Review Article

Pamukkale Medical Journal
doi:https://dx.doi.org/10.31362/patd.1091237

Time is skin: what does the emergency physician need to know about DRESS?

Zaman eşittir cilt: Acil servis hekimleri DRESS sendromu hakkında ne bilmeli?

Reşad Beyoğlu

Posted date:21.03.2021 Acceptance date:12.05.2022

Abstract

Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) syndrome, also known as Drug Induced Hypersensitivity Syndrome (DIHS), is an acute drug-induced hypersensitivity reaction. The pathogenesis of this syndrome, which can develop due to many drugs, especially antiepileptic agents, is not known exactly. This syndrome, which was denominated “hydantoin hypersensitivity” in 1950, was renamed as “DRESS syndrome” by Bocquet and his colleagues in 1996 and the first diagnostic criteria were determined. It is estimated that increased reactive metabolites due to inadequate detoxification of some drugs cause immunological reaction and it is thought that a similar reaction such as herpesvirus and Ebstein Barr Virus, as well as drugs, can cause DRESS syndrome.

Unlike syndromes that may develop due to other drugs, DRESS syndrome customarily commences 2-8 weeks after the commencement of the drug, and symptoms perpetuate to progress after discontinuation of the responsible drug. Symptoms such as fever, lymphadenopathy, hematological disorders, maculopapular rash and internal organ involvement are common in this syndrome.

Diagnosis of DRESS syndrome is often difficult, as the clinical manifestations are varied and the latent period after the initiation of drug use can be up to 3 months. Thus, it is thought that the diagnosis of DRESS should be in the minds of all doctors, especially emergency physicians because when this diagnosis is overlooked, its mortality is around 10-20% and it is a very serious clinical condition.

Key words: DRESS, drug rash with eosinophilia systemic symptoms, ED.

Beyoglu R. Time is skin: what does the emergency physician need to know about DRESS? Pam Med J 2023;16:…-….

Öz

Drug Rash with Eoshinophilia and Systemic Symptoms (DRESS) sendromu veya diğer adıyla da bilinen İlaçla indüklenen hipersensitivite sendromu (Drug Induced Hypersensitivity Syndrome (DIHS), ilaca bağlı akut bir hipersensitivite reaksiyonudur.

Başta antiepileptik ajanlar olmak üzere birçok ilaca bağlı gelişebilen bu sendromun patogenezi tam olarak bilinmemektedir. 1950 yılında “hidantoin hipersensitivitesi” olarak adlandırılan bu sendrom, 1996 yılında Bocquet ve arkadaşları tarafından “DRESS sendromu” olarak yeniden adlandırılmış ve ilk tanı kriterleri belirlenmiştir. Bazı ilaçların detoksifikasyonundaki yetersizliğe bağlı artan reaktif metabolitlerin immünolojik reaksiyona neden olduğu tahmin edilmektedir. İlaçların yanısıra herpesvirüs ve Ebstein Barr Virüsü gibi benzer bir reaksyonlar DRESS sendromuna yola açabildiği düşünülmektedir.

DRESS sendromunun diğer ilaçlara bağlı gelişebilen sendromlardan farklı olarak Klinik bulgularının genellikle ilacın kullanılmaya başlanmasından 2-8 hafta sonrasında başlaması ve sorumlu ilacın kesilmesiyle semptomların ilerlemeye devam etmesidir.

Ateş, lenfadenopati, hematolojik bozukluklar, makülopapüler döküntü ve ve iç organ tutulumları gibi bulgular bu sendromda rastlamak sıktır.

Klinik bulguların çeşitli olması ve ilaç kullanımının başlaması sonrasındaki latent periyodun 3 aya kadar uzun olabilmesi nedeniyle DRESS sendromunun tanısı sıklıkla güçtür. Bu nedenle DRESS sendromunun, başta acil servis hekimleri olmak üzere tüm doktorların aklında tutulması gerektiği düşünülmektedir. Tanısı gözden kaçtığında mortalitesi %10-20 civarında olup oldukça önemli bir klinik tablodur.

Anahtar kelimeler: DRESS, eozinofili ve sistemik semptomlarla seyreden ilaç reaksiyonu, acil servis.

