Objective: To investigate the clinical and pathologic features of patients with drug reaction with eosinophilia and systemic symptoms (DRESS) in Taiwan.

Design: Case series and retrospective analysis.

Setting: A medical referral center in Northern Taiwan.


Main Outcome Measures: Clinical characteristics for specific drugs and important prognostic factors in DRESS.

Results: Patients ranged in age from 6 to 90 years (mean age, 51 years). The female to male ratio was 1.3 to 1. The most common culprit drugs were allopurinol, phenytoin, and dapsone. Exanthematous eruption was the most common skin manifestation, but purpurae and blisters were also observed. Hepatic (80%), renal (40%), and pulmonary (33%) involvement were also common. The overall mortality rate was 10%. Allopurinol-induced DRESS was characterized by preceding chronic renal insufficiency and frequent renal involvement. Pancytopenia indicated a poor prognosis.

Conclusions: Drug reaction with eosinophilia and systemic symptoms has a variable clinical presentation, and its definition requires clarification. It may be a heterogeneous syndrome with some particular patterns related to different drugs. Early diagnosis and prompt discontinuation of offending drug regimens are essential.

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Severe Cutaneous Adverse Reactions (SCARs) to drugs are groups of drug hypersensitivity reactions with a heterogeneous clinical presentation. Although the prevalence of SCARs is low, they may result in prolonged hospitalization, substantial disability, and even death. One of these

See Practice Gaps at end of article

SCARs is drug reaction with eosinophilia and systemic symptoms (DRESS), also sometimes called drug-induced hypersensitivity syndrome. This syndrome was first described as exfoliative dermatitis following sulfanilamide treatment. It was then observed to result from different medications, including phenytoin, dapsone, allopurinol, and other anticonvulsants. However, these earlier reports described not only cases of DRESS but also cases of Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, and exanthematous eruption.

In 1996, the hypersensitivity syndromes with systemic involvement were named DRESS to decrease the ambiguity in clinical practice. Drug reaction with eosinophilia and systemic symptoms usually has a late onset, 3 to 8 weeks after use of the culprit drug, and is characterized by fever, skin eruption, prominent eosinophilia, lymphocyte activation, and multivisceral involvement. While DRESS is not universally agreed to represent a distinct entity, we have observed that it occurs in a subset of patients with certain features that are quite distinct from the features associated with other SCARs. Early in 1979, the original article focusing on phenytoin hypersensitivity described such reaction in detail and reminded physicians of the importance of prompt recognition and immediate cessation of treatment with the culprit drug. In addition, another study found that 31 of 53 patients with anticonvulsant hypersensitivity had multiorgan involvement. However, owing to the rarity

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of DRESS, large-scale studies are limited. The objective of the present study was to investigate the clinical features and prognosis of patients with DRESS in a medical center in northern Taiwan. In addition, we attempted to determine whether a correlation exists between specific drugs and reaction patterns.9

**METHODS**

A retrospective medical record review was conducted of all cases of suspected DRESS in the National Taiwan University Hospital database for patients hospitalized between 1998 and 2008. Potential cases were selected if they had a diagnosis of toxicoderma, erythroderma, or drug eruption with systemic involvement. We then recruited patients with DRESS using the inclusion criteria proposed by the European Registry of Severe Cutaneous Adverse Reactions (RegiSCAR).11 Clinical charts and sequential medical laboratory data obtained during hospitalization were reviewed. Demographic data, medication history, clinical course, laboratory results, and pathologic findings of all cases were analyzed.

**INCLUSION AND DIAGNOSTIC CRITERIA**

Two necessary inclusion criteria were reaction suspected to be drug related and hospitalization. Patients included also had to fulfill at least 3 of the following 7 criteria: acute skin eruption, fever with body temperature above 38°C, enlarged lymph nodes at 2 or more sites, involvement of at least 1 internal organ, lymphocyte count above or below the laboratory limits, eosinophil count above the laboratory limits, and platelet count below the laboratory limits.11 Hepatic and renal involvement were defined as liver enzyme levels more than twice the upper limit of the normal values or patients’ baseline levels, serum creatinine level more than twice the normal value or a deterioration of chronic renal insufficiency (CRI), and new onset of proteinuria or hematuria. Pulmonary involvement was considered when dyspnea or abnormal findings on chest radiographs were present and could not be explained by other reasons. Cardiomyocardial and pancreatic involvement were defined as elevation of cardiac or muscular enzymes and amylase levels, which is more specific for pancreatic damage. The normal ranges were defined as 1500/µL to 4000/µL for lymphocyte count and 120 to 320×10³/µL for platelet count. The definition of eosinophilia included an absolute eosinophil count of more than 700/µL or above 10% if the leucocyte count was lower than 4000/µL. (To convert lymphocytes, eosinophils, and leucocytes to ×10⁹/L, multiply by 0.001; to convert platelets to ×10⁹ per liter, multiply by 1.0.)

