DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS) SYNDROME FOLLOWING VACCINATION WITH THE ASTRAZENECA COVID-19 VACCINE (VAXZEVRIA)

Thomas O'Connor, Paul Ryan, MB, BCh, BAO, MD, FRCPC, Gillian Gibson MB, BCh, BAO, MRCPI, MD,
University College Cork Medical School, Department of Dermatology, Bon Secours Hospital, Cork, Department of Pathology, Bon Secours Hospital, Cork

Introduction

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a serious potentially life-threatening hypersensitivity syndrome usually occurring after exposure to a drug. Clinical features include skin rash, oedema, fever, lymphadenopathy and involvement of other organs. The aetiology is still being investigated. DRESS syndrome tends to occur after ingestion of a drug in a genetically predisposed individual. Reactivation of viruses including human herpes virus (HHV) 6, HHV7, Epstein Barr virus and human cytomegalovirus has been reported in patients with DRESS syndrome but the exact contribution to symptoms and severity is not yet established. [1] We report a case of DRESS syndrome following administration of the AstraZeneca Covid-19 vaccine (Vaxzevria).

Case Report

- A 45 year old woman presented with an 8 day history of a gradually worsening rash consisting of red papules on the face, trunk and extremities associated with facial and extremity oedema and chills. She complained of sore throat and hoarseness. She had no preceding medical conditions and was on no regular medication. She had taken levocetirizine and fexofenadine for the rash. She had received the AstraZeneca Covid-19 vaccine (Vaxzevria), first dose, 7 weeks prior to onset of the rash.
- On examination there was erythema and oedema of the eyelids and lips (Figure 1). There were multiple pink papules and plaques on the face, trunk and extremities, some with superficial scale. There were small pustules on the upper lip. There was oedema of the arms and legs with a coalescent erythema. There were violaceous patches on the feet (Figure 2) with some targetoid lesions and some central erosions. There was conjunctivitis, erythema of the pharynx and cervical lymphadenopathy.
- Blood results on admission showed an elevated eosinophil count 1.48 x 109/L (normal range 0.02-0.5 x 109/L), CRP 32.3 (normal range: <5.0), normal liver function tests, Covid-19 IgG weakly positive, Covid-19 PCR tests negative x 2, negative respiratory panel, negative serology for mycoplasma pneumonia, CMV, EBV, HHV6. CT scan showed serositis with mild fluid in the pleural and peritoneal cavities.
- Skin biopsy showed diffuse marked spongiosis with patchy vacuolar interface change and occasional dyskeratotic cells (Figure 3). There was a patchy lichenoid band of lymphocytes with perivascular lymphocytes and abundant eosinophils (Figure 4). These features were consistent with the clinical impression of DRESS syndrome.
- The patient was commenced on intravenous hydrocortisone on admission and was improving. However, 5 days later, on switching to oral prednisolone, she had a relapse with chills, malaise, conjunctivitis, generalized erythema and oedema. Her eosinophil count rose to 3.65 x 109/L. Her liver enzymes rose slightly. AST rose to 40 IU/L (normal range: 5-34 IU/L), ALT to 87 (normal < 55 IU/L), GGT to 39 IU/L (normal range 9-36 IU/L). Intravenous methylprednisolone was administered for 3 days with a marked improvement in her skin and a reduction in eosinophil count and liver enzymes. Oral prednisolone 60mg daily was commenced after the course of methylprednisolone and slowly weaned. At review 3 weeks later she still had some oedema of the face, arms and legs and at review 4 weeks later, on prednisolone 8mg daily, there was mild oedema remaining with a dusky purple color to the skin on the hands and feet. Liver enzymes remained normal with a very mild increase in eosinophil count 0.6 x 109/L.