Beyoğlu R. Zaman eşittir cilt: Acil servis hekimleri DRESS sendromu hakkında ne bilmeli? Pam Tıp Derg 2023;16:…-…

Reşad Beyoğlu, M.D. Emergency Medicine Specialist, Servergazi State Hospital, Department of Emergency Medicine, Denizli, Turkey, e-mail: resadbeyoglu@gmail.com (https://orcid.org/0000-0001-7321-5131) (Corresponding Author)

Introduction

Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) syndrome, also known as Drug Induced Hypersensitivity Syndrome (DIHS), is an acute drug-induced hypersensitivity reaction. The pathogenesis of this syndrome, which can develop due to many drugs, especially antiepileptic agents, is not known exactly. Increased reactive metabolites due to inadequate detoxification of some drugs are predicted to cause an immunological reaction. It is thought that similar reactions such as herpesvirus and Epstein Barr Virus, as well as drugs, can cause DRESS syndrome. This syndrome, which was denominated “hydantoin hypersensitivity” in 1950, was renamed as “DRESS syndrome” by Bocquet and his colleagues in 1996 and the first diagnostic criteria were determined.

Unlike syndromes that may develop due to other drugs, DRESS syndrome customarily commences 2-8 weeks after the commencement of the drug, and symptoms perpetuate to progress after discontinuation of the responsible drug. Symptoms such as fever, lymphadenopathy, hematological disorders, maculopapular rash and internal organ involvement are common in this syndrome.

Diagnosis of DRESS syndrome is often difficult, as the clinical manifestations are varied and the latent period after the initiation of drug use can be up to 3 months. Therefore, it is thought that the diagnosis of DRESS should be in the minds of all doctors, especially emergency physicians.

Literature review

Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) syndrome, additionally kenned as Drug Induced Hypersensitivity Syndrome (DIHS), is an acute drug-induced hypersensitivity reaction [1, 2]. The pathogenesis of this syndrome, which can develop due to many drugs, especially antiepileptic agents, is not known precisely [1]. Incremented reactive metabolites due to inadequate detoxification of some drugs are predicted to cause an immunological reaction [3]. It is thought that similar reactions such as herpesvirus and Epstein Barr Virus, as well as drugs, can cause DRESS syndrome [1, 3-5]. This syndrome, which was denominated “hydantoin hypersensitivity” in 1950, was renamed as “DRESS syndrome” by Bocquet and his colleagues in 1996 and the first diagnostic criteria were determined [3, 6, 7].

Unlike syndromes that may develop due to other drugs, DRESS syndrome usually starts 2-8 weeks after the start of the drug, and symptoms continue to progress after discontinuation of the responsible drug [7, 8].

Symptomes such as fever, lymphadenopathy, hematological disorders, maculopapular rash and internal organ involvement are common in this syndrome [1, 9].

Diagnosis of DRESS is often difficult, as the clinical manifestations are varied and the latent period after the initiation of drug use can be up to 3 months [8].

Although the exact incidence of DRESS is unknown, it is estimated at 1.2-6 cases/1 million/year. However, for common causative drugs like anticonvulsants and sulfonamides, the incidence is estimated to be one in 1000-10.000 drug exposures [3, 10].

Diagnosis of DRESS syndrome is often difficult, as the clinical manifestations are varied and the latent period after the initiation of drug use can be up to 3 months.

As it shown below, diagnostic criteria were established by the RegiSCAR working group to identify potential cases of DRESS syndrome [3].

(The presence of 3 or more of the manifestations other than the first two criteria is required)

- Need for hospitalization

- Presence of suspected drug use that may cause a reaction

- Acute skin rash

- Fever above 38°C

- LAP in at least 2 areas

- At least one internal organ involvement

- Blood findings

*Less or more than normal lymphocyte count

*Eosinophil elevation (in number or percentage)

*Platelet count below normal values

DRESS syndrome is a condition with a high mortality of 10-20%, so early diagnosis and treatment are very consequential particularly in ED [2, 3, 11, 12].

Although more than 50 drugs have been reported as the cause of DRESS syndrome, the most common drugs are aromatic anticonvulsants, allopurinol, and sulfonamides [3]. It was reported that anticonvulsant drugs carbamazepine and phenytoin were responsible for 43.6% of all DRESS syndrome cases, whereas severe cutaneous drug reaction due to valproic acid and topiramate was not observed [13].

