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DRESS Syndrome Following Vancomycin Use in Cardiac Surgery: A Case Report

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Abstract

The DRESS syndrome is a severe drug reaction characterized by a generalized skin rash, hyper eosinophilia, and visceral involvement. The incriminated medications include primarily antiepileptics, sulfonamides, allopurinol, and less frequently vancomycin.

We present here the case of a 45-year-old patient who developed a DRESS syndrome after taking vancomycin. This observation highlights the clinical presentation, diagnostic challenges, and associated pathogenesis and treatment of this syndrome.

Keywords

DRESS Syndrome, Vancomycin, Adverse Drug reaction, Cardiac surgery, RegiSCAR criteria, Drug toxicity DRESS Syndrome, Vancomycin, Adverse Drug reaction, Cardiac surgery, RegiSCAR criteria, Drug toxicity

Main Article

Observation

Mrs. N.C., a 45-year-old woman with a medical history including:

Repeated angina epiasodes in childhood without a history of acute rheumatic fever

A double mitral-aortic valve replacement on November 8, 2023, using a mechanical prosthesis

The patient presented to the emergency department of the Mohammed V Military Hospital with a febrile syndrome that had started a week earlier, characterized by chills and night sweats, along with a notion of superficial wall infection and a collection near the operative scar for which she was treated with antibiotics and local care (an antistaph).

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The patient's condition worsened during her hospital stay. Upon admission to the intensive care unit, she underwent a series of blood cultures, along with a transthoracic echocardiogram (TTE) and a transesophageal echocardiogram (TEE).

Three blood cultures returned positive for methicillin-resistant Staphylococcus aureus (MRSA).

ETT and ETO Findings

The echocardiography (ETT) revealed:

Double mechanical prosthetic valves in good function

Left ventricle not dilated, not hypertrophied, with good systolic function and a left ventricular ejection fraction (FEVG) of 58%

Right ventricle not dilatated, with preserved systolic function

No dilated ears

Doppler imaging showed mild mitral regurgitation and a fine, compliant tricuspid valve with a dry pericardium

The transesophageal echocardiogram (ETO) showed:

Two vegetations on the mitral and aortic prosthetic valves with an abscess of the trigone

Diagnostic and Treatment

Given these clinical, echocardiographic, and biological arguments, the diagnosis of endocarditis was rapidly suspected.

Upon receiving the identification of the germ and the antibiogram, a vancomycin (4g/24h) and rifampicin (1.2g/24h) antibiotic regimen was started. The patient benefited from a reduction in her symptoms with acheminement of the samples to the bacteriology laboratory.

Two samples returned positive: prosthetic valves and peripheral pus samples.

Evolution in Postoperative Care

The patient's condition worsened in the postoperative period in the intensive care unit (ICU) with the aggravation of renal and hepatic function, accompanied by the appearance of a cutaneous-mucous ictère (urine: 0.62g/l/0.42g/l; creatinine: 39mg/l/13mg/l; ASAT: 67/23UI/L; GGT: 96U/L; total bilirubin: 21mg/L; and TP below normal). A suspected overdose of vancomycin was suspected, and a vancomycin level was requested: 74.5 ug/ml (normal levels: residual serum level: 5-10 ug/ml, peak serum level: 20-40 ug/ml, and toxic level >= 80 ug/ml). The dose of vancomycin was reduced to 2g/24h, and the patient was transferred to the cardiac surgery service for further care.

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During this stay, the patient was readmitted to a dose of 4g/24h of vancomycin. The overall evolution was favourable, with the disappearance of fever and improvement of the inflammatory syndrome.

At day 21, the patient began to present an erythema on the face and neck, extending to the chest and back, accompanied by the onset of desquamation. In parallel, there was an aggravation of the inflammatory syndrome, along with a febrile syndrome (fever: 39-41°C, CRP in a rising trend from 43 to 155, and leukocytes from 6000 to 29000).