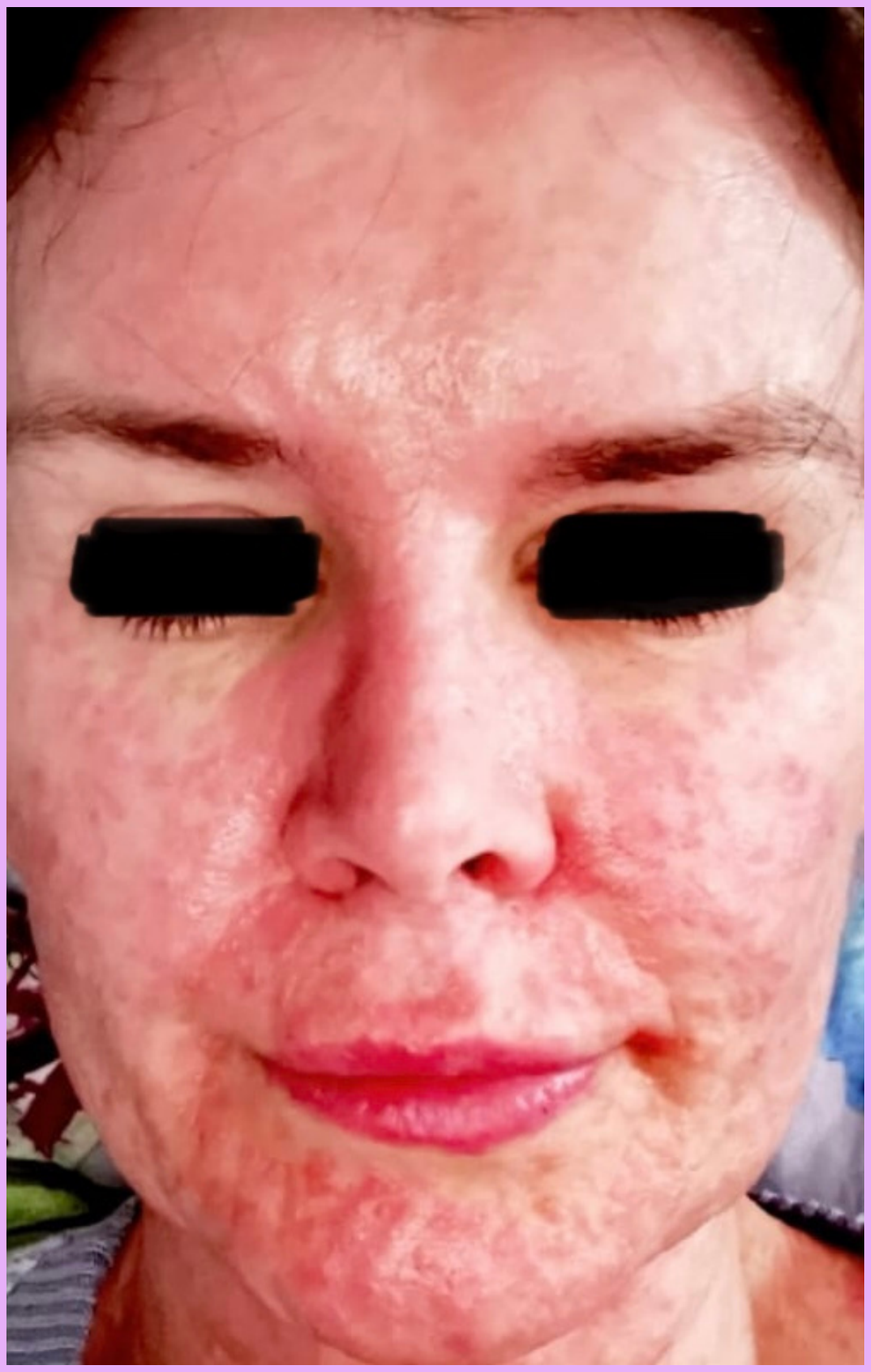

Figure 1: Erythema, oedema, papules and plaques and occasional pustules on the face

