Therapeutic management of DRESS: A retrospective study of 38 cases

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Background: There is no consensus regarding treatment for drug reaction with eosinophilia and systemic symptoms (DRESS).

Objectives: We report a single-center observational series of therapeutic management of DRESS.

Methods: We examined data for 50 consecutive patients admitted from March 2005 to June 2009 with a discharge diagnosis of DRESS (RegiSCAR score).

Results: For the 38 patients with a DRESS score of 4 or more, topical steroid treatment alone was initiated in 66% of cases. On admission, 13 patients received systemic steroids; in 7 of them, systemic steroid treatment was initiated or maintained for life-threatening organ failure, with kidney, lung, and/or nervous system involvement. Complications of DRESS, such as relapse, viral reactivation, and sepsis, were less frequent with topical steroid than with systemic steroids. None of the patients died during their stay in hospital.

Limitations: Retrospective nonblinded design and dermatologic recruitment are limitations. The variables underlying the choice of treatment study were not analyzed.

Conclusions: Systemic steroids may not be required for the management of mild forms of DRESS, and may thus be reserved for more severe cases. Prospective studies are required to evaluate strategies for treating DRESS. (J Am Acad Dermatol 2015;72:246-52.)

Key words: drug-induced hypersensitivity syndrome; drug reaction with eosinophilia and systemic symptoms; severe cutaneous adverse reactions; systemic corticosteroids treatment; therapeutic management; topical steroids.

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare, severe multiorgan adverse drug reaction.[1] Antiepileptic agents (phenobarbital, carbamazepine, phenytoin, lamotrigine), minocycline, allopurinol, dapsone, and sulfonamides are the most frequently reported causes of this condition.[2] The incidence of DRESS is unclear, but has been estimated at more than 1 case per 10,000 exposures for antiepileptic agents and sulfonamides.[3,4]

DRESS syndrome is defined as the presence of fever, skin eruption, hematologic abnormalities (leukocytosis, eosinophilia, atypical lymphocytosis), and systemic involvement.[5] The RegiSCAR epidemiologic network has refined the definition of this syndrome through retrospective validation of the

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DRESS score[6] and epidemiologic studies.[7] Various types of visceral involvement, including hepatitis, pulmonary infiltration, and interstitial nephritis, are directly linked to prognosis.[1,7] DRESS differs from other drug-related eruptions in terms of its late onset (2-6 weeks after first drug intake), prolonged course,[1,8] and the role of viral reactivation. In most cases, clinical signs resolve without sequelae, but they may persist for several weeks, or even months.[1,9] This syndrome may cause death,[8] usually as a result of liver or heart failure.[7,10-12]

DRESS management includes the cessation of treatment with the causal drug. To our knowledge, no controlled trial or large observational study has ever focused on curative treatment for DRESS. Systemic steroids (0.5-1 mg/kg/d) are often used initially, particularly for the management of visceral involvement, regardless of severity.[8,13-15] The use of topical steroids, to relieve symptoms, has been reported for mild forms.[14,16] We report here a single-center observational series focusing on the treatment of DRESS with topical and systemic steroids.

CAPSULE SUMMARY

- Systemic corticosteroids have been considered the primary treatment for drug reaction with eosinophilia and systemic symptoms.
- In our series, two thirds of patients with nonsevere drug reaction with eosinophilia and systemic symptoms received potent topical steroids. Systemic steroids were initiated or maintained only in case of at least 1 life-threatening visceral manifestation.
- Systemic steroids may not be required to manage mild forms of drug reaction with eosinophilia and systemic symptoms.

METHODS

Patients

We retrospectively screened all consecutive patients admitted to our department from March 2005 to June 2009 who received steroids and had a discharge diagnosis of DRESS. The final diagnosis was validated by a review committee (J-C. R., L. V-A., S. B.), using the RegiSCAR DRESS score,[6] with blinding to any risk factors. Each case was scored (4-5 = probable case; >5 = definite case); we considered only cases with a score of 4 or more.

We collected clinical and epidemiologic data, including demographic characteristics, information about exposure to drugs, the time interval between drug intake and the onset of symptoms, clinical presentation of fever, cutaneous features, lymph nodes, visceral involvement, biological data (peripheral blood absolute leukocyte count; eosinophilia; atypical lymphocytes; levels of bilirubin, gamma-glutamyltransferase, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, prothrombin, bilirubin, serum creatinine, and urea; presence of herpesviruses [qualitative polymerase chain reaction on blood], sternal puncture if necessary), and skin biopsy reports. Internal organ involvement was defined for each organ, according to Registry for Severe Cutaneous Adverse Reactions (RegiSCAR) score.[6] The drugs responsible for DRESS were defined as previously described.[7]

Treatment and course of the disease

We collected data concerning the treatment and course of the syndrome. We defined 2 groups on the basis of treatment strategy: treatment with potent or very potent topical steroids only (betamethasone or clobetasol) or with systemic steroids. Topical steroids were applied once or twice daily, but never under occlusion. Systemic steroids were administered orally or intravenously.

Statistical methods

The characteristics of the patients receiving topical and systemic steroids were described, relative to the total population as the denominator. Prevalence rates were calculated and variables associated with the choice of treatment strategy were investigated: age; sex; time from DRESS onset to drug withdrawal; duration of skin, liver, and kidney relapses; and durations of hospital stay and of treatment. The χ^2 statistics (or Fisher exact test, where indicated) and Mann-Whitney tests were used to analyze qualitative and quantitative data, respectively. Data were analyzed with software (Excel, Microsoft, Redmond, WA) and values of P less than .05 were considered statistically significant.

RESULTS

Description of the population

We analyzed data for 50 consecutive patients with a discharge diagnosis of DRESS; 38 patients had a RegiSCAR score of 4 or more, indicating probable DRESS, and were included in the study (Fig 1). The patients treated with topical and systemic steroids did not differ in age (median age: 49 ± 22 years [range: 16-87 years] vs 54 ± 22 years [range: 20-88 years], respectively, P = .66) or sex (number of female: n = 14/25 [56%] vs n = 5/13 [38%], respectively, P = .2) (data not shown).

The drugs implicated in these cases of DRESS are listed in Table I. In most patients (n = 33), a single drug