



Clinical Pharmacology & Toxicology Pearl of the Week

~ SCARs: Acute Generalized Exanthematous Pustulosis (AGEP) ~

Case:

- ✓ An 81-year-old woman was admitted to hospital with a urinary tract infection.
- ✓ She was started empirically on ceftriaxone 1 g IV q24h. Urine cultures were positive for *Proteus mirabilis* with sensitivities pending.
- ✓ Antimicrobial coverage was broadened to piperacillin-tazobactam on admission day 3 for worsening delirium.
- ✓ The following day, she was febrile and developed rapidly progressive erythematous macules over the chest, which progressed to small pustular lesions over the posterior trunk, neck, proximal extremities, and face. The mucous membranes, palms and soles were spared.

Background:

- ✓ AGEP is a severe, primarily drug-induced dermatosis with an incidence of 1-5 cases per million people per year. It has a low mortality rate of ~2-4%.
- ✓ The main culprits are antibiotics, primarily β -lactams and macrolides. Fluoroquinolones, anti-infective sulfonamides, terbinafine and diltiazem have also been implicated.
- ✓ Histology can help confirm the diagnosis. Typical findings are included in the AGEP validation score of the EuroSCAR study group, which can help confirm or rule out the diagnosis.

Clinical features:

AGEP is characterized by the abrupt onset of non-follicular pinhead-sized sterile pustules along with the following:

- ✓ An intertriginous predilection and fever $>38^{\circ}\text{C}$.
- ✓ Characteristic skin lesions appear within 24-48 hours of drug administration. There is rarely involvement of other internal organs.
- ✓ There may be mild mucous membrane involvement that is nonerosive and limited to one region (typically oral).
- ✓ It can closely mimic generalized pustular psoriasis and histology can help with this differentiation.
- ✓ The natural course includes post-pustular desquamation with resolution of skin lesions within 15 days of stopping the offending medication.



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AGEP validation score

Variable	Score	Variable	Score
<i>Morphology</i>		<i>Course</i>	
Pustules		Mucosal involvement	
Typical [±]	+2	Yes	-2
Compatible ^{**}	+1	No	0
Insufficient ^{***}	+0	Acute onset (<10 d)	
Erythema		Yes	0
Typical	+2	No	-2
Compatible	+1	Resolution <15 days	
Insufficient	+0	Yes	0
Distribution/pattern		No	-4
Typical	+2	Fever >38.75°C	
Compatible	+1	Yes	+1
Insufficient	+0	No	0
Postpustular desquamation		Polymorphonuclear neutrophils >7,000/mm ³	
Yes	+1	Yes	+1
No/insufficient	+0	No	0
		<i>Histology</i>	
		Other disease	-10
		Not representative/no histology	0
		Exocytosis of PMN	+1
		Subcorneal and/or intraepidermal non-spongiform or NOS pustule(s) with papillary edema or subcorneal and/or intraepidermal spongiform or NOS pustule(s) without papillary edema	+2
		Spongiform subcorneal and/or intraepidermal pustule(s) with papillary edema	+3

NOS = not otherwise specified.

Interpretation: =0: no AGEP; 1-4: possible; 5-7: probable; 8-12: definite.

Management:

- ✓ AGEP is a self-limiting disease with a good prognosis.
- ✓ Identification and avoidance of the trigger is key. Repeated exposures may increase subsequent reaction severity. The precipitating agent should be listed as an allergy in the patient's chart.
- ✓ Patch testing can be done after resolution of skin lesions to confirm the correct culprit drug.
- ✓ Antihistamines and topical steroids can be used to provide symptomatic relief when needed but do not affect the clinical course.

Case resolution:

- ✓ All antimicrobials were stopped and a pip-tazo allergy was added to the patient's chart.
- ✓ Pathology reported spongiosis of the epidermis with and overlying subcorneal pustule, superficial and mid dermis contained interstitial neutrophils and eosinophils, with an AGEF EuroSCAR score of 12 (definite AGEF).
- ✓ A recommendation was made to assess for ceftriaxone allergy upon discharge.

References:

1. Shear, Neil & Dodiuk-Gad, Roni. (2019). Advances in Diagnosis and Management of Cutaneous Adverse Drug Reactions: Current and Future Trends. 10.1007/978-981-13-1489-6.
2. Caruso C, Valluzzi RL, Colantuono S, Gaeta F, Romano A. β -Lactam Allergy and Cross- Reactivity: A Clinician's Guide to Selecting an Alternative Antibiotic. J Asthma Allergy. 2021 Jan 18;14:31-46.
3. Feldmeyer L, Heidemeyer K, Yawalkar N. Acute Generalized Exanthematous Pustulosis: Pathogenesis, Genetic Background, Clinical Variants and Therapy. Int J Mol Sci. 2016 Jul 27;17(8):1214.

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral and Specialist Link. You can also find us in the [Alberta Referral Directory](#) (ARD) by searching "Pharmacology" from the ARD home page. Click [HERE](#) for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in [Alberta Referral Directory](#) (ARD) by searching "Toxicology" from the ARD home page.

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