

# Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Syndrome: When the Medication is the Cause!!!

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**Abstract** Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is an idiosyncratic, potentially life-threatening hypersensitivity reaction to therapeutic medication. [1] The most common culprits historically being anticonvulsants followed by antibiotics, but most recent publications are beginning to show the opposite trend. [1] This case describes a 58-year-old-woman who presented for evaluation of a generalized skin rash associated with facial edema 4 weeks after treatment for Methicillin-resistant Staphylococcus aureus pneumonia with empyema.

**Keywords:** DRESS syndrome, vancomycin

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## 1. Case Presentation

A 58-year-old woman presented to the emergency department for evaluation of generalized skin rash associated with facial edema. Approximately five days prior to admission she started having nausea with recurrent episodes of nonbilious vomiting, which was followed a day later by 3-5 episodes per day of non-bloody diarrhea associated with abdominal cramping. Three days prior to admission she developed a pruritic red rash that involved the face, chest, back, abdomen and extremities and followed a day later by facial swelling, chills, and fever with a maximum temperature of 104 °F.

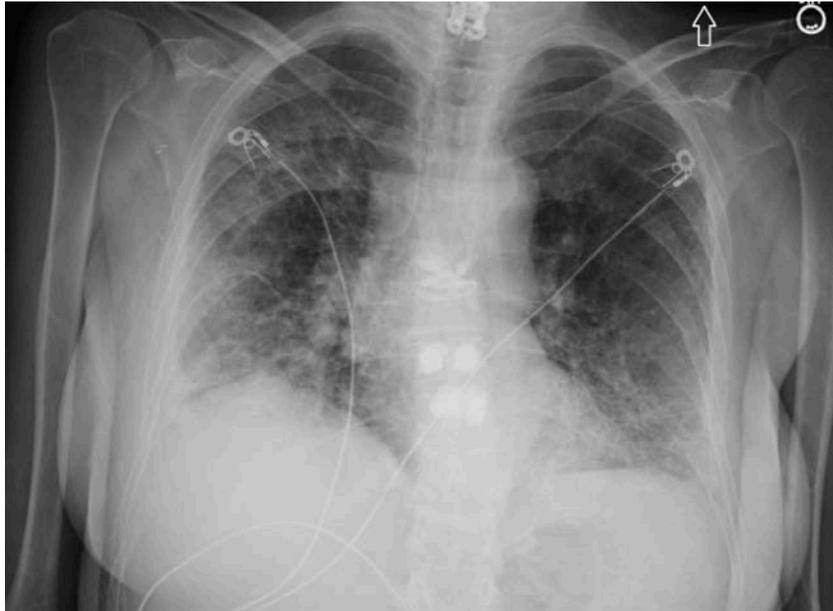
Her medical history is significant for chronic obstructive pulmonary disease, hypertension, anxiety, seizure disorder and cerebrovascular accident. Her medications included aspirin, levetiracetam amitriptyline and atorvastatin.

The patient was treated with intravenous vancomycin via a PICC line 4-weeks prior for Methicillin-resistant Staphylococcus aureus (MRSA) pneumonia associated with empyema. Vancomycin therapy was administered up until 1 week prior to readmission. CT chest from her prior admission showed multifocal mass-like areas of consolidation throughout the right lung, right-sided thick-walled loculated pleural fluid concerning for empyema and mediastinal and hilar lymphadenopathy. 1-week prior to admission her WBC, creatinine and GFR were within normal limits and eosinophils were elevated at 18% (normal:0-6%).

In the emergency department, her blood pressure was 112/72 mmHg, heart rate 126 and temperature of 101.7°F. She was breathing at 22 breaths per minute and saturating at 95% on room air. Physical examination was remarkable for facial swelling with periorbital edema, oral thrush, right basilar crackles, bilateral finger clubbing and an erythematous morbilliform rash involving the face, chest, back, abdomen extremities, palms and soles and associated with a 5 x 4 cm excoriation on the right lower back. No ulcer seen on the oral mucosa. Skin examination findings shown in [Figure 1](#).



