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## Case Report

# Acute generalized exanthematous pustulosis induced by flupentixol-melitracen: a previously unreported drug reaction

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## ABSTRACT

Acute generalized exanthematous pustulosis (AGEP) is a rare and severe cutaneous drug reaction, most often triggered by antibiotics or antifungals. Psychotropic medications are an uncommon cause. We report the case of a 60-year-old male who developed AGEP within 24-48 hours of initiating flupentixol-melitracen, a fixed-dose antipsychotic-antidepressant combination. Clinical features included widespread sterile pustules on an erythematous base, and histopathology confirmed the diagnosis. The eruption resolved rapidly upon drug withdrawal and topical corticosteroids. To the best of our knowledge, this is the first reported case of AGEP induced by flupentixol-melitracen. Clinicians should consider this rare association when evaluating drug-induced pustular eruptions.

**Keywords:** SCADR, AGEP, Flupentixol-melitracen, Drug reaction

## INTRODUCTION

Acute generalized exanthematous pustulosis (AGEP) is a rare, severe, and often drug-induced pustular eruption characterized by the rapid onset of sterile pustules on an erythematous base, typically accompanied by fever and neutrophilia. The condition is frequently misdiagnosed due to its resemblance to other pustular dermatoses. While antibiotics and antifungals are commonly implicated, reports involving psychiatric medications are exceedingly rare.<sup>1,2</sup> We present a unique case of AGEP triggered by flupentixol-melitracen, a fixed-dose antipsychotic-antidepressant combination.

## CASE REPORT

A 60-year-old male presented to our dermatology outpatient department with sudden onset of intense pruritus and erythematous maculopapular lesions over his back. Within 24-48 hours, the eruptions evolved into numerous sterile pustules that spread to his limbs. There were no systemic symptoms, mucosal involvement, or fever. Upon reviewing his history, it was discovered that

the patient had taken Flupentixol-Melitracen a day prior for lower back pain, a medication not previously used by him. No other new medications or infections were identified.

### Drug profile

Flupentixol-Melitracen is a combination of a typical antipsychotic and a tricyclic antidepressant. Flupentixol acts as a dopamine D2 receptor antagonist, offering antipsychotic and mood-stabilizing effects, while melitracen inhibits norepinephrine and serotonin reuptake, enhancing antidepressant action. Their synergistic effect is associated with fast onset and generally good tolerability.<sup>3</sup> However, to our knowledge, AGEP has not been previously reported as an adverse reaction to this combination.

### Clinical course and management

The drug was immediately discontinued. The patient was treated with topical corticosteroids and supportive care. Remarkable improvement was noted within 72 hours, with

drying of pustules followed by exfoliation. No systemic therapy was required.

### Histopathology

Biopsy from a pustular lesion showed: Intraepidermal spongiotic vesicles, subcorneal pustules, spongiosis with basal vacuolation, perivascular and interstitial infiltrate containing lymphocytes, neutrophils, and eosinophils and papillary dermal edema and red cell extravasation

These findings were consistent with the histopathological criteria for AGEP.<sup>1</sup>

### Differential diagnosis

Several conditions were ruled out:

*Pustular psoriasis*: Lacked chronicity and typical histology.

*DRESS syndrome*: No eosinophilia, systemic involvement, or delayed onset.<sup>2</sup>

*SJS/TEN*: No mucosal erosions or keratinocyte necrosis.

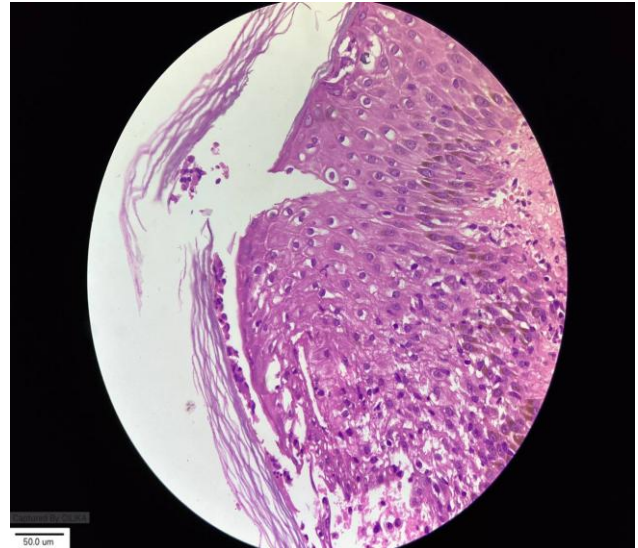
*Sneddon-Wilkinson disease*: Chronic and intertriginous in distribution.

*Infectious dermatitis*: Sterile pustules and negative cultures excluded this.

*Contact dermatitis*: Unlikely due to widespread nature and lack of exposure history. The EuroSCAR validation score strongly supported a diagnosis of AGEP.<sup>2</sup>



**Figure 1: Multiple, coalescing erythematous sterile, non-follicular papulo pustules (forearms).**



**Figure 2: The biopsy shows intra-epidermal vesicles with spongiosis, superficial pustules, and vacuolations under basal cells. There is perivascular inflammation with lymphocytes, neutrophils, and eosinophils, along with mild dermal edema and red cell extravasation. No granuloma is seen.**



**Figure 3: Clinical improvement was noted within 72 hours, with drying of pustules followed by exfoliation, after discontinuation of the drug.**

### DISCUSSION

AGEP is a self-limiting but alarming dermatologic condition, typically triggered by medications. Most cases involve beta-lactam antibiotics or antifungals.<sup>2</sup> The sudden onset, typical morphology, and rapid resolution upon drug withdrawal in our case indicate a probable causal relationship between flupentixol-melitracen and AGEP.

T-cell-mediated hypersensitivity and cytokine release are proposed mechanisms behind AGE<sup>4</sup>. Though psychotropics have been known to cause cutaneous reactions, this is, to the best of our knowledge, the first case reporting AGE<sup>4</sup> associated with this particular drug combination.

## CONCLUSION

This case adds to the growing awareness of uncommon triggers for AGE<sup>4</sup>. Flupentixol-melitracen, though widely regarded as safe, may rarely cause severe cutaneous drug reactions. Prompt identification and discontinuation of the offending drug is critical for favorable outcomes. More case documentation will help in better understanding its cutaneous adverse effect profile.

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