Cases of typical manifestation of Stevens-Johnson syndrome and toxic epidermal necrolysis were excluded. For the identification of culprit drugs, the criteria of Naranjo et al12 were used for determination of causality for DRESS.

**STATISTICAL ANALYSIS**

We used nonparametric tests for analysis. The Wilcoxon rank sum test was adopted for 2-sample comparison for allopurinol- or phenytoin-induced DRESS with other drug-induced DRESS. The Kruskal-Wallis test was adopted for comparison within these 3 groups. We also used the Fisher exact test for nominal variables. The results were expressed as means (SDs) or as numbers. A P value of less than .05 was considered statistically significant for all tests.

**RESULTS**

A total of 60 patients (26 male and 34 female) diagnosed as having DRESS were enrolled in this study. The mean age was 51 years (age range, 6-90 years; median, 54.5 years), with no difference in age between male and female groups. Most patients were treated in internal medicine departments and dermatology departments, but some were treated in pediatric and neurology departments.

**CULPRIT DRUGS**

Drugs that were newly and persistently administered within 3 months before the onset of symptoms were evaluated as possible culprit drugs. We used the criteria of Naranjo et al12 to identify the culprit drugs. Allopurinol was the most common culprit drug (19 of 60 [32%]), followed by phenytoin (11 of 60 [18%]) and dapsone (10 of 60 [17%]) (Figure 1). Other culprit drugs included carbamazepine (3 of 60 [5%]); cotrimoxazole (3 of 60 [5%]); penicillin (3 of 60 [5%]); nonsteroidal anti-inflammatory drugs, including sulindac, diclofenac, and meloxicam (3 of 60 [5%]); lamotrigine (2 of 60 [3%]); antituberculous drugs (2 of 60 [3%]); and unknown Chinese medicines (2 of 60 [3%]). Two cases were classified as uncertain owing to concomitant use of multiple drugs (one with carbamazepine and imipramine and the other with phenytoin and ceftriaxone).

**CLINICAL FEATURES AND COURSES**

The average drug reaction latency period for all patients was 20.7 days (range, 3-76 days). It was 27.0 days for the allopurinol group, but the longer latency period was not statistically significant (P = 0.8). Fever (temperature ≥38°C) was reported in 52 patients (87%), and palpable lymphadenopathy was recorded in 17 patients (17 of 55 [31%]). Twenty-nine patients were reported to have lesions in at least 1 mucosal area (48%), always including the oral mucosa. All patients revealed a diffuse exanthematous eruption (Figure 2A), some with typical facial edematous erythema (Figure 2B), and in some cases this was followed by exfoliative dermatitis (7 of 60 [12%]) or accompanied by blistering or purpuric eruption (6 of 60 [10%]) (Figure 2C).
Elevation of liver enzyme levels was the most common finding related to internal organ involvement: 48 patients (80%) had levels double that of normal, with or without hyperbilirubinemia. Renal involvement was present in 24 patients (40%), and the frequency of renal involvement was significantly higher in the allopurinol group than in the other patients (68% [n=13] vs 33% [n=10]) (P = .02). The rates of lung (n=20), cardiomuscular system (n=9), and pancreas involvement (n=3) were 33%, 15%, and 5%, respectively (Figure 3A). Of 9 patients with cardiomuscular involvement, none was observed to have specific cardiac enzyme elevation.

