Case Report ISSN 2639-944X

Journal of Medical - Clinical Research & Reviews

Acute Generalized Exanthematous Pustulosis (AGEP): Case Report

Dandhara De Lima Cardoso Almeida[1]*, Lorena Marquez Rizzi[1], Bárbara Eugênio Custódio Silva[1], Daniel Sossai Altoé[2] and Antônio Chambo Filho[3]

[1]Resident Doctor of the Gynecology and Obstetrics Service of the Santa Casa de Misericórdia Hospital in Vitória/ES, Brazil.

[2]Student of the Medicine course at the Escola Superior de Ciências da Santa Casa de Misericórdia de Vitória/ES, Brazil.

[3]Professor of Gynecology and Obstetrics, responsible for the Gynecology and Obstetrics Service at Hospital Santa Casa de Misericórdia de Vitória/ES, Brazil.

***Correspondence:**

Dandhara De Lima Cardoso Almeida, Resident Doctor of the Gynecology and Obstetrics Service of the Santa Casa de Misericórdia Hospital in Vitória/ES, Brazil.

Received: 02 Oct 2023; **Accepted:** 30 Oct 2023; **Published:** 05 Nov 2023

Citation: Dandhara De Lima CA, Rizzi LM, Silva BEC, et al. Acute Generalized Exanthematous Pustulosis (AGEP): Case Report. J Med - Clin Res & Rev. 2023; 7(11): 1-4.

ABSTRACT

Acute generalized exanthematous pustulosis (AGEP) is a clinical and rare condition characterized by the sudden development of multiple non-follicular sterile pustules that are pruritic, primarily appearing in intertriginous areas. This study reports a case of AGEP during pregnancy in a 24-year-old patient, at a gestational age of 35 weeks and 3 days. She was admitted to the obstetric ward with a presentation of pustular exanthematous lesions on the lips, chest, abdomen, face, and upper limbs. The treatment was initiated with a pulse therapy of methylprednisolone at 1 gram per day for 3 days, and albendazole for 5 days. The patient remained hospitalized until she reached 37 weeks of gestation, and a cesarean section was eventually recommended due to failed induction, and the procedure occurred without complications.

Keywords

Pregnancy, Acute generalized exanthematous pustulosis and pregnancy complications.

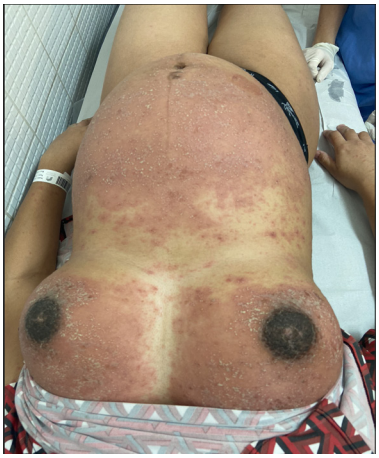
Introduction

Acute generalized exanthematous pustulosis (AGEP) is a clinical condition characterized by the sudden development of multiple non-follicular sterile pustules that are pruritic, primarily appearing in intertriginous areas. Regarding its etiology, it is estimated that in 90% of cases, it is caused by drugs or acute viral infections, dietary supplements, chemotherapy, and radiation [1]. This condition is rare, with an estimated incidence of 1-5 patients per million per year, and it is a severe type of cutaneous adverse reaction. The outcome is favorable in the majority of cases.

Case Report

M. M. V. S., a 24-year-old primigravid at 35 weeks and 3 days of gestational age, was admitted to the obstetric ward with a presentation of pustular exanthematous lesions on her lips, chest, abdomen, face, and upper limbs. These lesions were painful and pruritic, along with a fever and headache, which had been present for the past 7 days. She had been taking cephalexin 500 mg for 5 days with no improvement. She had no prior significant medical history, reported no allergies, and denied the use of medications. The patient also mentioned that her family members did not exhibit similar symptoms. However, her mother, with whom she had daily contact, had been diagnosed with COVID-19.

Upon physical examination upon admission, the patient was afebrile but had multiple pustular lesions on her chest, abdomen, dorsal/lumbar region, lips, and auricular pavilion. These lesions were erythematous and tender to the touch, with scaling noted on the lips and ears (Figures 1 and 2). No obstetric abnormalities were observed during the obstetric physical examination. The patient had irregular prenatal care, and obstetric ultrasound showed fetal weight at the 96th percentile. The cause of this alteration could not be determined, as the patient did not undergo laboratory testing during the second and third trimesters.