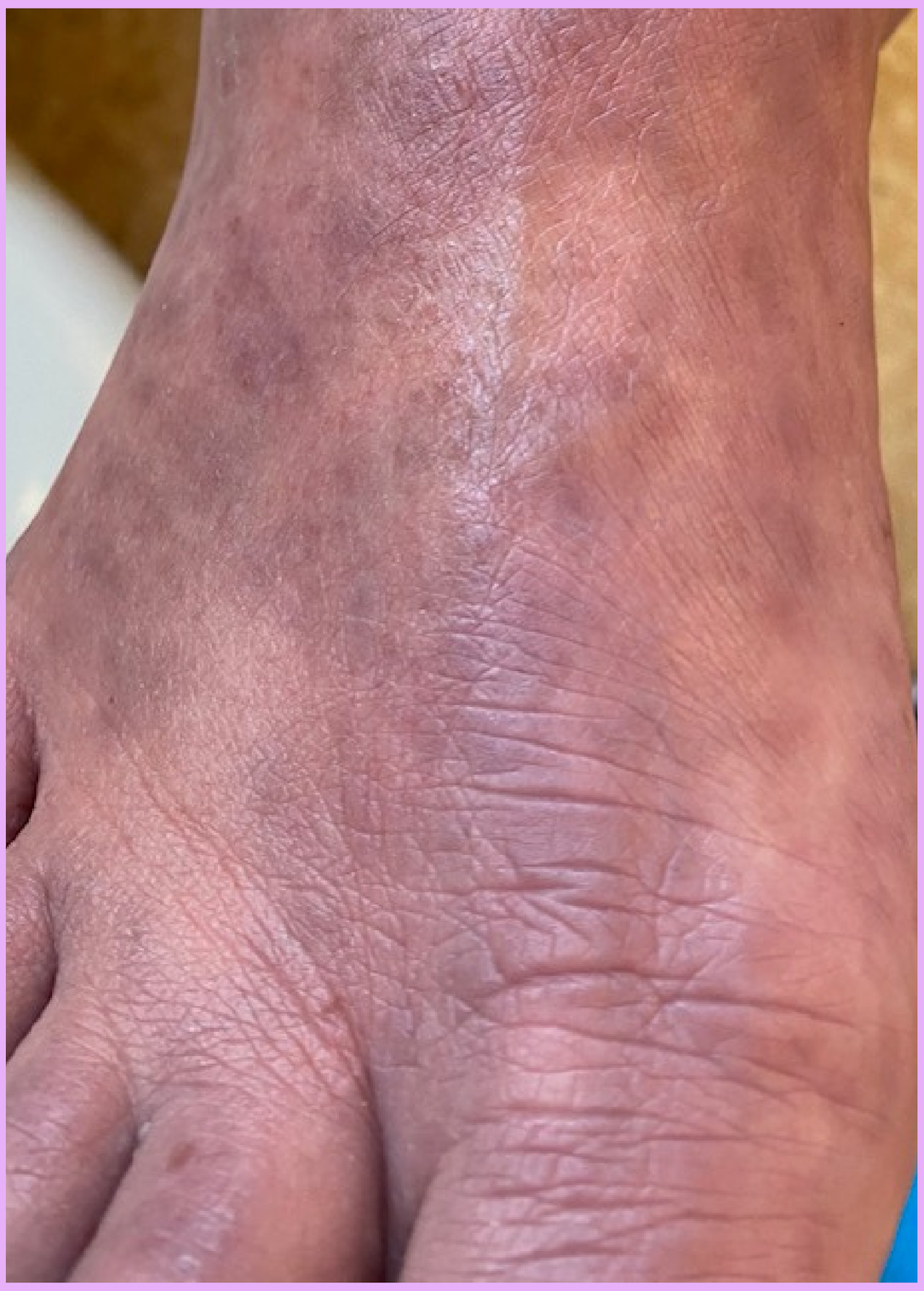

Figure 2: Violaceous patches on the feet with targetoid lesions

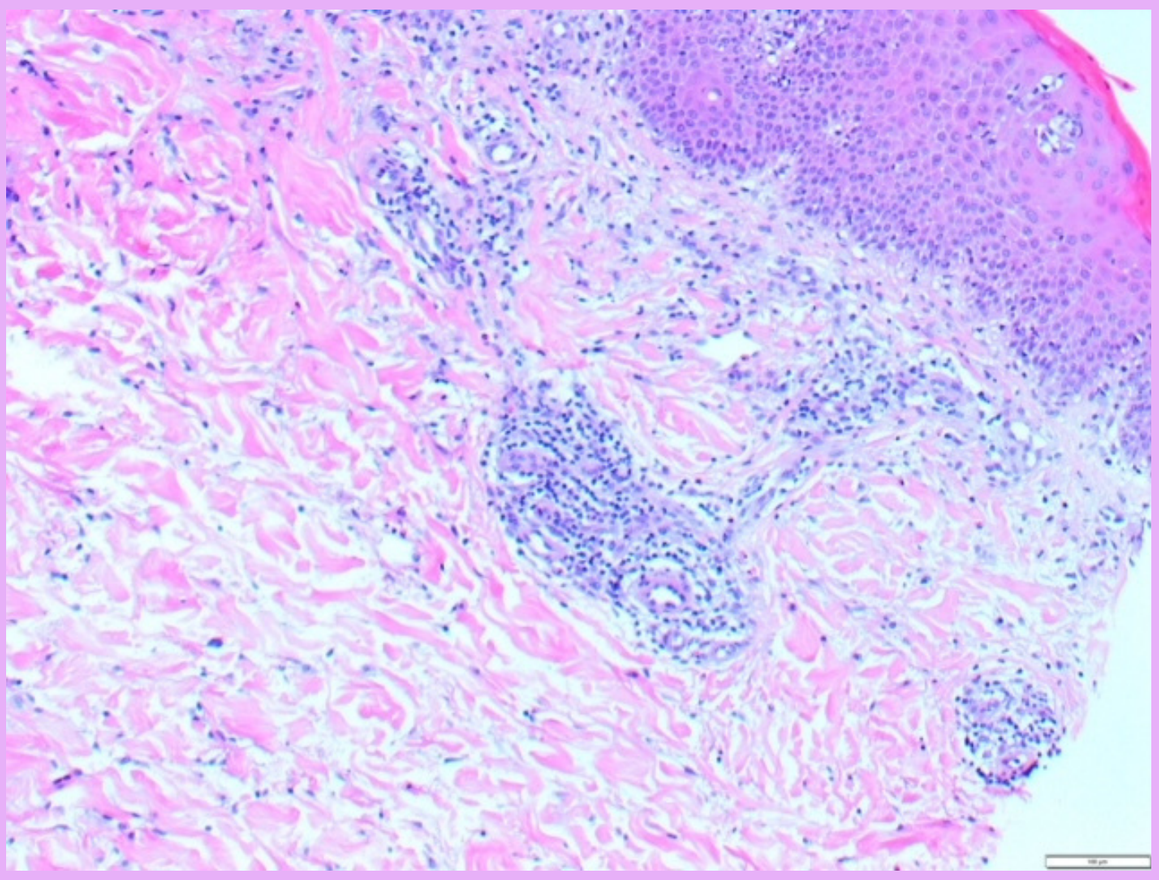

Figure 3: Low power view: epidermal spongiosis and interface change with superficial dermal perivascular