**Figure 1.** Morbilliform rash on the abdomen



**Figure 2.** Chest x-ray showing bilateral pulmonary parenchymal opacities more prominent on the right (improved from prior admission)

Laboratory analysis revealed WBC 21.90 (elevated), eosinophils 11 (elevated) on admission, bands 3 (elevated), atypical lymphocyte 3 (elevated), LDH 600 (elevated), procalcitonin 13.24 (elevated), CRP > 8.0 (elevated), lactate 3.1 (elevated), alkaline phosphatase 137 (elevated) and COVID 19 negative. Creatinine 2.84 (elevated) and GFR 17. Urinalysis shows 1+ protein, 2+ blood, 3+ leukocyte with WBC >182. Vancomycin 2.1 (reference range 5.0 -45.0). Hemoglobin, platelet, AST and ALT are within normal limits. Chest shows improved aeration of the right lung, see [Figure 2](#).

She was admitted to the ICU. Further workup revealed a negative hepatitis panel, blood cultures with no growth, negative CMV, EBV, HHV 6 and HIV tests. Her urine culture showed <10,000 CFU/mL of gram-negative bacilli but negative clostridium difficile stool antigen test and negative shiga-like toxin antigen. Her respiratory culture grew MRSA, her urine eosinophils were negative, histone antibodies were negative, ANA titer was 1:80 and double stranded DNA was negative. Given her clinical picture of a generalized, erythematous, morbilliform rash associated with pruritus, fever, facial edema, recent use of vancomycin and the presence of eosinophilia and atypical lymphocyte, a diagnosis of drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome was made. The patient was started on methylprednisolone and over the course of 5 days the skin rash improved and the eosinophilia normalized. She did not receive vancomycin during this hospitalization.

## 2. Discussion

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare drug-induced hypersensitivity reaction that results in systemic symptoms. [1] The mortality risk of patient with DRESS syndrome is approximately 10% and is usually associated with prior use of certain medications. [1,2] Previous studies have shown a higher incidence of DRESS associated with

anticonvulsants such as carbamazepine; however, a recent large retrospective electronic health records analysis reported the primary drug class associated with this condition is antibiotics comprising 74% of the cases. [3] Vancomycin being the primary culprit corresponding to 39% of the patients with anticonvulsants accounting for only 20%. [3] Concomitantly the CDC antibiotic stewardship program has reported an increased use of vancomycin by 32% between 2006-2012 alone. DRESS syndrome is thought to be multifactorial with a genetic predisposition and a link to infection or reactivation of viruses including herpes virus-6, herpes virus-7, Epstein-Barr virus, and cytomegalovirus. [2]

Clinical presentation of DRESS syndrome include fever, pruritus, morbilliform rash, facial edema and lymphadenopathy, usually occurring 2 to 8 weeks after the first drug interaction but can occur earlier in patients with prior exposure to the drug. [1,2] They are two scoring systems, including the one we used in our patient, the European Registry of Severe Cutaneous Adverse Reaction (RegiSCAR) criteria. [2] Using the RegiSCAR criteria our patient met all required findings including acute onset morbilliform rash, recent use of vancomycin and requirement for hospitalization. She also had supporting findings of fever (101.7), involvement of the gastrointestinal tract and kidneys with leukocytosis, atypical lymphocytes, and eosinophilia. The patient had gastroenteritis presented with vomiting and diarrhea, and kidney involvement as well as hematuria, proteinuria, and acute kidney injury.

Therapy with vancomycin for MRSA pneumonia was completed 1 week prior to admission so there was not a need to continue vancomycin. Antibiotics were not restarted given that clinical presentation and radiographic and clinical improvement in her pneumonia. On the day of admission, she was started on methylprednisolone which was tapered and transitioned to oral prednisone. On day 4 of admission the methylprednisolone dose was decreased from 40 mg IV every 6 hours to prednisone 60 mg daily but due to worsening eosinophilia (23) and rash the

following day the methylprednisolone was increased back to 60 mg every 8 hours. On day 4 given that her facial swelling, pruritus, vomiting, and diarrhea were all improving the methylprednisolone was transitioned to oral prednisolone once again and was tapered slowly to complete a total of 8 weeks of steroid therapy. Prior to discharge the skin rash, pruritus, facial swelling, eosinophilia, and creatinine had all improved and the nausea, vomiting and diarrhea resolved.

### 3. Conclusion

DRESS syndrome is a complex, rare, and potentially life-threatening condition which presents with a wide array of clinical features. The significance of promptly ruling out other causes of the clinical presentation of patients with DRESS syndrome and starting steroid therapy in a timely fashion is therefore paramount in a

physician's management of their patient. With the cessation of the offending therapeutic medication and appropriate steroid therapy patients can recover remarkably as gauged by both clinical and laboratory improvement.

### References

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