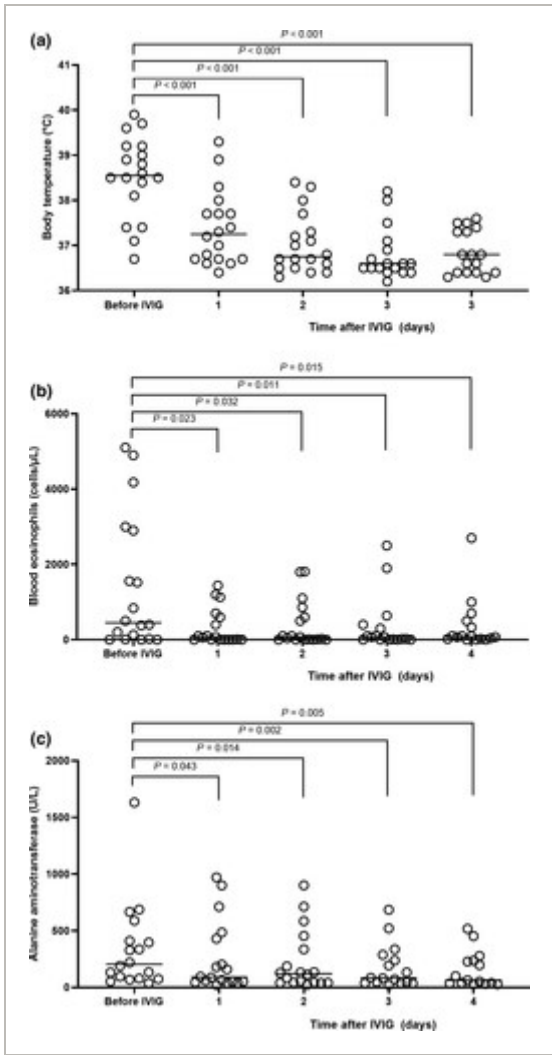


FIGURE 1

[Open in figure viewer](#) | [PowerPoint](#)

Changes in clinical parameters before and after intravenous immunoglobulin (IVIG) treatment in patients with drug reaction with eosinophilia and systemic symptoms syndrome. (a) Changes in fever. (b) Changes in blood eosinophil count. (c) Changes in alanine aminotransferase levels

Fourteen patients showed rapid improvement in general condition 24 h after IVIG treatment initiation. The remaining four patients showed improvement within 72 h. Eosinophil counts and ALT levels improved significantly within 4 days after IVIG injection (Figure 1). Fever

resolved in a median of 1 day (range, 0–3), rashes disappeared in a median of 8 days (range, 2–13), and liver enzyme values returned to normal levels in a median of 13 days (range, 0–27) after IVIG administration. One patient (no. 14) transferred to another hospital after IVIG treatment initiation and was lost to follow-up.

Patients were administered systemic steroids for a median of 36.5 days (range, 3–131). Eleven patients completed the primary steroid treatment, but six had worsening symptoms during the systemic steroid taper, so their time was increased. Ultimately, 16 patients completed treatment without complications during the follow-up period.

Few adverse reactions to the IVIG treatment were reported. Two patients experienced facial flushing and mild headache; this was relieved by ibuprofen. No patient had any severe allergic reactions, and no patients considered discontinuing IVIG due to adverse reactions.

DISCUSSION

Drug reaction with eosinophilia and systemic symptoms syndrome involves delayed-type hypersensitivity reactions mediated by the adaptive immune system with organ damage as the major cause of morbidity and mortality (up to 10%)¹; in severe cases, organ transplantation should be considered.¹² IVIG has been successfully combined with corticosteroids and may have a role in cases refractory to systemic steroid administration.^{3, 7, 8}

Drug reaction with eosinophilia and systemic symptoms syndrome is thought to be a T cell-mediated reaction related to human leukocyte antigen (HLA) type and racial factors.¹³ It is hypothesized to occur in individuals with drug detoxification defects that lead to an increase in reactive metabolites and subsequent immunologic reaction coupled with reactivation of specific viruses such as HHV-6.⁴ Changes in regulatory T cells and B cells have been found in DRESS syndrome.¹⁴