inflammatory infiltrate and vascular telangiectasia (H & E, x 100)

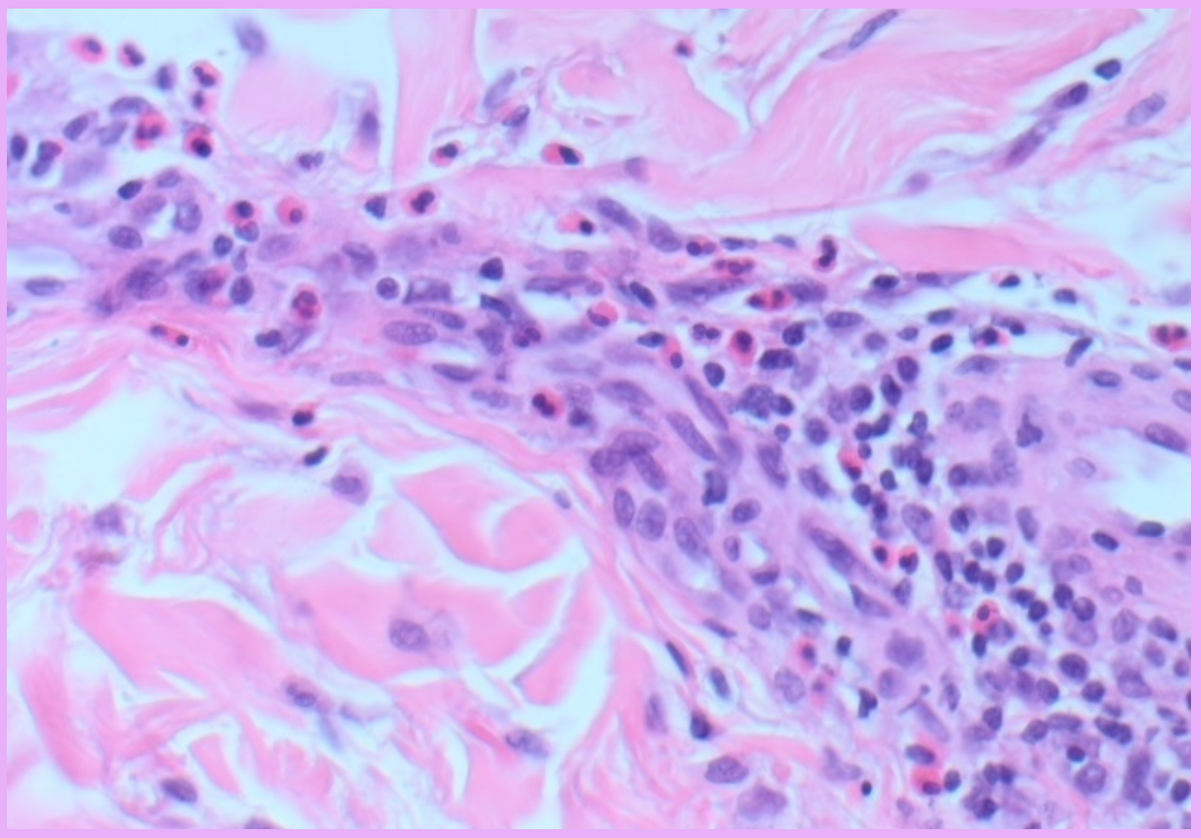

Figure 4: High power view of dermal perivascular inflammatory infiltrate comprising lymphocytes and abundant eosinophils (H & E, x 400)

