

of psoriatic arthritis or Crohn's disease, while general practitioners might find it not challenging to deal with comorbidities and comedication. In contrast, any other manifestation should be regarded as 'severe'. This includes localized psoriasis in difficult to treat areas as well as any manifestation other than chronic plaques. 'Severe' psoriasis would be the dermatologists' domain.

The way we practice medicine is based on evidence as well as available resources. The above-mentioned definitions could be adapted accordingly: in countries with limited access to dermatologists, the role of non-dermatologists will inevitably be more important, while in countries with easy access, 'moderate' cases could be seen by dermatologists.

In summary, the 'innovation storm' in dermatology provides opportunities and challenges, which can best be managed jointly with colleagues from other specialties. There is no 'one size fits all' solution, as – besides evidence – the respective healthcare systems define how we practice medicine. Re-addressing patient stratification will decide whether treating inflammatory skin diseases in the year 2020 remains a task for the medical community, or a domain of few (opinion) leaders.

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A breathtaking DRESS due to amoxicillin–clavulanate presenting as polymorphic eruption of the pregnancy

Editor

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a delayed-type drug hypersensitivity reaction with potential life-threatening complications. To our knowledge,

DRESS has never been described in pregnancy. Here, we report on a pregnant woman presenting with erythematous plaques on the abdomen, developing cardiac tamponade due to eosinophilic perimyocarditis and an interstitial pneumonitis 5 weeks after exposure to amoxicillin–clavulanate.

A 31-year-old woman at 26 weeks gestation presented with pruritic confluent erythematous plaques on the abdomen (Fig. 1a,b) starting 1 week earlier periumbilical. Furthermore, she was having arthralgia without fever. Five weeks earlier, she had been treated with amoxicillin–clavulanate for cystitis. With differential diagnosis polymorphic eruption of pregnancy (PEP), beginning pemphigoid gestationis and subacute lupus erythematoses biopsies were taken for histopathology and immunofluorescence.

Four days later, she was admitted to the hospital with chest pain and progressive dyspnoea upon exertion. Physical examination revealed tachycardia, jugular venous distention and bilateral lung crackles. There was no fever (after taking acetaminophen), facial oedema or lymphadenopathy.

Laboratory studies showed inflammation with eosinophilia, mildly elevated liver enzymes and elevated cardiac enzymes (Table 1). Chest X-ray, high resolution computed tomography, electrocardiogram (ECG) and echocardiography demonstrated bilateral interstitial pneumonitis, perimyocarditis and a developing cardiac tamponade. Pericardiocentesis released 500 mL yellow transparent fluid, showing leucocytosis of $3.51 \times 10^9/L$ with 45% eosinophilia. The skin biopsy showed high dermal perivascular and spongiotic dermatitis with marked eosinophilia (Fig. 1c). Additional laboratory studies comprising autoimmune antibodies, complement consumption and extensive microbiological tests including screening for parasites were all negative.

The diagnosis DRESS induced by amoxicillin–clavulanate was made after classifying our patient as 'probable' with five points according to the European registry of severe cutaneous adverse reactions (RegiSCAR) scoring system.¹ Seronegative eosinophilic granulomatosis with polyangiitis, systemic lupus erythematosus and hypereosinophilic syndrome, whether or not combined with a second diagnosis of PEP, was excluded as diagnostic criteria were not met. Oral prednisolone was started 1 mg/kg for 2 weeks followed by gradual tapering, resulting in rapid clinical improvement. She had an uncomplicated delivery at 37 weeks gestation. Penicillin series patch testing after pregnancy according to ENDA recommendations showed a positive reaction to amoxicillin, confirming our diagnosis.^{2,3} An extensive search by our librarian PubMed, Embase, Web of Science and Google Scholar (including meeting abstracts and no language restriction) did not identify any published case of DRESS during pregnancy.

Diagnosing DRESS is challenging with a wide spectrum of clinical presentations, as well as a delayed onset of symptoms – usually 2–6 weeks after initiation of drug therapy.

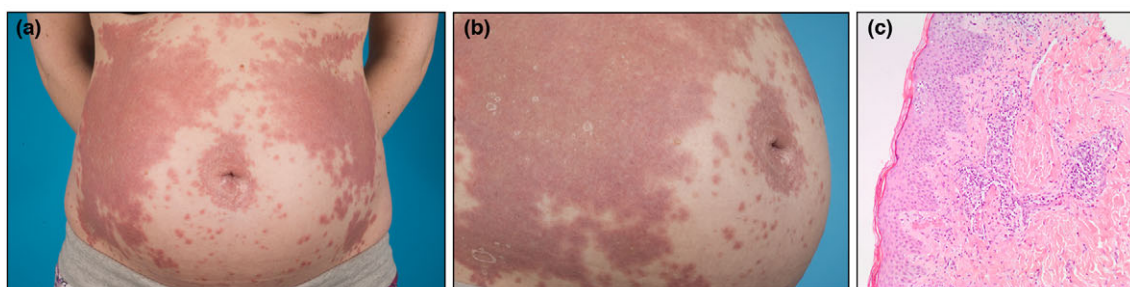


Figure 1 (a) At 26 weeks gestation, a total body examination demonstrated confluent erythematous squamous plaques on the abdomen, including the umbilical region. The back and limbs showed no skin aberrations. (b) A detail of the erythematous plaques. (c) Histopathology of a skin biopsy shows high dermal perivascular infiltrate and spongiotic dermatitis with eosinophilia.

Table 1 Overview of laboratory results at presentation

Test		Unit	Normal range
Leucocytes	17	$\times 10^9/L$	4–10
Eosinophils	1.4	$\times 10^9/L$	<0.50
Erythrocyte sedimentation rate (ESR)	55	mm/h	0–20
C-reactive protein (CRP)	6	mg/dL	0–5
Aspartate aminotransferase (AST)	60	IU/L	<31
Alanine aminotransferase (ALT)	86	IU/L	<34
Troponin T	0.340	Ug/L	0–0.050
Creatinine kinase (CK)	39	U/L	0–145

RegiSCAR has therefore developed a scoring system to define DRESS more accurately. DRESS should be highly suspected in the presence of a cutaneous eruption, fever, lymphadenopathy, hypereosinophilia and liver involvement, especially when other potential causes have been excluded.⁴ However, the pattern of cutaneous eruption and the types of organs involved are non-specific. Periumbilical involvement of skin lesions is not typical for PEP and should raise suspicion of alternative diagnoses such as drug hypersensitivity as the underlying cause.

Eosinophilic (peri)myocarditis is an unrecognized manifestation of DRESS reported in only 2% of patients.⁴ The gold standard to diagnose myocarditis is an endomyocardial biopsy. However, in clinical practice, the diagnosis is based on criteria using ECG, echocardiography and cardiac enzymes whether or not combined with cardiovascular magnetic resonance imaging.⁵ Of the 22 cases with DRESS-associated myocarditis, three occurred following ampicillin exposure. Despite treatment, 12 patients died and two patients suffered from long-term heart failure.⁶

In summary, this is the first report of DRESS in pregnancy following exposure to amoxicillin–clavulanate. In both pregnant as well as non-pregnant patients appearing with a skin eruption,

systemic symptoms and eosinophilia, a thorough investigation of drug exposure(s) up to 6 weeks before presentation is mandatory as this is crucial for early recognition. Prompt withdrawal of the causative agent and treatment with corticosteroids can be lifesaving.

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