Intravenous immunoglobulins contain antibodies that regulate immune responses by inhibiting cytotoxic T cells. IVIG interferes with the generation and activation of cytotoxic T cells and decreases their activity by blocking important cell surface molecules like antigen-specific T cell receptor.^{15, 16} In addition, IVIG contains soluble CD4 and CD8¹⁷ glycoproteins, which serve as ligands for HLA-I and HLA-II on antigen presenting cells. They compete with major histocompatibility complex class II-restricted autoreactive T lymphocytes in binding HLA-II, resulting in immune tolerance.¹⁸ Thus, IVIG has been used as a steroid-tapering agent in various inflammatory diseases.^{19, 20}

Based on these findings, IVIG treatment in patients with steroid hyporesponsive DRESS syndrome might be effective. Although the benefits of IVIG treatment in severe adverse drug reactions have not been completely elucidated, immunomodulatory and anti-inflammatory activity may exist.

Despite the potential benefits of IVIG, its effectiveness as an adjunct to systemic corticosteroids in steroid hyporesponsive DRESS syndrome remains unclear. Although IVIG has been successfully used to treat adults,^{3, 5, 7, 8} in one recent study, most patients suffered severe adverse effects.⁹ However, a recent pediatric study showed minimal adverse effects of IVIG.⁶ In our cohort, facial flushing and mild headache during IVIG administration were observed in two patients. No other adverse effects were noted.

To the best of our knowledge, we described the largest series of adult patients with DRESS syndrome who were hyporesponsive to systemic corticosteroids and treated successfully with the addition of IVIG. Sixteen patients showed complete remission of DRESS syndrome during the follow-up period. In most patients, fever and systemic symptoms rapidly improved after IVIG initiation. All patients had severe organ involvement and worsening symptoms despite high-dose steroid therapy but responded well to IVIG.

Generally, IVIG is considered safe,²¹ and most adverse reactions are transient and mild.²² According to a previous study, pretreatment with analgesics, antihistamines, nonsteroidal anti-inflammatory drugs, or systemic steroids may be beneficial.²²

The study has some limitations. It was retrospective without a control group. Given the rarity of steroid hyporesponsive DRESS syndrome and the positive experience at our institution with IVIG add-on treatment for this condition, we could not find patients with steroid hyporesponsive DRESS syndrome who were not treated with IVIG.

In conclusion, steroid hyporesponsive DRESS syndrome continues to be a therapeutic challenge, although our results suggest a beneficial effect of IVIG when used with systemic steroids. In addition, we found that administration of pretreatment medication resulted in fewer than expected side effects. Our study suggests an important role for IVIG in DRESS syndrome, especially in patients with a severe clinical course that is not responsive to systemic steroid treatment.

CONFLICTS OF INTEREST

The authors declared no competing interests for this work.

AUTHOR CONTRIBUTION

D.W.S. and Y.I.K. wrote the manuscript. D.W.S. designed the research. D.W.S. and J.Y. performed the research. D.W.S. and Y.I.K. analyzed the data.

Supporting Information



Filename	Description

Filename	Description
cts13201-sup-0001-TableS1.docx Word document, 30.8 KB	Table S1

Please note: The publisher is not responsible for the content or functionality of any supporting information supplied by the authors. Any queries (other than missing content) should be directed to the corresponding author for the article.

REFERENCES



1 Mustafa SS, Ostrov D, Yerly D. Severe cutaneous adverse drug reactions: Presentation, risk factors, and management. *Cur Allergy Asthma Rep.* 2018; **18**: 26.

[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

2 Shiohara T, Iijima M, Ikezawa Z, Hashimoto K. The diagnosis of a DRESS syndrome has been sufficiently established on the basis of typical clinical features and viral reactivations. *Br J Dermatol.* 2007; **156**: 1083- 1084.

[Wiley Online Library](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

3 Galvão VR, Aun MV, Kalil J, Castells M, Giavina-Bianchi P. Clinical and laboratory improvement after intravenous immunoglobulin in drug reaction with eosinophilia and systemic symptoms. *J Allergy Clin Immunol Pract.* 2014; **2**: 107- 110.