Discussion

- DRESS is a drug-induced hypersensitivity reaction which occurs usually 2 to 8 weeks after exposure to the culprit drug. Multiple organs can be affected by this hypersensitivity and patients vary in their clinical presentation. It has an associated mortality of around 10%. [2]
- There are a number of drugs that can cause DRESS in people with a genetic predisposition. The most common include anticonvulsants, antibiotics, antiretrovirals and allopurinol. DRESS has been reported rarely after Influenza vaccination. [3,4,5]
- Our patient was taking no other medication prior to the onset of her symptoms. Thus we believe that in her case DRESS syndrome was precipitated by her first dose of AstraZeneca COVID-19 vaccine (Vaxzevria). We are unaware of any other cases of DRESS syndrome reported after the AstraZeneca vaccine. A case has been reported of a severe cutaneous adverse reaction to the Janssen Ad26.COV2.S COVID-19 vaccine with a differential diagnosis of acute generalized exanthematous pustulosis (AGEP), DRESS or AGEP-DRESS overlap. [6]
- DRESS syndrome is treated by withdrawal of the offending agent, supportive care, monitoring for systemic involvement and corticosteroids. Relapses can occur with a steroid taper as occurred with our patient. Symptoms can persist for up to a year in some patients.[7]
- Organ damage can be very severe in some patients leading to permanent impairment of organ function. Liver transplantation has been necessary in some patients as has long term hemodialysis. Several autoimmune diseases including thyroiditis, type 1 diabetes mellitus, systemic lupus erythematosus have been reported from a few months to several years after recovery from DRESS syndrome.[8] Thus patients require careful follow up after recovery and clinicians need to be aware of the possibility of autoimmune sequelae.
- We present this case to highlight the importance of a vaccination history in a patient presenting with clinical features suspicious for DRESS syndrome. This is particularly relevant in the case of vaccines requiring 2 doses as the second dose should be withheld, as should boosters of the same vaccine. DRESS syndrome often has a longer latent period than other drug reactions and thus the drug history should include exposures in the preceding eight weeks.

References

- 1.Roujeau JC, Dupin N. Virus reactivation in drug reaction with eosinophilia and systemic symptoms (DRESS) results from a strong drug-specific immune response. J Allergy Clin Immunol Pract 2017;5:811-12
- 2. Chen Y.C., Chiu H.C., Chu C.Y. Drug reaction with eosinophilia and systemic symptoms. A retrospective study of 60 cases. Arch Dermatol 2010: 146: 1373-1379
- 3. Hewitt N, Levinson M, Stephenson G. Drug reaction with eosinophilia and systemic symptoms associated with H1N1 vaccination. Intern Med J 2012;42:1365-1366
- 4. Solak B, Dikicier BS, Kara RO, Erdem T. DRESS syndrome potentially induced by allopurinol and triggered by influenza vaccine. BMJ Case Rep 2016; 2016: bcr206214563
- 5. AishGriffin WJ, Martin GE, McLean C, Cheng AC, Giles ML. (2020) A case of drug reaction with eosinophilia and systemic symptoms (DRESS) without a typical precipitant. MJA 2020; 212(7): 300-312)
- 6. Lospinoso K, Nichols CS, Malachowski SJ, Mochel MC, Nutan F. A case of severe cutaneous adverse reaction following administration of the Janssen Ad26,COV2.S COVID-19 vaccine. JAAD Case Reports 2021;13:134-7
- 7. Tetard F, Picard D, Janela B, Joly P, Musette P. Prolonged evolution of drug reaction with eosinophilia and systemic symptoms: Clinical, virologic and biological features. JAMA Dermatol 2014;150:206-207.
- 8. Kano y, Tohyama M, Aihara M, Matsukura S, Watanabe H, Sueki H, Iijima M, Morita E, Nohara H, Asada H., et al. Sequelae of 145 patients with drug-induced hypersensitivity syndrome/drug reaction with eosinophilia and systemic symptoms: Survey conducted by the Asian Research Committee on severe cutaneous adverse reactions (ASCAR). J Dermatol 2015;42: 276-282