The laboratory results also showed liver failure with increased values of liver enzymes: ASAT: 35, ALAT: 53, PAL: 204, GGT: 168, and a low TP of 22%. The hypothesis of a DRESS syndrome was advanced due to the cutaneous eruption, hyper eosinophilia of 569 (N: < 500), liver and cardiac failure with a RegiSCAR score of 6.

The erythrodermia generalized, and an oedema of the face was associated. A second vancomycin level was requested and returned above the serum level: 63.9 ug/ml. Serological and auto-immunity tests were negative.

The imputability of vancomycin was considered; this antibiotic was stopped immediately, and the patient was switched to tigecycline: 50mg/12h, along with systemic corticosteroids at a dose of 1mg/kg.

The patient's clinical condition rapidly deteriorated, requiring intensive care unit admission, mechanical ventilation, and the reintroduction of vasoactive drugs. An echocardiogram (ETT) was performed, which objectified a membrane in front of the mitral valve of 03 mm.

Given the persistence of fever, a series of blood cultures was performed, which was in favour of a Klebsiella pneumoniae type BMR. The antibiotic regimen was reinforced with a beta-lactam: imipenem/cilastatine, associated with a polymyxin family peptide: 3000mi/8h.

Mycological samples returned positive for Candida tropicalis, and the patient was switched to voriconazole: 200mg/12h.

A hormonal balance was performed, which objectified an unreported hyperthyroidism in our patient, which may be a consequence of the DRESS syndrome.

Under this treatment, the patient's clinical and biological parameters gradually normalized. The biological balance remained stable, and the liver function normalized progressively.

The overall evolution is favourable, without any reappearance of sepsis signs despite the change in antibiotic therapy. The transoesophageal echocardiogram performed later is also normal.

The patient is transferred to the cardiac surgery service.

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Discussion

The DRESS syndrome is a rare but serious form of drug-induced toxicity that can be associated with multiple organ dysfunctions. The cases linked to vancomycin are rare but potentially fatal, with an estimated risk between 1 in 1,000 and 1 in 10,000 exposures (1). Hepatic failure is the main cause of mortality reported in the literature (2).

The pathophysiology of DRESS involves a delayed hypersensitivity reaction mediated by T lymphocytes, reactivation of herpes viruses, and genetic predisposition. It is the result of a delayed hypersensitivity mechanism mediated by TH2 CD8+ cytotoxic T cells that secrete TNFα, IFNγ, interleukins (IL 4, 5, 13), and eotaxin, a chemokine recruiting eosinophilic polymorphonuclear cells (3). Recent research suggests the involvement of new signalling pathways such as JAK-STAT in the pathophysiology of the disease, opening up the possibility of new therapeutic approaches (4).

The diagnosis of DRESS syndrome is highly dependent on clinical suspicion, particularly in the context of recent medication administration within the two to six weeks prior. The European Registry of Severe Cutaneous Adverse Reactions (regiSCAR) has developed a scoring system that can guide clinicians towards specific laboratory tests, but its primary utility lies in retrospective confirmation of cases. (5)

DATA table: RegiSCAR Criteria for Classifying DRESS as Certain, Probable, Possible, or Excluded : (6)

Visceral alterations, sometimes leading to transfer to intensive care, can manifest initially, such as in the case of fulminant hepatitis, or evolve during the course of other conditions like hemophagocytosis, hepatic cytolysis, renal insufficiency, pulmonary involvement, cardiac insufficiency, pancreatitis, and encephalitis. The DRESS syndrome, responsible for multi-organ failure, is the main cause of death in this syndrome.(7)

When a DRESS suspicion arises, it is crucial to perform additional tests to confirm the diagnosis and initiate prolonged surveillance. Recently, the French Society of Dermatology's Toxidermy Group has issued guidelines for managing DRESS.

The initial examinations will primarily focus on: Complete Blood Count (CBC) Analysis and Visceral Organ Assessment.

The observed anomalies in DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms) may include lymphopenia, mononucleosis syndrome, hyperlymphocytosis, hyper eosinophilia, anemia, and thrombocytopenia,

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The most common visceral organ injuries include signs of hemophagocytic syndrome, characterized by elevated lactate dehydrogenase (LDH); hypertriglyceridemia, hyperferritinemia; hyponatremia, bicytopenia, pancytopenia; hepatic cytolysis, renal insufficiency, which may be functional or non-functional; eosinophilia; pneumonia, and encephalitis.