Hematologic abnormalities included lymphocytosis (15 of 60 [25%]), lymphocytopenia (27 of 60 [45%]), the presence of atypical lymphocytes (38 of 60 [63%]), eosinophilia (31 of 60 [52%]), and thrombocytopenia (15 of 60 [25%]) (Figure 3B). IgG reactive to Epstein-Barr virus and cytomegalovirus was detected in 9 patients, but IgM reactive to these viruses was not detected. Blood was tested in only 1 patient for human herpesvirus (HHV) 6, and the results were positive for serum IgG antibody but negative for DNA on polymerase chain reaction.

In total, 17 patients underwent skin biopsy, and 6 patients underwent bone marrow biopsy during the course of their drug reaction. In 13 of the 17 skin biopsy cases (77%), specimens showed various degrees of basal vacuolization, dyskeratosis, lymphocyte exocytosis, dermal edema, and superficial perivascular inflammation, resulting in a pathologic diagnosis of erythema multiforme (Figure 4A). The perivascular inflammation was most commonly infiltrated by lymphocytes with or without eosinophils, but no atypical cells were observed. The skin biopsy specimens of 2 patients (12%) revealed only perivascular infiltration by mixed cells. The skin specimens from 1 patient revealed lymphocytic vasculitis (Figure 4B), while the findings in the final skin biopsy case were pigment incontinence without obvious interface activity.

As for the cases of bone marrow biopsy, 5 of the 6 showed hypocellularity with a decrease in both myeloid and erythroid series, and 1 showed hypercellularity and an increased myeloid and/or erythroid ratio to 5:1 with substantial myeloid hyperplasia. In all 6 specimens, an increased quantity of megakaryocytes and increased in-
terstitial infiltration with small lymphocytes without cellular dysplasia were observed. However, no definite evidence of hemophagocytosis was observed in bone marrow specimens from our patients.

TREATMENT OUTCOMES AND PROGNOSSES

Forty-five of our 60 patients (75%) were treated with regimens of systemic corticosteroids of different durations. Either intravenous methylprednisolone sodium succinate, (40-120 mg/d) or oral prednisolone (30-60 mg/d) was administered with titration. The indications included severe or multiorgan involvement and prominent systemic symptoms with exclusion of infection. Intravenous immunoglobulin (IVIG) was also administered in 2 of these 45 patients; one recovered, but the other died. None of the 60 patients was treated with other immunosuppressants. Six patients also received antibiotic treatment, either before or after positive culture results. Ten patients received treatment with only supportive care, including oral antihistamines or topical antipruritic agents.

In our study, 6 patients eventually died, for an overall mortality rate of 10%. One patient died of multiorgan failure, and 5 died of profound shock, either septic or cardiogenic. Of the 6 deaths, allopurinol was the culprit drug in 4 cases, lamotrigine in 1, and suspected Chinese medicine in 1. Five of the 6 patients who died had pancytopenia shortly before death (83%) (Table 1).

Acute renal failure developed in 5 of 60 patients (8%). One of these died of multiorgan failure, and 1 patient required long-term hemodialysis. Although the incidence of liver involvement was high (up to 80%), only 4 cases progressed to hepatic failure, and most of them subsequently resolved. One patient showed symptoms of hyperthyroidism 1 month after the initial presentation of DRESS and later developed Graves disease. Six patients had complications of bacteremia and fungemia during hospitalization (10%), and 3 of them eventually died of septic shock. The identified pathogens included Escherichia coli, methicillin-resistant Staphylococcus aureus, Acinetobacter baumannii, and Candida albicans. The patients with septic shock tended to have multiple pathogens.
Since it was originally defined in the 1980s, DRESS, or drug-induced hypersensitivity syndrome, has become well known by dermatologists because of its distinctive features and potential to cause death. Because of the condition’s rarity, variable presentation, and usually delayed recognition, its clinical and biological features are still under debate.

In this study, allopurinol was the most common culprit drug (n=19 [32%]). This finding differs from the findings of 2 European studies9,13 but is consistent with the results of a previous study in Taiwan14 (Table 2). In previous pharmacogenetic research, the genotype of HLA-B*5801 was observed to have a strong association with allopurinol-induced SCARs. However, the prevalence of HLA-B*5801 is much higher in Han Chinese (up to 20%) than in Europeans and Japanese, as is the odds ratio (OR) for the prevalence of this genotype among those with allopurinol-induced SCARs compared with the general population.15-17 Moreover, the prescription of allopurinol for asymptomatic hyperuricemia is probably more common in Taiwan.18 The second most common culprit drug in the present study was phenytoin, but other aromatic anti-epileptic agents, such as carbamazepine and phenobarbital, were used less frequently in our study. In contrast, DRESS due to dapsone treatment was more common in our hospital, which is one of the few medical centers in Taiwan authorized to prescribe dapsone.

