

Which prophylaxis is senseful after contrast-induced drug rash with eosinophilia and systemic symptoms? The role of double prophylaxis and chemical cross-reactivity

I am intrigued by the recent publication by Griffith Brookles *et al.*¹ presenting two cases with drug rash with eosinophilia and systemic symptoms (DRESS) following the application of an iodinated contrast medium (ICM). Their study offers valuable insights into their prophylaxis of delayed ICM-induced hypersensitivity reactions, especially DRESS. However, I wish to underscore a few concerns pertinent to the presentation of some facts and result interpretation.

- (1) Two prophylactic measures were taken (change of contrast agent to a non-culprit one and anti-allergic medication). Why the anti-allergic medication was used is not clear and is not mentioned in the manuscript.¹

Presumably, the treating physicians were not sure whether the ICM change alone (see below) would prevent the recurrence of DRESS or not. The use of two prophylactic measures means that the reader does not know which prophylaxis was effective. Since the treatment of DRESS is very difficult and some cases are resistant to therapy despite treatment with corticosteroids, the value of the medication described is doubtful. Moreover, there is no evidence that continuation of anti-allergic medication resulted in suppression of DRESS. Therefore, such medication should not be recommended for DRESS prophylaxis, as corticosteroids can, for example, worsen diabetic metabolism.

Although the authors provide recommendations for management in patients with DRESS, we lack information on the dosage of the proposed corticosteroid medication.¹

In general, late-type (non-immediate) reactions, such as DRESS, are not suitable for premedication.² Switching to another ICM

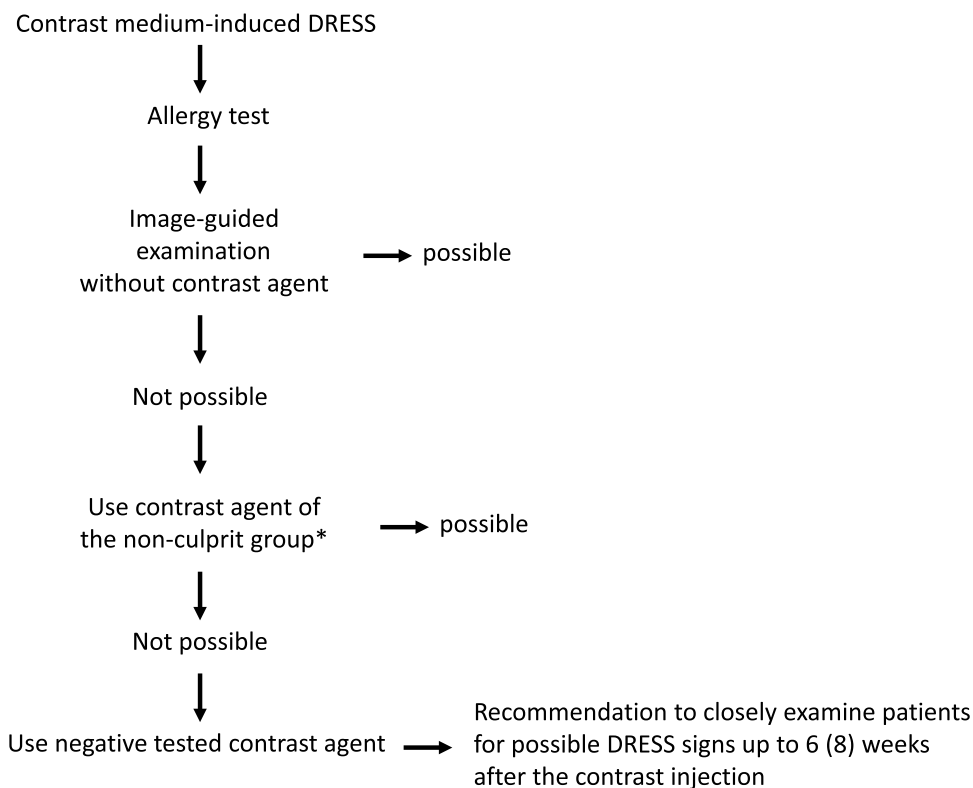


Figure 1 Flowchart showing the recommended procedure in patients with a history of contrast medium-induced drug rash with eosinophilia and systemic symptoms. *Patients in whom iodinated contrast media-induced drug rash with eosinophilia and systemic symptoms should receive gadolinium-containing contrast media, and vice versa.

(i.e. a non-culprit ICM) serves as adequate prophylaxis. This measure was also used in the two patients described and probably brought the observed benefit.¹ This measure is correct and sensible.

- (2) Although the switch to a non-culprit is a useful measure, the information on the so-called cross-reactivity is unclear (e.g. 'The results showed a negative prick test and a positive IDT at 48 h to iohexol, while iopromide, iobitridol, and gadoteric acid tested negative for cross-reactivity¹'). Based on the chemical structural formulas, it is clear that there are possible cross-reactions between iohexol and iopromide, while these are not to be expected between iohexol and iobitridol or gadoteric acid.³ Patients with proven allergy to two or more contrast agents do not necessarily have cross-reactivity; polyvalent allergy is also possible. Clinical experience shows that every patient has an individual reaction pattern with respect to allergic and non-allergic contrast media. The so-called chemical cross-reactivity plays a minor role and should not be overestimated in the clinical context.³
- (3) Like several other authors, Griffith Brookles *et al.*¹ mention that patients treated with beta-blockers are at higher risk of developing hypersensitivity reactions to ICM. Evidence in the medical literature suggests that beta-blockers do not increase the frequency of anaphylaxis, but are associated with greater risk for severe anaphylaxis, and for anaphylaxis refractory to treatment.⁴

Taken together, it can be assumed that there is a desire for effective prophylaxis of contrast hypersensitivity reactions, including DRESS. Since DRESS is very rare, there are currently no recommendations in the guidelines of the professional societies (European Society of Cardiology and European Society of Urogenital Radiology). According to the current state of science, no further CM administration should be given to patients who have developed DRESS following CM injection. If contrast-enhanced imaging is urgently indicated, we should preferentially switch from iodinated to gadolinium-containing CM (or vice versa). If this is not possible, a non-culprit CM (i.e. a negative tested CM) should be applied (Figure 1). In this context, it is very important to precisely document undesirable CM reactions.⁵

Further studies are necessary to show whether a switch to non-culprit CM plus anti-allergic medication is the effective prophylaxis. Based on the current data, anti-allergic medication does not seem to have any

prophylactic effects in DRESS. On the contrary, anti-allergic medication can create the illusion of safety that does not exist and may induce side effects by themselves. The switch to a non-culprit CM should be systematically investigated in patients with DRESS. Future studies should also show whether the focus should be on the so-called cross-reactivity or not.

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Data availability

All available data are included in the manuscript; no further data exists.

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