Dermatology Case Reports

Case Report Open Access

From Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) to severe DRESS

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Abstract

Drug Reaction with Eosinophilia and Systemic Symptoms, or DRESS, is a rare drug reaction and can be life-threatening in some cases. This is a report of a 55-years-old woman who presented to the Emergency Room of our hospital with a diffuse morbilliform eruption, approximately one month after starting to take Allopurinol for her gout. In addition to the dermatological manifestations, she developed other systemic manifestations (hepatic and cardiovascular) very rapidly and expired as a result of complications secondary to DRESS.

Case Presentation

A 55-year-old African American woman presented to the Emergency Room (ER) of our hospital with a diffuse morbilliform eruption and edema of her face and neck approximately four weeks after being started on Allopurinol. One week prior to the presentation to the ER, she developed a generalized pruritic erythematous rash, for which she was given Famotidine; two days prior to the presentation she was also given oral and topical Hydrocortisone as she continued to be symptomatic. After neither of these two approaches worked, she presented to the ER again.

On physical exam, she was in mild distress secondary to pruritus. A solitary nodular mass, fixed and painless to palpation, measuring 2 cm by 2 cm was present in the posterior aspect of her neck. A diffuse, morbilliform rash was present which covered her entire body with sparring of the palms, soles and her oral mucosa. In addition to her pruritus, she also endorsed a stiff and bloated abdomen.

She was admitted to the medicine floor, Allopurinol was discontinued and was started on Prednisolone. Triamcinoloe 0.1% topical ointment and calamine lotion were also simultaneously started to treat her generalized pruritus. Over the next two days, her condition remained stable, but on the third day after admission, she became hemodynamically unstable requiring transfer to the Intensive Care Unit.

Her laboratory values during the course of her hospitalization are presented in Table 1 below.

Later, she was transferred to another facility for cardiac catheterization, which revealed a normal coronary angiography. She expired as a result of complications. Sections of the heart (Figure 1) and skin (Figures 2A and 2B) obtained at autopsy are presented below.

	On Admission	At the time of transfer to the ICU	At the time of transfer to another facility
Eosinophils (x10^9/L)	13% (2.4)	-	15% (3.41)
AST (U/L)	63	-	218
ALT (U/L)	176	-	187
Lactate Dehydrogenase(U/L)	703	-	970
Troponin (ng/mL)	-	34.39	-
Lactic Acid (mmol/L)	-	5.4	-
EBV IgM (U/mL)	-	-	<10
EBV IgG (U/mL)	-	-	444

Table 1: Laboratory values during the course of her hospitalization.

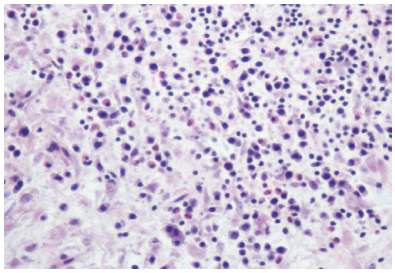

Figure 1: Mixed inflammatory infiltrate that includes eosinophils in the myocardium (Original magnification 40x).

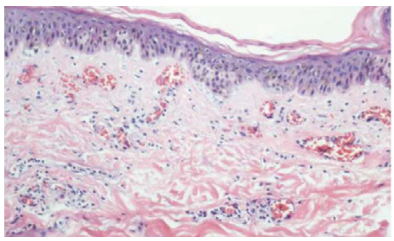

Figure 2A: Spongiosis, perivascular lymphocytic infiltrates, and eosinophils in the dermis (Original magnification 4x).

Discussion

Drug Reaction with Eosinophilia and Systemic Symptoms, or DRESS, is a rare and potentially life-threatening form of Severe Cutaneous Adverse Reactions (SCARs); other SCARs include Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis [1].