Compared with patients described in European studies, the patients with DRESS in Taiwan seemed to have higher rates of liver and renal involvement (Table 2). In our study, 48 patients were observed to have liver involvement (80%), but only 1 patient had a history of chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) coinfection. However, 2 patients with a history of chronic HBV or HCV infection in our series did not develop a 2-fold increase in their baseline level of liver enzymes, suggesting that chronic HBV or HCV infection may not be a risk factor for liver involvement. The high renal involvement rate in this study may be related to the large proportion of allopurinol-induced DRESS, which showed a statistically significant difference in renal involvement rate (Table 3). Moreover, of 5 cases that progressed to acute renal failure, 4 of them also included acute interstitial nephritis.

In our study, 19 patients were diagnosed as having allopurinol-induced DRESS. We observed some differ-

### Table 1. Clinical Details of the Mortality Cases in Our Study

<table>
<thead>
<tr>
<th>Patient Sex/ Age, y</th>
<th>Underlying Diseases</th>
<th>Culprit Drugs</th>
<th>Skin Eruption</th>
<th>Pathologic Diagnosis (Skin/BM)</th>
<th>Internal Organ Involvement</th>
<th>Pancytopenia</th>
<th>Cause of Death</th>
<th>Systemic Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/21</td>
<td>Posttraumatic epilepsy</td>
<td>Lamotrigine</td>
<td>Ex</td>
<td>EM/NA</td>
<td>Multiple</td>
<td>Y</td>
<td>Multiorgan failure</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>M/46</td>
<td>CRI, CHF</td>
<td>Allopurinol</td>
<td>Ex</td>
<td>NA/NA</td>
<td>Kidney</td>
<td>N</td>
<td>Septic shock</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>F/72</td>
<td>CRI</td>
<td>Allopurinol</td>
<td>ED, erosions</td>
<td>EM/NA</td>
<td>Liver, kidney</td>
<td>Y</td>
<td>Septic shock</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>F/75</td>
<td>Allopurinol</td>
<td>Ex, erosions</td>
<td>EM/hypocellular</td>
<td>Multiple</td>
<td>Y</td>
<td></td>
<td>Corticosteroids, antibiotics</td>
<td></td>
</tr>
<tr>
<td>F/89</td>
<td>CRI, CAD</td>
<td>Allopurinol</td>
<td>Ex</td>
<td>EM/hypocellular</td>
<td>Multiple</td>
<td>Y</td>
<td>Cardiogenic shock</td>
<td>Corticosteroids, IVIG, antibiotics</td>
</tr>
<tr>
<td>F/39</td>
<td>None</td>
<td>Suspected Chinese medicine</td>
<td>Ex</td>
<td>EM/hypocellular</td>
<td>Multiple</td>
<td>Y</td>
<td></td>
<td>Corticosteroids, IVIG, antibiotics</td>
</tr>
</tbody>
</table>

Abbreviations: BM, bone marrow; CAD, coronary artery disease; CHF, congestive heart failure; CRI, chronic renal insufficiency; ED, exfoliative dermatitis; EM, erythema multiforme; IVIG, intravenous immunoglobulins; Ex, exanthematous eruption; N, no; NA, not available; Y, yes.

a Defined as positive results of blood culture.

b Negative blood culture results; no elevation of cardiac enzyme levels.

