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**Case Presentation**

**Acute generalized exanthematous pustulosis due to dextromethorphan**

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**Abstract**

Acute generalized exanthematous pustulosis (AGEP) is a rare, severe, pustular, cutaneous reaction. We report a case in which a patient developed AGEP after the intake of 3 different antitussive agents containing dextromethorphan as the only ingredient in common.

**Keywords: Acute Generalized Exanthematous Pustulosis, immunology, dextromethorphan, antitussive agents, drug eruptions.**

We present a 25- year old woman referred to our department because of a pustular eruption she suffered less than 24 hours after the intake of a cough suppressant compound (Iniston®).

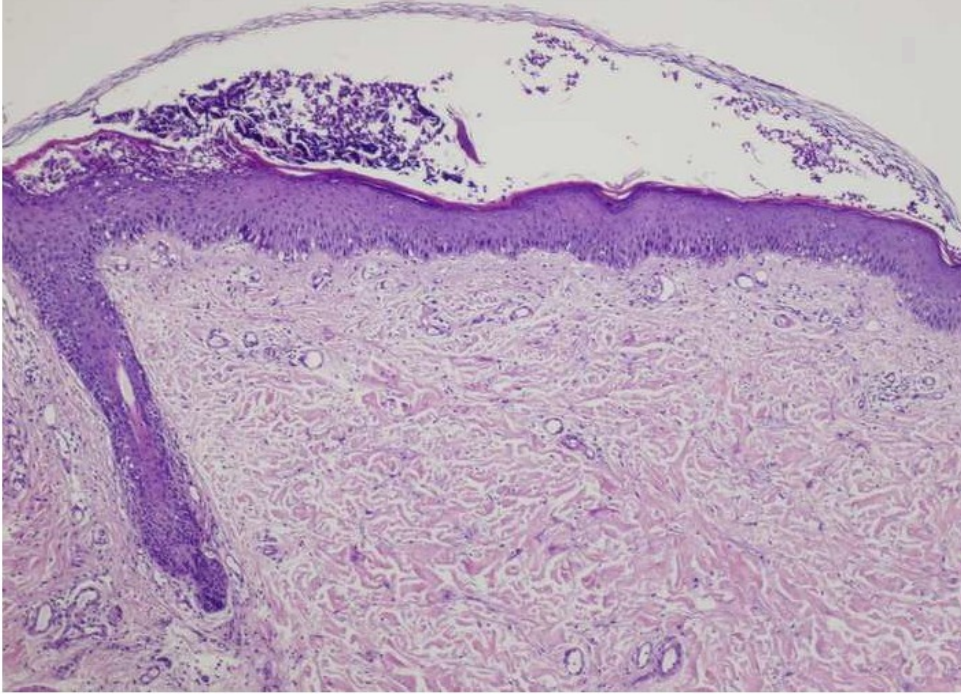


**Figure1.** AGEP. Numerous non-follicular pustules on widespread edematous erythema.

The patient did not take any other drugs or antibiotics apart from the antitussive agent. She did not suffer from any viral illness and her past medical history was unremarkable except for two episodes of pustular eruption as a child with the intake of Benylin® and Frenadol®. In all three medications there was only one common active compound or excipient: dextromethorphan, a weak opioid with antitussive properties.

The patient, otherwise healthy, exhibited a generalized pustular eruption, with hundreds of small, non-follicular pustules over an erythematous-edematous skin, which was starting to scale in flexural areas. The mucous membranes were not affected and Nikolsky sign was negative on both affected and healthy skin. The patient had a temperature of 38.5° and a significant leukocytosis with neutrophilia was observed in the blood count ( $20.8 \times 10^9$  leukocytes with 93% neutrophils) (Figure 1).

The skin biopsy supported a diagnosis of AGEP with many features related to this entity such as subcorneal intraepidermal pustules, marked edema of the papillary dermis, and perivascular infiltrates with neutrophils and some eosinophils within the dermis (Figure 2).



**Figure 2.** HE 4x. AGEP. Subcorneal pustule filled with neutrophilic granulocytes. Slight edema of the superficial dermis, as well as a sparse perivascular lymphocytic infiltrate.

With the suspicion of AGEP related to dextromethorphan, based on both the classic criteria of Roujeau [1] and the score from the EuroSCAR group [2], we decided to discontinue the intake of the drug. Our patient fulfilled four out of the five classic criteria proposed by Roujeau et al.[1]: acute pustular eruption, fever  $>38^{\circ}\text{C}$ , neutrophilia (with or without eosinophilia), and subcorneal or intraepidermal pustules on biopsy. We did not verify the last criterion, spontaneous resolution in less than 15 days, because the patient was treated with oral corticosteroids (prednisone 0.5 mg/kg) and supportive care with complete clearing of the eruption within 7 days.

The differential diagnosis excluded considering both clinical presentation and histopathology were DRESS, Sweet Syndrome, Stevens-Johnson syndrome, and most importantly, pustular psoriasis (which usually shows classic psoriatic features in the histopathology, a previous history of disease, and lack of recent medication).

AGEP is one of the most recognizable drug reaction patterns. Once the diagnosis is established, a confirmation of the culprit drug is desirable, but often remains unclear. In our case, the patient tested herself in the same way a drug provocation test would do. Patch testing of the patient with the offending agent generally shows a weak sensitivity and has been associated with reports of generalized AGEP flares [3]. AGEP is believed to involve drug specific T cells ( $\text{CD4}^{+}$  and  $\text{CD8}^{+}$ ) and the production of  $\text{IL8-CXCL8}$  [4]. As a result we decided to use the in vitro lymphocytic transformation test, which gives a sensitivity of the 78% and specificity of the 81%. It was performed twice, with a 4-month interval between tests. The control antigens were *Candida albicans* and *Trichophyton rubrum*. The sample reacted against the controls but the result was negative for dextromethorphan in both tests.

We present, to our knowledge so far, the first case of AGEP related to dextromethorphan. Given the wide use of this substance in prescribed and over the counter drugs, clinicians should be aware of this potential complication.

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