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Drug Reaction with Eosinophilia and Systemic Symptoms (Dress) Syndrome: A Rare Case Report

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Abstract

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a multisystem involvement with fever, lymphadenopathy, and hematologic abnormalities.

Most patients with DRESS syndrome can fully recover, while some may have a prolonged journey of illness.

Here, we present a rare case of a 47-year-old male patient who had fever, rash, lymphadenopathy, elevated liver enzymes, eosinophilia, sore throat, and diffuse pruritic macular rash 10 days after the use of NSAIDs for a low back pain that started two weeks ago. Symptoms resolution was achieved by 14 days of systemic corticosteroid therapy in addition to stop the causative drug.

Introduction

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome or drug-induced hypersensitivity reaction (DIHS) is a severe cutaneous drug reaction characterized by fever, lymphadenopathy, hematologic abnormalities, multisystem involvement, and viral reactivation. Several features distinguish it from the more commonly encountered morbilliform drug reaction. This review will cover the clinical features, workup, and recommended treatment approach to patients with DRESS [1].

There is a latency of 2–8 weeks between drug exposure and the onset of skin rash in DRESS syndrome, which is more than in most other drug reactions. The most common culprits are antiepileptics like carbamazepine, lamotrigine, or phenytoin in 35%, NSAIDs in 13%, sulfonamides like sulfasalazine, dapsone, trimethoprim-sulfamethoxazole, or sulfadiazine in 12%, antibiotics such as vancomycin, minocycline, or penicillin in 11%, and allopurinol in 6% of cases [2].

Some studies have revealed the genetic association in DRESS syndrome; notably, HLA-B*58:01 is associated with allopurinol hypersensitivity, and HLA-B*13:01 is associated with dapsone hypersensitivity. DRESS syndrome occurs as a result of the activation of T cells specific to each drug, making the reaction drug-specific. It often results in reactivation of viruses, especially human herpesviruses, a phenomenon thought to be due to the expansion of regulatory T cells [3].

We reported a rare case of a male patient who had DRESS syndrome after the use of NSAIDs for his back pain. Stopping the drug with the administration of corticosteroids were the definite treatment.

Case Presentation

A 47-year-old male patient was presented to the emergency department with two days of fatigue, sore throat, rash and a high fever. Past medical history was remarkable only for a new lower back pain two weeks ago which was treated with NSAIDs. Family history demonstrated type two diabetes mellitus in his mother, Hashimoto disease in his sister. Vital signs were as follows.

His blood pressure was 10.5/50 mmHg, his pulse was 88/min, his respiration rate was 22/min, his temperature was 39.8 C0. Physical examination showed a diffuse maculopapular rash on his head, trunk soles and palms. Oral cavity and mucosal membranes were spared. He had a mild degree of generalized edema in his body. Initial laboratories revealed a white blood cell count of 13.1 ×103/μL, with 57% neutrophils, 33% lymphocytes, and 4% eosinophils. Other initial laboratory tests are shown in Table 1. A blood smear demonstrated many pleomorphic atypical reactive lymphocytes. Blood culture was negative. Advanced laboratory studies such as serological tests for hepatitis and human immunodeficiency viruses, polymerase chain reaction tests for common viral infections, autoimmune serology for antimitochondrial, antiliver kidney microsomes, and antinuclear antibodies were all negative. Complement levels (C3 and C4) were within the normal range. We performed chest-x-ray, echocardiography and were normal. Abdominal and pelvis ultrasound revealed mild hepatosplenomegaly.

Table 1: Laboratory Tests

	Admission	Hospital stay	Discharge	Normal range
Wight blood cell count ×103/µL	13.1	19.7	8	4–10
Hemoglobin, g/dL	10.5	10.1	10	13.0– 17.0
Platelets×105/mcl	300	350	199	150– 400
Creatinine mg/dl	1.1	1.3	1.0	0.3-1.2
Urea mg/dl	41	60	29	20-40
Glucose mg/dl	85	90	80	65-110
Mean corpuscular volume, fL	94	91	88	83.0– 101.0
Mean corpuscular hemoglobin, pg	27	29	29	27.0– 32.0
Mean corpuscular hemoglobin concentration, g/dL	35	33	31	31.5– 34.4
RDW, %	13	13	11	11.6– 14.5
Lymphocytes, ×103/µL	4	9	4	1–3
Eosinophils, ×103/µL	0.8	7	0.3	0–0.5
Alkaline phosphatase, U/L	350	450	200	40–150
Alanine aminotransferase, U/L	199	244	230	0–55
Aspartate aminotransferase, U/L	88	241	55	5–34
C-reactive protein, mg/L	29	3	3	0–5

Drug reaction was suspected. We started with anti-histamine and hydrocortisone with no clear improvement. After six hours, the blood pressure dropped to 90/40 mmHg, pulse 100/min, respiratory rate 26/min, and temperature 40 C0. We suspected a sepsis origin. We started broad spectrum antibiotics intravenously (ceftriaxone, piperacillin-tazobactam, and vancomycin). A repeated blood culture showed no growth. On the third day of admission, we transferred the patient to the intensive care unit for oxygen and because his laboratory results showed leukocytosis (33 × 103/µL) with eosinophilia (7.8 × 103/µL) as well as increasing aspartate aminotransferase (512 U/L), alanine aminotransferase (1200 U/L), and alkaline phosphatase (401 U/L).