While the most common symptom of DRESS syndrome is fever (90%-100%), the second most common symptom (70%-97%) is skin manifestations and it usually occurs 1-8 weeks following the start of treatment (Figure 1) [2, 9, 14, 15].

Mucosal involvement is seen in 60% of cases, and the most common site is the oral mucosa (Figure 2) [14, 15]. The most common hematological disorder is Eosinophilia (>50%) [2, 14, 16, 17] and the most common systemic symptom is liver abnormalities (60%) [1, 3, 18].

It is recommended that patients presenting to the emergency department with signs and symptoms suggestive of hypersensitivity should be questioned whether they have been on medication within the last six months. Detailed physical examination, vital signs (especially temperature measurement) and laboratory tests should not be forgotten.

Figure 1. Diffuse maculopapular rash, more prominent on the back, chest, and arms

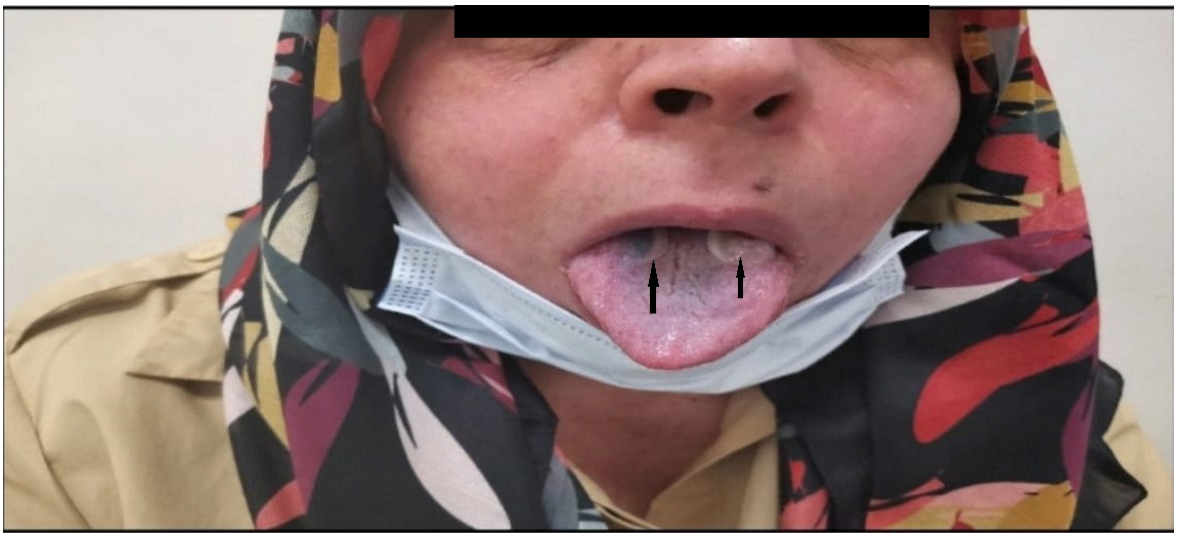

Figure 2. Oral mucosal erosion

Laboratory tests should include LFT, complete blood count (especially eosinophil) and KFT. Since the most important cause of mortality in these patients is liver failure, liver enzymes should be followed up [2, 14].

There are many expert opinions that glucocorticoids and intravenous immunoglobulin (IVIG) are beneficial, especially in the treatment of severe cases [19].

As a conclusion, When emergency physicians detect any new drug use, especially aromatic anticonvulsants, allopurinol, and sulfonamides, any rash or skin lesions accompanying systemic complaints (fever, hematological disorders, LFT disorder, etc.), DRESS syndrome should also be taken into account and dermatology consultation should be requested and it should not be forgotten that early diagnosis of the disease and discontinuation of the responsible drug in the early period will contribute to the reduction of mortality and morbidity in these cases.

Conflict of interest: No conflict of interest was declared by the authors.