[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

4 Dredge DC, Parsons EC, Carter LP, Staley KJ. Anticonvulsant hypersensitivity syndrome treated with intravenous immunoglobulin. *Pediatr Neurol.* 2010; **43**: 65- 69.

[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

5 Lee JH, Park HK, Heo J, et al. Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) syndrome induced by celecoxib and anti-tuberculosis drugs. *J Korean Med Sci.* 2008; **23**: 521- 525.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

6 Marcus N, Smuel K, Almog M, et al. Successful intravenous immunoglobulin treatment in pediatric severe DRESS syndrome. *J Allergy Clin Immunol Pract.* 2018; **6**: 1238- 1242.

[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

7 Kito Y, Ito T, Tokura Y, Hashizume H. High-dose intravenous immunoglobulin monotherapy for drug-induced hypersensitivity syndrome. *Acta Derm Venereol.* 2012; **92**: 100- 101.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

8 Santhamoorthy P, Alexander KJ, Alshubaili A. Intravenous immunoglobulin in the treatment of drug rash eosinophilia and systemic symptoms caused by phenytoin. *Ann Indian Acad Neurol.* 2012; **15**: 320- 322.

[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

9 Joly P, Baptiste J, Tetart F, et al. Poor benefit/risk balance of intravenous immunoglobulins in DRESS. *Arch Dermatol*. 2012; **148**: 543- 544.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

10 Kardaun SH, Sidoroff A, Valeyrie-Allanore S, 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; **156**: 609- 611.

[Wiley Online Library](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

11 Bocquet H, Bagot M, Roujeau JC. Drug-induced pseudolymphoma and drug hypersensitivity syndrome (Drug Rash with Eosinophilia and Systemic Symptoms: DRESS). *Semi Cutan Med Surg*. 1996; **15**: 250- 257.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

12 Venulet J. Role and place of causality assessment. *Pharmacoepidemiol Drug Saf*. 1992; **1**: 225- 234.

[Wiley Online Library](#) | [Google Scholar](#)

13 Mennicke M, Zawodniak A, Keller M, et al. Fulminant liver failure after vancomycin in a sulfasalazine-induced DRESS syndrome: fatal recurrence after liver transplantation. *Am J Transplant*. 2009; **9**: 2197- 2202.

[Wiley Online Library](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

14 Tohyama M, Hashimoto K. New aspects of drug-induced hypersensitivity syndrome. *J Dermatol*. 2011; **38**: 222- 228.

[Wiley Online Library](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

15 Trepanier P, Chabot D, Bazin R. Intravenous immunoglobulin modulates the expansion and cytotoxicity of CD8+ T cells. *Immunology*. 2014; **141**: 233- 241.

[Wiley Online Library](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

16 Pereira FA, Mudgil AV, Rosmarin DM. Toxic epidermal necrolysis. *J Am Acad Dermatol*. 2007; **56**: 201- 203.

[Crossref](#) | [Web of Science®](#) | [Google Scholar](#)

17 Blasczyk R, Westhoff U, Grosse-Wilde H. Soluble CD4, CD8, and HLA molecules in commercial immunoglobulin preparations. *Lancet*. 1993; **341**: 789- 790.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

18 Azimi M, Aghamohammadi A, Och HD, Rezaei N. Soluble molecules in intravenous immunoglobulin: benefits and limitations. *Expert Rev Clin Immunol*. 2016; **12**: 99- 101.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

19 Hernandez-Bautista V, Yamazaki-Nakashimada MA, Vazquez-Garcia R, Stamatelos-Albarran D, Carrasco-Daza D, Rodriguez-Lozano AL. Treatment of Kimura disease with intravenous immunoglobulin. *Pediatrics*. 2011; **128**: 1633- 1635.

[Crossref](#) | [Web of Science®](#) | [Google Scholar](#)

20 Orson FM. Intravenous immunoglobulin therapy suppresses manifestations of the angioedema with hypereosinophilia syndrome. *Am J Med Sci*. 2003; **326**: 94- 97.