The additional examinations will include a chest radiograph, blood gas analysis, electrocardiogram, and potentially, an echocardiogram (TTE and TEE) in cases of severe eosinophilia or elevated cardiac enzymes. It is crucial to systematically search for bacterial and viral infections, including blood cultures, blood tests for bacterial infections, and urine tests for bacterial infections.

Procalcitonin levels can increase in response to various stimuli, including bacterial endotoxins, viral infections, and certain medications. In the context of DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms), an increase in procalcitonin levels does not necessarily indicate a bacterial infection. This is because the immune response to the medication can also lead to a systemic inflammatory reaction, resulting in elevated procalcitonin levels. (8)

Vancomycin, a commonly used antibiotic, has been reported to trigger the development of DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms) syndrome in a limited number of case reports and series. A 2016 review of hypersensitivity reactions associated with vancomycin, covering the period from 1982 to 2015, identified 71 cases of total hypersensitivity, including 16 cases of DRESS syndrome. Unfortunately, the RegiSCAR scoring methods were only documented in four of these cases. (8)

A retrospective review over three years, conducted by Lam et al. on 32 cases of DRESS syndrome in the LACounty and KeckMedical centers, revealed that 12 cases were associated with vancomycin. All DRESS cases in this series were diagnosed using the regiSCAR scoring system. (9)

The principles of DRESS treatment require immediate discontinuation of the suspected drug, constituting a medical emergency. This approach is justified due to the severity of general signs and organ damage, the severity of which can sometimes jeopardize the prognosis. Mortality associated with DRESS is estimated between 5 and 10%, resulting in particular from complications such as pulmonary involvement, heart disease, hemodynamic failure or fulminant hepatitis. (10)

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There are no consensus criteria for classifying the severity of DRESS syndrome. However, the presence of pulmonary, cardiac, intestinal, neurological involvement, or macrophage activation syndrome always indicates severe involvement.

Regarding liver involvement, it can be considered severe if transaminase levels exceed 15 to 20 times normal, or if the prothrombin rate (especially factor V) decreases, indicating hepatocellular failure. Similarly, kidney involvement is considered severe if creatinine deteriorates rapidly on an organ profile. (11)

In cases of DRESS syndrome with mild or moderate severity, the relative efficacy of topical corticosteroids at a dose of 30 g/day compared to systemic corticosteroid therapy at moderate doses (0.5 mg/kg/day) remains to be demonstrated.

In the presence of severe DRESS or macrophage activation syndrome, systemic corticosteroid therapy at a dose of 1 mg/kg/day is necessary, often initiated with high-dose methylprednisolone boluses. In all cases, whether it is local or systemic corticosteroid therapy, the reduction must be done very gradually over a period of 3 to 6 months in order to prevent relapses. (12)

Intravenous immunoglobulins are not recommended as the only treatment but can be considered in some severe DRESS cases when used together with corticosteroids. This can be done if the treatment with corticosteroids alone does not work, or if the patient becomes dependent on the corticosteroids. (13)

Finally, reporting to the pharmacovigilance system should not be neglected.

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Figures:

