



Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) or Stevens - Johnson syndrome (SJS): Does the Name Matter!

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Keywords

Rash, Eosinophilia, Dress, Steven-johnson syndrome-toxic epidermal necrolysis, AGEP, SCARs, Hypersensitivity drug reaction, Share syndrome

Case

The case is of 23-year-old Caucasian male who fell from 30 feet height in a suicidal attempt. He sustained multiple orthopedic fractures including hips, left lower ribs, and right radius at the elbow. He had multiple orthopedic surgeries with fixation of his fractures including pins, plates and screws. He presented to the hospital with fever, tachycardia, and malaise. He was discharged initially to long-term acute care (LTAC) for continued recovery. After 3 weeks in the LTAC he developed pinhole infection of his hip and right forearm which was reported methicillin resistant staphylococcal infection (MRSA) positive and was started on Vancomycin. After 5 days in the LTAC, where he developed a generalized rash on his chest that was pruritic and erythematous but not painful. The rash became progressively worse spreading to the upper thighs and face. The patient was switched to linezolid out of concern for drug rash with vancomycin. This was continued for 3 days and then stopped. The patient was given a dose of levofloxacin and steroid, however, due to increasingly high fever, rash progressing to the face with facial edema, and tachycardia to 160's, the patient was transferred to acute care facility. Patient has had multiple blood cultures and wound cultures of elbow that have been negative. He was evaluated by the psychiatrist at the LTAC because of the suicidal tendency and was started on aripiprazole 5 mg QHS.

His electronic record showed that he had positive wound culture that grew MRSA. His CBC showed 12% eosinophilia, anemia with Hg of 9.7 g/dl, but no leukocytosis. Normal complete metabolic panel and liver function tests. A skin biopsy showed eosinophilic infiltration throughout the dermis. The course is consistent with

DRESS syndrome or SJS/TEN. His complement levels (C3, C4), rheumatoid factor, cryoglobulin, and further blood cultures were negative.

He developed DVT secondary to immobilization during his stay at the LTAC and was started on Coumadin with therapeutic INR. His examination revealed normal Cardiovascular, respiratory, and abdominal examination. His exposed hardware of the right elbow showed no infection, however, his hip pin site repeatedly grew MRSA infection and he was continued on linezolid. He was treated with oral steroids and topical corticosteroids and he made steady recovery of his skin rash. His aripiprazole was stopped for DRESS syndrome concern.

Discussion

Cutaneous adverse reaction to drugs (SCARs) is a spectrum of diseases that includes acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS) and epidermal necrolysis (Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS-TEN)). Drug reactions are not uncommon in hospitalized patients and affecting 2% to 3% [1]. Only a fraction of these reactions (2%) are considered severe to seek medical attention [1].

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These skin conditions have many histological and biological features in common [2,3]. Diagnosis of these syndromes is mainly based on clinical grounds, and overlap between the various clinical entities do occur making accurate diagnosis on clinical grounds almost impossible. Most of these syndromes are characterized by a latency period of 2-6 weeks between the exposure to drug and the cutaneous findings which is required for type-IV hypersensitivity to develop. Cutaneous manifestations are common and present in 70%-100% of cases.

Eosinophilia is considered the most frequently occurring hematological abnormality (> 50%) of the cases. Other hematological abnormalities observed were thrombocytopenia, anemia, neutropenia, and the presence of large activated atypical lymphocytes.

Hepatic involvement in the form of hepato-cellular necrosis with high liver enzymes was the most common visceral abnormalities encountered in these cases. Renal dysfunction in the form of proteinuria, decreased renal functions, and high creatinine were observed most often with allopurinol and other antibiotics. Minocycline causes eosinophilic pneumonitis (33%) of the cases [4]. It was speculated that the different symptoms associated with each drug were in some way related to the degree of chemical specificity and its reactive metabolites that accumulate in the bodily systems [5].

AGEP drug reaction is presented with pustular eruption that occurs soon after drug administration. The usual offending drugs are, aminopenicillin, pristinamycin, diltiazem, [6,7].

DRESS syndrome on the other hand, is also known as drug-induced hypersensitivity syndrome. It is a severe, systemic drug reaction with dermal eosinophilia, and internal organ involvement (liver, kidney, heart). It is characterized by high fever, facial edema, lymphadenopathy, and morbilliform rash. This rash can progress to involve large part of the skin with erythematous reaction and exfoliative dermatitis [8-10].

Overlap syndrome between SCARs do occur e.g. AGEP can presented with facial edema, atypical blisters and mucous involvement [6,11,12]. Cases similar to SJS-TEN with eosinophilia have been also described [13,14]. Internal organ involvement is not common in AGEP even through lymphadenopathy, slight elevation of liver enzymes, and reduced creatinine clearance may be observed [6,14].

DRESS syndrome can also be confused with SJS-TEN on clinical grounds, as pustules may be found in 20% of cases [15]. Vesicles, blisters, atypical target lesions and mucous membrane involvement have been reported [8,15]. Cases of overlap syndrome between DRESS and

TEN have also been reported in the literature, making accurate classification of these SCARs difficult if not impossible under certain circumstances [16]. Clinicians may have difficulty diagnosing these SCARs with certainty. Bouvresse, et al. [17], for example, reported that 7/10 of their patients could not be classified because several diagnoses of SCARs were possible. If we consider these diseases as a spectrum of severity, on one hand mild drug reaction with mild skin involvement and excellent prognosis, and on the other end of the spectrum severe symptoms with systemic and skin manifestation that poses a grave risk with high morbidity and mortality like SJS-TEN.

The conventional criticism to this paper is that distinguishing between the different entities of drug reaction is important for diagnosis and management. However, I would argue that in many of these cases tissue biopsy are rarely taken and treatment principles including stopping the culprit drug and/or steroids are the same and differed only according to the severity of illness.

In conclusion, for patients with severe skin reaction due to drugs, determining and removing the offending drug is more important than a precise diagnosis. Complications are very rare after AGEP, but are infrequent after DRESS which is mostly auto-immune [18]. These complications are nearly always present after SJS-TEN [19]. The mortality depends on the severity of the underlying disease process, it can range from 2% in AGEP and up to (20%-25%) in SJS-TEN [20]. Since most of these SCARs are due to participation of T-cell with type-IV delayed hypersensitivity reaction it might be logical to consider these diseases as one spectrum ranging from mild (AGEP) to severe (SJS-TEN). An inclusive term that encompasses all these disorders may be "Skin and Systemic Hypersensitivity Adverse Reaction (SHARE) syndrome".

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