[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

21 Bichuetti-Silva DC, Furlan FP, Nobre FA, et al. Immediate infusion-related adverse reactions to intravenous immunoglobulin in a prospective cohort of 1765 infusions. *Int Immunopharmacol*. 2014; **23**: 442- 446.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

22 Ruetter A, Luger TA. Efficacy and safety of intravenous immunoglobulin for immune-mediated skin disease: current view. *Am J Clin Dermatol*. 2004; **5**: 153- 160.

[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

[Download PDF](#)



Today's discovery, tomorrow's medicine

About ASCPT



Membership & Events



Contact ASCPT



© 2021 American Society for Clinical Pharmacology and Therapeutics

About Wiley Online Library

Privacy Policy

Terms of Use

Cookies

Accessibility

Publishing Policies

Help & Support

Contact Us

Training and Support

DMCA & Reporting Piracy

Opportunities

Subscription Agents

Advertisers & Corporate Partners

Connect with Wiley

The Wiley Network
Wiley Press Room

Copyright © 1999-2021 John Wiley & Sons, Inc. All rights reserved

Table S1. Baseline clinical characteristics of the patients

Patient No.	Age	Sex	Culprit drug	Naranjo scale	Latent period (days)	Mucosal involvement	LAP	Hepato-megaly	Facial edema	Blood eosinophil (cells/ μ L)	ALT (U/L)	Renal impairment	Atypical lymphocyte (%)	LDH (U/L)	HHV-6 reactivation	RegiSCAR score*
1	75	F	Dapsone	4	21	No	I, A	No	No	5200	711	No	21	1076	Yes	8
2	54	M	Dapsone	3	28	No	I, A	No	Yes	900	920	No	34	1209	No	6
3	60	M	Sulfasalazine, Naproxen	5 5	42	No	I, A, IA, C	No	Yes	4300	220	Yes	11	1170	No	9
4	37	F	D-penicillamine	4	20	No	IA	No	No	20	96	No	1	707	No	5
5	83	F	Allopurinol	2	92	No	IA	No	No	240	134	Yes	1	791	No	7
6	80	F	Ciprofloxacin	5	38	No	IA	Yes	No	40	170	No	0	662	No	5
7	54	F	Vancomycin, Diclofenac	4	24	Yes	No	No	No	4900	337	No	0	1608	No	6
8	69	M	Ceftriaxone	4	8	No	A	No	No	0	72	Yes	1	1196	Yes	5
9	34	F	Dapsone	5	18	No	A, C	No	Yes	5000	485	No	7	1262	No	9
10	51	M	Vancomycin	5	15	No	IA	No	No	700	98	No	0	588	-	4
11	71	F	Diazepam	3	43	Yes	No	No	Yes	1130	143	Yes	0	581	No	6
12	33	M	Dapsone	4	32	No	IA	Yes	Yes	5100	432	No	4	1905	No	8
13	59	F	Carbamazepine	4	28	Yes	I, A, C, IA	No	No	1520	1631	No	5	1742	Yes	8
14	18	M	Carbamazepine	4	28	No	A, C, IA	Yes	No	1810	589	No	7	1747	No	8
15	20	M	Dapsone, Minocycline	8 8	22	Yes	I, A	Yes	No	600	127	No	16	1370	No	7
16	40	M	Anti-TB drugs	4	25	No	C	Yes	No	2700	228	No	2	925	No	7
17	34	M	Carbamazepine	4	39	No	A,C, IA	Yes	Yes	3000	239	No	10	1446	No	8
18	78	F	Vancomycin,	4	32	No	A,C	No	No	1440	41	No	2	1066	No	7

ALT, alanine aminotransferase; A, axillary; C, cervical; HHV-6, human herpesvirus 6; I, inguinal; IA, intra-aortic; LAP, Lymphadenopathy, LDH, Lactate dehydrogenase; RegiSCAR, the Registry of Severe Cutaneous Adverse Reaction; TB, tuberculosis

*DRESS RegiSCAR score¹⁰ is defined as follows: <2: no case; 2-3: possible; 4-5: probable; >5: definite