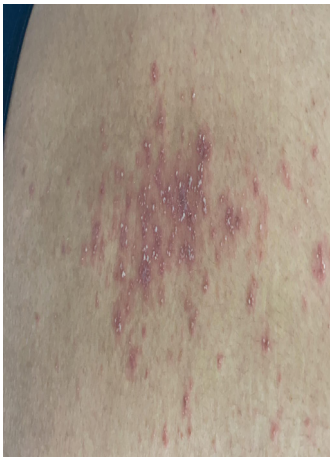


Figure 1: Lesions to the chest and abdomen.; **Figure 2.** Multiple sterile non-follicular pustules.

The requested laboratory tests did not show leukocytosis, although C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were elevated. Liver and kidney function remained normal, and there were no electrolyte imbalances. Skin biopsies were performed on the affected area, revealing agranulosis with parakeratosis in the epidermis, subcorneal and intra-corneal pustules rich in neutrophils, mild spongiosis, and exocytosis of neutrophils. In the papillary dermis, there was edema, a presence of a mixed infiltrate with neutrophils and a few eosinophils, perivascular flow, and no vasculitis, which supported the clinical diagnosis of Acute Generalized Exanthematous Pustulosis (Figure 3). As for the pustule culture, no bacterial growth was observed.

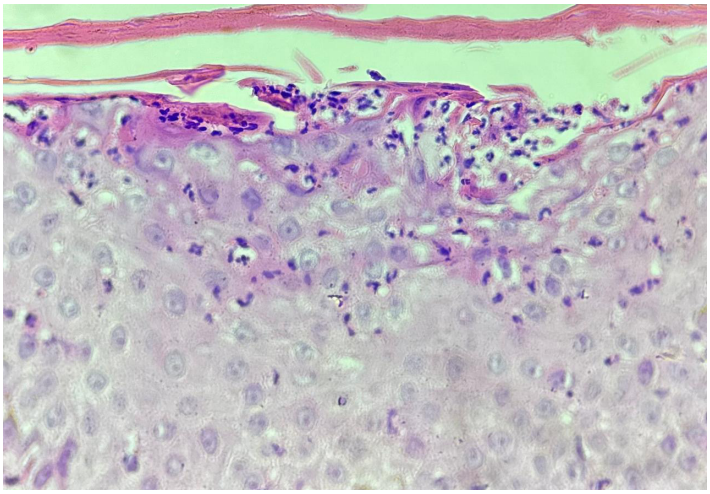
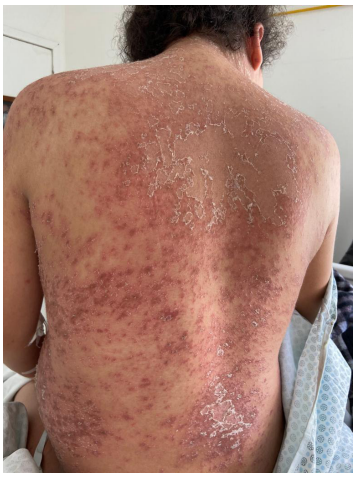
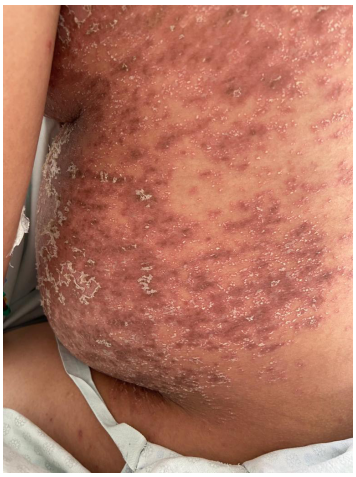


Figure 3: Histophatological: subcorneal and/or intraepidermal spongiotic pustules, marked and frequent papillary dermal edema, perivascular infiltrates with neutrophils, and exocytosis of some eosinophils

A consultation was sought from the hospital's Dermatology Department, which raised the diagnostic hypothesis of Acute Generalized Exanthematous Pustulosis (AGEP). Treatment was initiated with cefalotin for 7 days, along with a pulse therapy of methylprednisolone at 1 gram per day for 3 days, and albendazole for 5 days. Despite partial improvement of the lesions after the pulse therapy, the patient continued to complain of itching and reported the emergence of new lesions on the back (Figures 4 and 5). Therefore, prednisone at a dose of 40 mg per day was administered. After 5 days of hospitalization, there was a progression with desquamation of the lesions (Figures 6 and 7). After 3 days of using the aforementioned dose of prednisone, it was decided to increase it to 60 mg per day. Additionally, topical treatment with a formula containing 3% urea, 5% calamine, 0.002% betamethasone, and 1% silicone in grapeseed oil cream was initiated.