For a case to be diagnosed as DRESS, it is accepted that a variable

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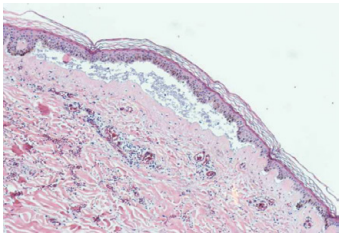

Figure 2B: Spongiosis, perivascular lymphocytic infiltrates, and eosinophils in the dermis (Original magnification 10x).

combination of the following seven criteria be present [2]: 1) It has to be drug-induced; 2) Onset about 2-6 weeks after starting an offending agent; 3) A rash that persists; 4) Involvement of at least one internal organ; 5) Lymphocyte abnormalities; 6) Eosinophilia; 7) reactivation of latent viruses; and for a presentation to be classified as DRESS and to be included in the European based Regis CAR study group, three or more criteria are required [2]. Our patient met the following criteria: hospitalization; reaction suspected to be drug related; an acute skin rash; involvement of at least one internal organ; eosinophilia. Furthermore, using their scoring system, we assigned points as follows:

- -1 point since she did not have fever.
- +1 point for skin rash covering > 50% of BSA.
- +1 point for a skin rash suggesting DRESS.
- +2 points since two organs were affected (heart and liver).
- +2 points since eosinophil count was greater than 1.5×10^9 /L.

The total score of five makes this presentation a probable case of DRESS [2]. Edema involving the face is also a very specific finding in DRESS, and this was present in our patient as well. A small list of drugs has been associated with DRESS, and amongst them Allopurinol has been shown to be the most common with an average latency period of 27 days [1]. Our patient's symptoms first started about four weeks after initiating therapy with Allopurinol, in line with published data on latency [3]. Amongst laboratory findings, the work by Chen Y et al. [1] demonstrated that 80% of their study group had liver enzymes double that of normal, and our patient had this finding as well. IgG reactive to Epstein-Barr virus (EBV) was seen in 9 in the work by Chen Y et al. [1], and this was seen in our patient as well.

A clear etiology for the cause in our patient and for DRESS patients in general remains elusive. Several possible mechanisms described include: accumulation of drug metabolites due to a genetic deficiency in detoxifying enzymes; associations seen with specific human leukocyte antigens (HLA); and a possible virus-drug reaction [4,5]. Reactivation of Human Herpes Viruses (HHV) have occurred at the time of drug induced hypersensitivity reactions [6]. Cytomegalovirus (CMV), and EBV have also been associated drug-induced hypersensitivity syndrome [5]. Of the associated viruses, the published literature is most in favour of an active EBV infection causing the hypersensitivity syndrome which may have been a contributing factor in our patient, however, only her IgG, not IgM, was elevated.

At this time no specific histopathologic finding is available to either rule DRESS in or out [7]. A skin biopsy in a patient DRESS would reveal, mild spongiosis in the epidermis, lymphocytic infiltrate in the superficial dermis, papillary dermal edema as well as dilated vasculature in the dermis [8]. Eosinophils may also be present in the inflammatory infiltrate. In addition to the dermatological manifestations, other possible organ involvement includes the lymph nodes, liver, heart, lungs, and kidneys [9]. In fact, the most common cause of death in patients with DRESS is liver failure. Organ involvement can even persist for weeks to months after the medication withdrawal.

In a patient presenting with DRESS, the first step in management is to remove the offending drug. Corticosteroids are first line therapy for patients with DRESS and in many cases need to maintained for weeks to months to treat the continuing organ involvement. On the other hand, treatment with IVIG increases the possibility of HHV-6 reactivation and worsening of outcomes [9]. Finally, DRESS is considered to be severe when management in an ICU becomes necessary or the patient dies from complications such as end organ failure [10].

Conclusion

DRESS, while rare, can develop into severe DRESS very rapidly. When a patient presents with the findings described in this case, keeping DRESS at the top of a health care provider's consideration will help lead to better outcomes. Prompt withdrawal of the offending medications and administration of corticosteroids are the first and most important steps in managing this syndrome.

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