We reached the diagnosis of DRESS syndrome. As a result, we stopped the antibiotics.

We administrated a course of 40 mg intravenous methylprednisolone followed by a 14-day tapering course of 80 mg oral prednisolone.

The patient showed great resolution of his symptoms. There was an improvement to his rash. His laboratories were normal (eosinophil count 0.3 × 103/µL) except for liver function tests. They went normal after one month. We discharged him to be back later. The patient gained complete health in the fourth week.

Discussion

Some studies have revealed the genetic association in DRESS syndrome; notably, HLA-B*58:01 is associated with allopurinol hypersensitivity, and HLA-B*13:01 is associated with dapsone hypersensitivity [4,5].

The pathophysiology of DRESS/DIHS is still not yet completely understood. Viral reactivation, particularly HHV6, Epstein Barr virus, and CMV, is not only common among patients with DRESS/DIHS and has been implicated in the pathophysiology of this disease. It is also associated with poor outcomes and increased mortality. Documentation of viral reactivation is dependent on the timing of the ELISA or PCR, as there is a sequential pattern of HHV reactivation in patients with DRESS/DIHS [1].

DRESS syndrome is a complex syndrome with a broad spectrum of clinical features. The clinical manifestations are not immediate and usually appear 2 to 8 weeks after introduction of the triggering drug. 23 Common features consist of fever, rash, LAP, hematological findings (eosinophilia, leukocytosis, etc.), and abnormal liver function tests, which can mimic viral hepatitis. [6].

The skin manifestations of DIHS are maculopapular rash, erythema multiforme, exfoliative dermatitis, acute generalized exanthematous pustular dermatosis-like eruption, and erythroderma [1].

Leukocytosis with atypical lymphocytes and eosinophilia of varying degree is a prominent feature of the syndrome [7].

The European RegiSCAR devised a scoring system based on clinical features, the extent of skin involvement, organ involvement, and clinical course to help clinicians confirm or exclude the diagnosis of DRESS syndrome. [8].

Our patient had a RegiSCAR score of 7, which makes him a case of definite DRESS syndrome (Table 2). Liver abnormalities occur in up to 70% of patients and are characterized by a marked increase in serum alanine aminotransferase value. Severe hepatitis portends a prolonged course characterized by multiple exacerbations and remissions of both rash and liver disease [9,10].

Table 2: The RegiSCAR score and its components. Total score: 8 (<2 no DRESS syndrome, 2–3 possible DRESS syndrome, 4–5 probable DRESS syndrome, ≥6 definite DRESS syndrome). DRESS, drug reaction with eosinophilia and systemic symptoms; RegiSCAR, Registry of Severe Cutaneous Adverse Reactions.

Fever (≥38.5°C)	yes	1
Enlarged lymph nodes (≥2 sites, ≥1 cm)	yes	1
Atypical lymphocytes	yes	1
Eosinophilia (700–1,499 or 10–19.9%)	yes	1
Skin rash		
Extent >50%	Yes	1
At least two of: edema, infiltration, purpura, scaling	Yes	1
Biopsy suggesting DRESS syndrome yes 0	Yes	0
Internal organ involved	two organs (liver and spleen)	0
Resolution delay	>15 days	0
At least three biological investigations done and negative to exclude an alternative diagnosis	yes (antinuclear antibodies, blood cultures, serology for HAV/HBV/HCV)	1

Our patient had an elevated serum liver function test (ALT, AST).

The mainstay of treatment is systemic corticosteroids. Rapid resolution of rashes and fever occurs within several days after starting systemic corticosteroids: the usual dosage is prednisolone 40-60 mg/day. However, systemic corticosteroids need to be tapered over 6 8 weeks to prevent the relapse of various symptoms of this syndrome [7].

For our situation, the patient showed brilliant clinical reaction with the commencement of systemic corticosteroids. Given the high changeability in the clinical show, the analysis of DRESS disorder as a rule requires a serious level of doubt and clinical judgment.

Conclusion

DRESS syndrome is a very challenging case in medicine. Because of its rarity, we should give high suspicion of patient who present with fever, cutaneous lesion, internal organs involvement and hematological abnormalities after the administration of a new drug. Early recognition of such serious case will reveal in a good outcome.

Declaration of Competing Interest

The authors report no declarations of interest. Sources of funding

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Written informed consent was obtained from the patient's parents for publication of this case report and accompanying images, in line with local ethical approval requirements. No other requirements were stipulated.

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