References

1. Choudhary S, McLeod M, Torchia D, Romanelli P. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome. J Clin Aesthet Dermatol 2013;6:31-37.
2. Criado PR, Criado RFJ, Avancini JM, Santi CG. Drug reaction with Eosinophilia and Systemic Symptoms (DRESS) / Drug-induced Hypersensitivity Syndrome (DIHS): a review of current concepts. An Bras Dermatol 2012;87:435-449. https://doi.org/10.1590/s0365-05962012000300013
3. Cacoub P, Musette P, Descamps V, et al. The DRESS syndrome: a literature review. Am J Med 2011;124:588-597. https://doi.org/10.1016/j.amjmed.2011.01.017
4. Husain Z, Reddy BY, Schwartz RA. DRESS syndrome: part I. clinical perspectives. J Am Acad Dermatol 2013;68:693(e1-14). https://doi.org/HYPERLINK "https://doi.org/10.1016/j.jaad.2013.01.033"10.1016/j.jaad.2013.01.033
5. Fernando SL. Drug-reaction eosinophilia and systemic symptoms and drug-induced hypersensitivity syndrome. Australas J Dermatol 2014;55:15-23. https://doi.org/10.1111/ajd.12085
6. Bocquet H, Bagot M, Roujeau JC. Drug-induced pseudolymphoma and drug hypersensitivity syndrome (Drug Rash with Eosinophilia and Systemic Symptoms: DRESS). Semin Cutan Med Surg 1996;15:250-257. https://doi.org/10.1016/s1085-5629(96)80038-1
7. Callot V, Roujeau JC, Bagot M, et al. Drug-induced pseudolymphoma and hypersensitivity syndrome. Two different clinical entities. Arch Dermatol 1996;132:1315-1321. https://doi.org/10.1001/archderm.1996.03890350057010
8. Alkhateeb H, Said S, Cooper CJ, Gaur S, Porres Aguilar M. DRESS syndrome following ciprofloxacin exposure: an unusual association. Am J Case Rep 2013;14:526-528. https://doi.org/10.12659/AJCR.889703
9. Shiohara T, Inaoka M, Kano Y. Drug-induced Hypersensitivity Syndrome (DIHS): a reaction ınduced by a complex ınterplay among herpesviruses and antiviral and antidrug ımmune responses. Allergol Int 2006;55:1-8. https://doi.org/10.2332/allergolint.55.1
10. Cabañas R, Ramírez E, Sendagorta E. Spanish guidelines for diagnosis, management, treatment and prevention of DRESS syndrome. J Investig Allergol Clin Immunol 2020;30:229-253. https://doi.org/10.18176/jiaci.0480
11. Chen YC, Chiu HC, Chu CY. Drug reaction with eosinophilia and systemic symptoms: a retrospective study of 60 cases. Arch Dermatol 2010;146:1373-1379. https://doi.org/10.1001/archdermatol.2010.198
12. Chiou CC, Yang LC, Hung SI, et al. Clinicopathological features and prognosis of drug rash with eosinophilia and systemic symptoms: a study of 30 cases in Taiwan. J Eur Acad Dermatol Venereol 2008;22:1044-1049. https://doi.org/10.1111/j.1468-3083.2008.02585.x
13. Yang CY, Dao RL, Lee TJ, et al. Severe cutaneous adverse reactions to antiepileptic drugs in Asians. Neurology 2011;77:2025-2033. https://doi.org/10.1212/WNL.0b013e31823b478c
14. Emre S, Akoglu G, Metin A, Demirseren DD, Kurtoğlu G. Evaluation of clinical features of 11 cases with DRESS syndrome. Türkderm 2013;47:218-222. https://doi.org/10.4274/turkderm.71324
15. Tetsuo Shiohara, Yoshiko Mizukawa. Drug-induced hypersensitivity syndrome (DiHS)/drug reaction with eosinophilia and systemic symptoms (DRESS): an update in 2019. Allergol Int. 2019;68:301-308. https://doi.org/10.1016/j.alit.2019.03.006
16. Tsyrulnik A, Landman A. Drug rash with eosinophilia and systemic symptoms: two emergency department cases. West J Emerg Med 2011;12:559-562. https://doi.org/10.5811/westjem.2010.11.2077
17. Criado PR, Avancini J, Santi CG, Amoedo Medrado AT, Rodrigues CE, de Carvalho JF. Drug reaction with eosinophilia and systemic symptoms (DRESS): a complex interaction of drugs, viruses and the immune system. Isr Med Assoc J 2012;14:577-582.