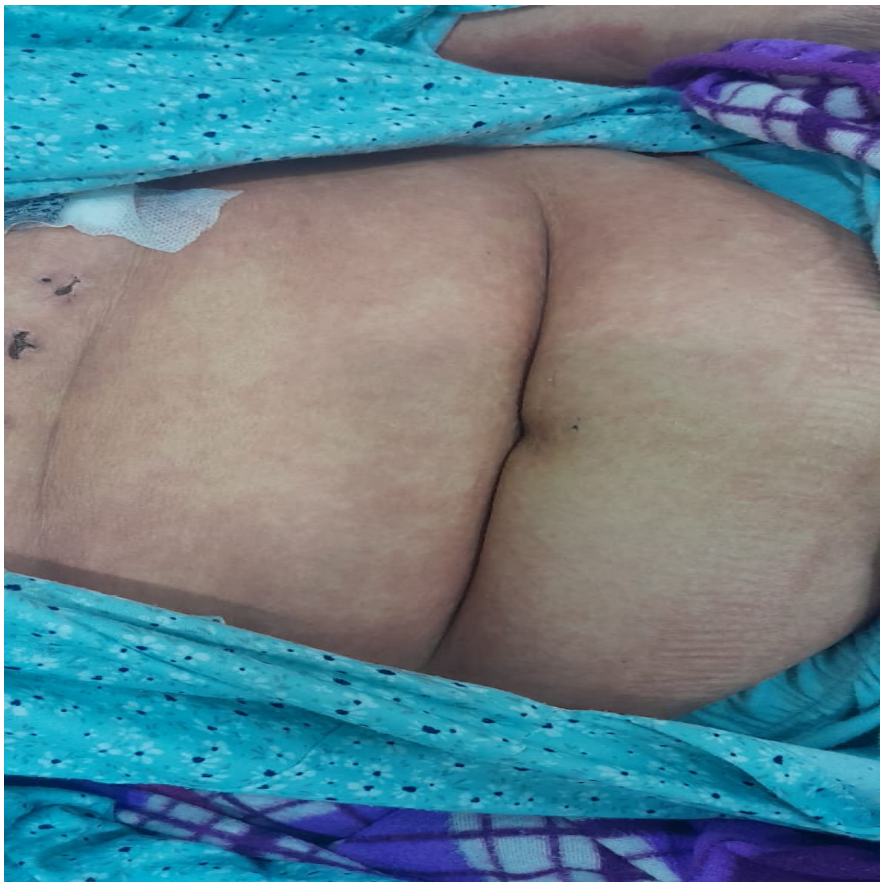

Figure 1: erythema progressing to generalized erythroderma

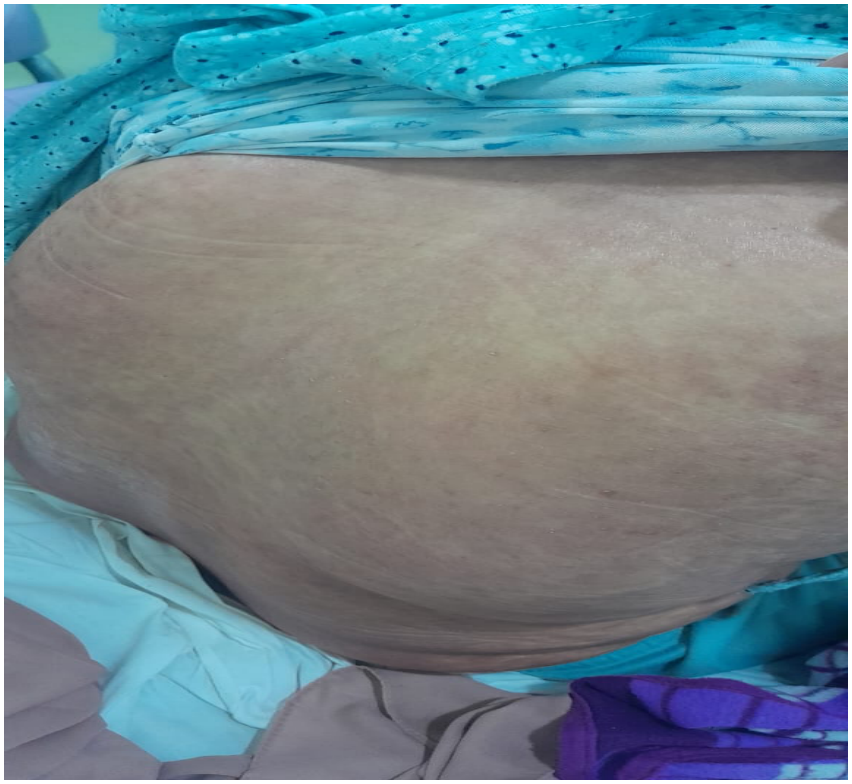

Figure 2: erythema progressing to generalized erythroderma

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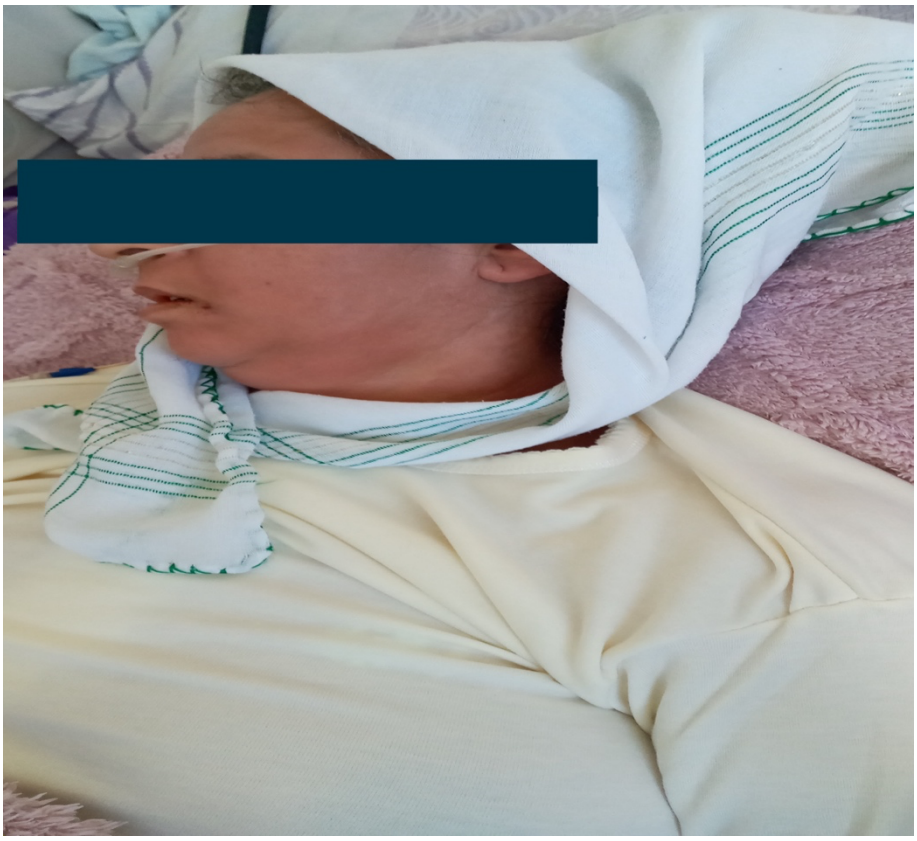

Figure 3: facial edema

Tables :

Score	- 1	0	1	2	Minimum	Maximum
Fièvre ≥ 38,5 °C	Non/U	Oui			-1	0
Polyadénopathies		Non/U	Oui		0	1
Eosinophilie		Non/U			0	2
Eosinophilie			0,7-1,499 G/L	≥ 1,5 G/L		
Eosinophilie, si leucocytes < 4 G/L			10-19,9 %	≥ 20 %		
Lymphocytes atypiques		Non/U	Oui		0	1
Atteinte cutanée					-2	2
Étendue de l'exanthème (% surface cutanée)		Non/U	≥ 50 %			
Exanthème évocateur de Dress	Non	U	Oui			
Biopsie cutanée en faveur du Dress	Non	Oui/U				
Atteinte viscérale[a]					0	2
Foie		Non/U	Oui			
Rein		Non/U	Oui			
Poumon		Non/U	Oui			
Muscle/cœur		Non/U	Oui			
Pancréas		Non/U	Oui			
Autre organe		Non/U	Oui			
Régression ≥ 15 jours	Non/U	Oui			-1	0
Évaluation d'autres causes						
Facteurs antinucléaires						
Hémocultures						
Sérologies VHA/VHB/VHC						
Chlamydia/Mycoplasma						
Si non positif ou ≥ 3 négatif			Oui		0	1
Score total					-4	9

U : non connu ; VHA : virus hépatite A ; VHB : virus hépatite B ; VHC : virus hépatite C.

