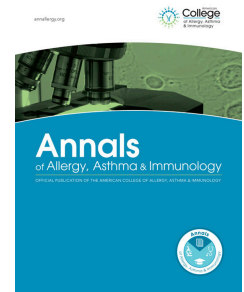


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Vancomycin Induced DRESS Syndrome

A Case Series Examining Vancomycin Induced DRESS Syndrome

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Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare but potentially life threatening drug-induced hypersensitivity reaction. Vancomycin accounts for approximately two-thirds of DRESS cases due to antibiotics². This is important to recognize in light of increasing use of Vancomycin; a review of antimicrobial usage in acute care hospitals in the U.S. reports Vancomycin as the most commonly used antimicrobial³. The following case series describes two cases of DRESS associated with Vancomycin in our institution.

A 30 year old male was transferred to our hospital for evaluation of fever, rash and lymphadenopathy. He had been diagnosed with mitral valve MSSA endocarditis and had completed 6 weeks of cefazolin, however had recurrent symptoms 6 months later and was found to have subacute endocarditis, at which time Vancomycin was initiated. The patient developed fevers, malaise, and a diffuse rash one month after starting Vancomycin. CT abdomen showed hepatosplenomegaly with diffuse lymphadenopathy. At this time, he was transferred to our hospital for further management. Upon presentation to our hospital, he had worsening leukocytosis, worsening renal function, and lactic acidosis. A skin biopsy showed extensive perivascular eosinophilic dermatitis, likely in the setting of drug reaction, at which time DRESS syndrome was suspected and diagnosed with regiSCAR score, which was calculated as 6, indicating definite DRESS. Vancomycin was discontinued; another antibiotic was not started as he had completed a 4 week course with repeat blood cultures negative. He was subsequently started on high dose methylprednisolone with significant improvement of his rash, and his kidney function returned to baseline. He was discharged on oral steroids with gradual taper.

Our second patient was a 63 year old woman with history of rheumatoid arthritis, and hyperlipidemia. She was recently admitted to our hospital with a nonhealing right foot ulcer, found to have osteomyelitis on MRI of the foot, and was started on intravenous ampicillin/sulbactam and vancomycin. Subsequent wound cultures grew MSSA resistant to Ampicillin and ampicillin/sulbactam was discontinued. Patient continued to receive Vancomycin to complete 8 weeks of therapy. She came back to our hospital 4 weeks following discharge with complaints of fevers (Tmax 101.0 F), malaise, and a diffuse macular, erythematous, and blanching rash that she first noticed the evening prior to presentation following her daily dose of Vancomycin. Her symptoms were initially attributed to possible Red Man Syndrome due to rapid infusion of the Vancomycin. However, she was noted to have increasing eosinophilia (differential count 38%; absolute count 6,802 cells/microliter) as well as a worsening rash and transaminitis, and the diagnosis of DRESS Syndrome secondary to Vancomycin was made at that time. Her regISCAR score was 5 at the time, indicating definite DRESS Syndrome. Vancomycin was then discontinued and she was started on oral steroids, with rapid improvement of rash and eosinophilia. The following day, she was discharged with instructions to continue linezolid for 6 weeks total as well as a gradual taper of prednisone.

DRESS syndrome is a severe drug-induced reaction. A 2-9 week latency period is followed by onset of symptoms: fevers, lymphadenopathy, transaminitis, kidney injury, and/or rash. Classically described in association with antiepileptics and allopurinol, other drugs have also been implicated. The diagnosis of DRESS Syndrome is often missed in clinical practice due to its highly variable manifestation. Vancomycin has been reported as a possible cause of DRESS in medical literature. Minhas et al had identified 16 cases of Vancomycin-induced DRESS in a

systematic review of literature from 1982 to 2015⁴. More recently, Lam et al reported 12 cases of DRESS likely caused by Vancomycin over 3 year period. This apparent increase in number of cases of DRESS syndrome caused by Vancomycin over the years could be due to increase in use of Vancomycin or increased recognition of DRESS.

DRESS Syndrome is a diagnosis of exclusion. Steven-Johnson Syndrome/toxic epidermal necrolysis, acute generalized exanthematous pustulosis, erythroderma, and adult T-cell leukemia/lymphoma are diagnoses that can present very similarly to DRESS Syndrome, and should all be considered prior to making a confirmatory diagnosis.⁶ A commonly used tool in diagnosis is the regiSCAR scoring system.

The management of DRESS Syndrome largely relies on a timely diagnosis. The most important factor is prompt withdrawal of the offending drug. While patch testing has previously been used in diagnosis of type 1 hypersensitivity, its utility in diagnosis of DRESS is currently under investigation. Cutaneous lesions are often managed with topical steroid treatment for symptomatic relief, and systemic steroids are indicated to shorten the length and severity of symptoms. There is no currently published randomized clinical trial studying systemic corticosteroid therapy in the management of DRESS Syndrome, however patients have been noted to relapse with abrupt withdrawal or taper of systemic steroid therapy. The French Society of Dermatology has been noted to recommend the use of systemic steroid therapy at stress dosing for patients with transaminitis more than five times what is normal, any indication of renal involvement, pneumonia, cardiac involvement, or hemophagocytosis.⁶ They also recommend the usage of IVIG for patients with severe renal or respiratory failure as well as the use of ganciclovir as adjunctive therapy for patients with confirmed HHV-6.⁶ Other studies have mentioned the use of NAC (N-acetylcysteine) due to its detoxifying ability. Scant studies have

mentioned plasmapheresis and rituximab therapy as well⁶. Our patients responded well to discontinuation of Vancomycin and high dose steroids.

The clinical outcomes for patients with DRESS can be variable. In general, recovery is expected in most patients after withdrawal of the culprit drug and initiation of steroids.⁷ In an analysis of 172 reported cases of DRESS, the reported mean time to recovery was 6.4 +/- 9.4 weeks (range 0.5-90 weeks).¹

Though recovery is generally expected with cessation of offending drug and initiation of corticosteroids, DRESS is a potentially life threatening syndrome, with mortality rates reportedly 5-10%.^{1,12-15} As more literature is published on the various presentations of DRESS, more awareness is expected to be raised and thus a more timely approach to treatment may be obtained, as treating the disease in a timely fashion is ultimately the most important prognostic indicator.

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RegiSCAR Scoring for DRESS Syndrome**Table 1**

RegiSCAR Group Study Criteria	No	Yes	Unknown
Fever ≥ 38.5 C	-1	0	1
Enlarged lymph nodes (≥ 2 sites, > 1 cm)	0	1	0
Atypical lymphocytes	0	1	0
Eosinophilia	0		0
700-1,499 or 10-19.9%		1	
$\geq 1,500$ or $\geq 20\%$		2	
Skin rash	0		0
Extent $> 50\%$	0	1	0
At least 2 of : edema, infiltration, purpura, scaling	-1	1	0
Biopsy suggestive of DRESS	-1	0	0
Internal organ involved	0		0
1		1	
≥ 2		2	
Resolution in > 15 days	-1	0	1
≥ 3 negative biological investigations to exclude alternative diagnosis	0	1	0