### Table 2. Comparison of Clinical Features of DRESS Between Different Studies

<table>
<thead>
<tr>
<th>Clinical Feature</th>
<th>Roujeau and Stern13</th>
<th>Peyrière et al12</th>
<th>Chiou et al14</th>
<th>Present Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common culprit drugs</td>
<td>Aromatic anticonvulsants, sulfonamides</td>
<td>Aromatic anticonvulsants, abacavir</td>
<td>Allopurinol, carbamazepine</td>
<td>Allopurinol, phenytoin, dapsone</td>
</tr>
<tr>
<td>Fever</td>
<td>87</td>
<td>69</td>
<td>72</td>
<td>87</td>
</tr>
<tr>
<td>Skin eruption</td>
<td>Exanthematous</td>
<td>Exanthematous</td>
<td>Exanthematous</td>
<td>Exanthematous</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>75</td>
<td>18</td>
<td>50</td>
<td>31</td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>30</td>
<td>57</td>
<td>48</td>
<td>52</td>
</tr>
<tr>
<td>Atypical lymphocytes</td>
<td>NA</td>
<td>7</td>
<td>45</td>
<td>63</td>
</tr>
<tr>
<td>Hepatic involvement</td>
<td>51</td>
<td>52</td>
<td>87</td>
<td>80</td>
</tr>
<tr>
<td>Renal involvement</td>
<td>11</td>
<td>10</td>
<td>53</td>
<td>40</td>
</tr>
<tr>
<td>Mortality rate</td>
<td>10</td>
<td>10-40</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

Abbreviation: DRESS, drug reaction with eosinophilia and systemic symptoms;

a Unless otherwise indicated, data are reported as percentages of patients.
In our 19 patients with allopurinol-induced DRESS, 7 had taken diuretics, but only 2 of them had taken thiazide diuretics (trichlormethiazide). We also found that preceding CRI was a characteristic clinical feature of allopurinol-induced DRESS and increased the risk of renal involvement (relative risk, 24.00; 95% CI, 1.69-340.99) (P = .002). Because previous research has revealed that CRI increases the risk of allopurinol-related SCAR (OR, 4.7 compared with 135 allopurinol-tolerant cases),15 we believe that the higher rates of preceding CRI do not simply reflect the higher incidence of receiving allopurinol treatment in patients with CRI. Whether the DRESS was induced by allopurinol had no statistically significant effect on the overall outcome.

On the other hand, 11 patients in the phenytoin group had a shorter duration of skin eruption (Table 3). To our knowledge, this characteristic has never been mentioned in comparison of phenytoin-related and carbamazepine-related hypersensitivity syndromes.16 More data are needed to support this preliminary observation. Moreover, neither history of CRI nor frequency of renal involvement differed between the phenytoin group and other groups (data not shown).

In our series, profound shock was the major cause of death. Four patients who died were in the allopurinol group and had a history of CRI. Further analysis revealed that these 4 patients had thrombocytopenia, a history of CRI, multiorgan involvement, and pancytopenia (Table 4), all characteristics that distinguished them from surviving patients. In our study, pancytopenia seemed to be the most significant factor of a poor prognosis, possibly reflecting the fact that suppressed bone marrow indicates a poor outcome. Although none of our cases presenting with pancytopenia fulfilled the diagnostic criteria for hemophagocytic syndrome,22 we cannot completely rule out this possibility because of the unusual presentation of pancytopenia in DRESS and the underdiagnosis of hemophagocytic syndromes.23

In the present study, there was no difference in corticosteroid use between mortality and nonmortality patients. In contrast to another study in Taiwan, which revealed pronounced eosinophilia in all 3 mortality cases, we did not find a significant difference in the presence of extreme eosinophilia between the 2 groups.14 One pos-

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**Table 3. Comparison Between Patients in Allopurinol, Phenytoin, and Other Groups**