[a] Après exclusion de tout autre diagnostic : 1, un organe ; 2, deux organes ou plus.

Score final < 2 : diagnostic exclu ; score final 2 à 3 : diagnostic possible ; score final 4 à 5 : diagnostic probable ; score final > 5 : diagnostic certain.

Table 1: xxx

Acknowledgements

This research was conducted to investigate and analyze the resulting data. The findings presented reflect the independent efforts of the authors, who designed, executed, and interpreted the study. All results and conclusions are based solely on the authors' analysis and interpretation.

References

1. Cariou ME, Kaabar M, Cailliez P, Lorléac'h A, Prades-Grandgirard N, Jacobzone-Lévêque C, Schmitt F. Dress (Drug reaction with eosinophilia and systemic symptoms) suite à la prise de vancomycine : à propos d'un cas. Ann Biol Clin 2013 ; 71(2) : 190-5 doi :10.1684/abc.2013.0807
2. Cacoub P, Musette P, Descamps V, Meyer O, Speirs C, Finzi L,et al. The DRESS syndrome : a litterature review. Am J Med 2011 ; 124 : 588-97.
3. Duong TA, Valeyrie-Allanore L, Wolkenstein P, Chosidow O. Severe cutaneous adverse reactions to drugs. Lancet 2017;390: 1996–2011.
4. Kim D, Kobayashi T, Voisin B, Jo J-H, Sakamoto K, Jin S-P, et al. Targeted therapy guided by single-cell transcriptomic analysis in drug-induced hypersensitivity syndrome: a case report. Nat Med 2020;26: 236–43.
5. Sumon Roy, Vinay P. Goswamy, Kirolos N. Barssoum, Devesh Rai, "Vancomycin-Induced Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Syndrome Masquerading as Elusive Sepsis", Case Reports in Immunology, vol. 2019, Article ID 1625010, 5 pages, 2019. https://doi.org/10.1155/2019/1625010
6. Descamps V, Ben Saïd B, Sassolas B, Truchetet F, Avenel-Audran M, Girardin P, et al. Prise en charge du drug reaction with eosinophilia and systemic symptoms (DRESS). Ann Dermatol Venereol 2010 ; 137 : 703-8.
7. Eshki M, Allanore L, Musette P, et al (2009) Twelve-year analysis of severe cases of drug reaction with eosinophilia and systemic symptoms: a cause of unpredictable multiorgan failure. Arch Dermatol 145:67–72
8. J. S. Minhas, P. G. Wickner, A. A. Long, A. Banerji, and K. G. Blumenthal, "Immune-mediated reactions to vancomycin: A systematic case review and analysis," Annals of Allergy, Asthma & Immunology, vol. 116, no. 6, pp. 544–553, 2016.
9. Barbara D. Lam, BA,a Melanie M. Miller, BA,a Adam V. Sutton, MD, MBA,a,b David Peng, MD, MPH,a,b and Ashley B. Crew, MDa,bVancomycin and DRESS: A retrospective chart review of 32 cases in Los Angeles, California DOI :https://doi.org/10.1016/j.jaad.2017.05.041
10. Cho Y-T, Yang C-W, Chu C-Y. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS): An Interplay among Drugs, Viruses, and Immune System. Int J Mol Sci 2017;18: 1243
11. Le DRESS (Drug reaction with eosinophilia and systemic symptoms)DRESS: drug reaction with eosinophilia and systemic symptomsAnnales de dermatologie et de vénéréologie - FMC 1 (2021) 55—58
12. Ingen-Housz-Oro S, Duong T-A, de Prost N, Colin A, Fardet L, Lebrun-Vignes B, et al. Traitement des toxidermies graves. Ann Dermatol Venereol 2018;145: 454–64.
13. Giavina-Bianchi P, Huang S-W. Intravenous Immunoglobulin May Be Beneficial as an Add-on Therapy in DRESS. J Allergy Clin Immunol Pract 2018;6: 1243–5.