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Allopurinol (n=19)</th>
<th>P Value b</th>
<th>Phenytoin (n=11)</th>
<th>P Value b</th>
<th>Others (n=30)</th>
<th>P Value c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time interval, mean (SD), d</td>
<td>27.0 (17.1)</td>
<td>.08</td>
<td>14.3 (6.1)</td>
<td>.20</td>
<td>19.1 (10.2)</td>
<td>.04 d</td>
</tr>
<tr>
<td>Duration of skin eruption, mean (SD), d</td>
<td>29.1 (11.1)</td>
<td>.03 d</td>
<td>12.5 (5.7)</td>
<td>.02 d</td>
<td>25.3 (24.5)</td>
<td>&lt;.001 d</td>
</tr>
<tr>
<td>Mucosal involvement, Y/N</td>
<td>14/5</td>
<td>.02 d</td>
<td>4/7</td>
<td>.99</td>
<td>11/19</td>
<td>.03 d</td>
</tr>
<tr>
<td>Liver involvement, Y/N</td>
<td>15/4</td>
<td>.41</td>
<td>8/3</td>
<td>.32</td>
<td>27/3</td>
<td>.37</td>
</tr>
<tr>
<td>Renal involvement, Y/N</td>
<td>13/6</td>
<td>.02 d</td>
<td>1/10</td>
<td>.23</td>
<td>10/20</td>
<td>.002 d</td>
</tr>
<tr>
<td>History of CRI, Y/N</td>
<td>14/5</td>
<td>-.001 d</td>
<td>0/11</td>
<td>.99</td>
<td>2/28</td>
<td>&lt;.001 d</td>
</tr>
<tr>
<td>History of DM, Y/N</td>
<td>7/12</td>
<td>.02 d</td>
<td>2/9</td>
<td>.23</td>
<td>2/28</td>
<td>.02 d</td>
</tr>
<tr>
<td>Overall outcome, M/D</td>
<td>4/15</td>
<td>.19</td>
<td>0/11</td>
<td>.99</td>
<td>2/28</td>
<td>.25</td>
</tr>
</tbody>
</table>

Abbreviations: CRI, chronic renal insufficiency; DM, diabetes mellitus; M/D, mortality/discharge; N, no; Y, yes.

a Allopurinol group vs others.
b Phenytoin group vs others.
c Allopurinol group vs phenytoin group vs others.
d Significant difference.

**Table 4. Comparison Between Mortality and Nonmortality Patients**

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Mortality</th>
<th>Nonmortality</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extreme eosinophilia, Y/N a</td>
<td>2/4</td>
<td>21/33</td>
<td>.27</td>
</tr>
<tr>
<td>Thrombocytopenia, Y/N</td>
<td>4/2</td>
<td>11/43</td>
<td>.03 b</td>
</tr>
<tr>
<td>Liver involvement, Y/N</td>
<td>5/1</td>
<td>45/9</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Renal involvement, Y/N</td>
<td>4/2</td>
<td>20/34</td>
<td>.21</td>
</tr>
<tr>
<td>History of CRI, Y/N</td>
<td>4/2</td>
<td>12/42</td>
<td>.04 b</td>
</tr>
<tr>
<td>Multiorgan involvement, Y/N c</td>
<td>4/2</td>
<td>8/46</td>
<td>.01 b</td>
</tr>
<tr>
<td>Pancytopenia, Y/N</td>
<td>5/1</td>
<td>0/54</td>
<td>&lt;.001 b</td>
</tr>
<tr>
<td>Systemic steroid use, Y/N</td>
<td>5/1</td>
<td>39/15</td>
<td>&gt;.99</td>
</tr>
</tbody>
</table>

Abbreviations: CRI, chronic renal insufficiency; N, no; Y, yes.

SI conversion factors: To convert eosinophils and leukocytes to 10^9/L, multiply by 0.001.
a Extreme eosinophilia was defined as follows: leukocyte count greater than 4000/µL and absolute count greater than 1500/µL or leukocyte count less than 4000/µL and differential count greater than 20%.
b Significant difference, Fisher exact test.
c More than 2 organs involved.
sible cause of this discrepancy may be that more patients in our study had received corticosteroid therapy (5 of 6) than in the earlier study (1 of 3).

Because of the variable clinical presentation of DRESS, whether it can be considered a specific entity is still under debate. In fact, the patients in our study exhibited many similar features, although we observed some characteristic differences between drugs, possibly indicating a spectrum of DRESS. We believe that clinicians should be aware of this syndrome not only because of its usually delayed diagnosis but also because of its severity and life-threatening potential.

In conclusion, we examined the clinical and pathologic features of 60 cases of DRESS in Taiwan. Although the existence of the disease entity of DRESS cannot be denied, its definition needs clarification because of the variability of the symptoms and signs involved. It may represent a disease spectrum related to severity and with some characteristic differences depending on the culprit drug.

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Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Chen and Chu. Acquisition of data: Chen and Chu. Analysis and interpretation of data: Chen and Chu. Drafting of the manuscript: Chen and Chu. Critical revision of the manuscript for important intellectual content: Chiu and Chu. Statistical analysis: Chen and Chu. Administrative, technical, and material support: Chiu. Study supervision: Chiu and Chu.

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