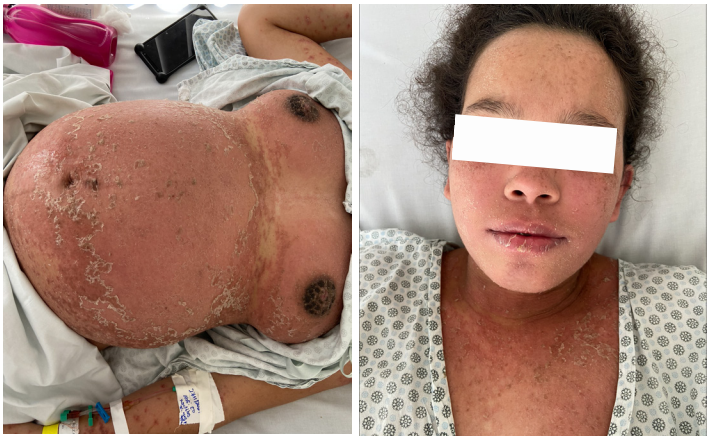
Figures 4 and 5: Emergence of new lesions on the back, despite pulse therapy with corticosteroids.

After a discussion regarding the risk-benefit of starting corticosteroid treatment, taking into consideration the possibility of gestational diabetes, it was decided to continue with corticosteroid therapy. Subsequently, maternal-fetal monitoring was conducted through cardiotocography and obstetric ultrasound. The patient remained hospitalized until she reached 37 weeks of gestation, at which point labor was induced using misoprostol. However, a cesarean section was eventually recommended due to failed induction, and the procedure occurred without complications.

Following the birth, the patient remained hospitalized for an additional 4 days. Upon discharge, she was prescribed prednisone at 40 mg per day, to be continued for 15 days before starting the corticosteroid taper. Additionally, the patient was referred for follow-up at the hospital's Dermatology outpatient clinic and for postpartum care.

Discussion

AGEP is a clinical condition defined by the sudden appearance of numerous non-follicular sterile pustules (smaller than 5 mm) that are pruritic, associated with edema and erythema in the surrounding area. Regarding its etiology, it is estimated that in 90% of cases, it is caused by drugs or acute viral infections, dietary supplements, chemotherapy, and radiation [1].



Figures 6 and 7: Progression with desquamation of the lesions.

As observed in the reported case, the literature describes that the skin lesions primarily affect the facial region and/or intertriginous areas, progressing to the trunk and lower limbs within a few hours in the majority of cases [2]. Such lesions can be associated with systemic symptoms such as high fever, asthenia, diarrhea, lymphadenopathy, delirium, dehydration, tetany, and seizures. Other cutaneous manifestations have also been documented in the literature, including facial edema, lesions resembling Stevens-Johnson Syndrome, and, in approximately 20% of cases, mucosal lesions, mainly in the mouth and on the tongue [3].

Laboratory analysis often reveals leukocytosis in most cases, primarily due to neutrophilia, and eosinophilia may be present in about a third of patients. Furthermore, laboratory studies may show elevated ESR and CRP [1]. Although this was not observed in the reported patient, reduced creatinine clearance occurs in 30% of cases, and occasional hypocalcemia, along with a slight increase in aminotransferases, can also be seen [3]. As for the pustular content, while secondary staphylococcal infection may occur, most pustules are non-microbial [4].

Typical histopathology of AGEP reveals subcorneal and/or intraepidermal spongiotic pustules, marked and frequent papillary dermal edema, perivascular infiltrates with neutrophils, and exocytosis of some eosinophils, consistent with the histopathological findings described in the clinical presentation (Figure 3). Vasculitis and/or some single-cell necrosis of keratinocytes may also be present [5]. The studies suggest that AGEP is a T-cell-mediated immune disease. After contact with the causative agent, antigen-presenting cells present the antigen through MHC molecules, leading to the activation of specific CD4 and CD8 T cells. When activated, these cells migrate to the dermis and epidermis and use mechanisms that induce keratinocyte apoptosis within the epidermis, leading to tissue destruction and the formation of epidermal vesicles. At the onset of AGEP, the contents of the vesicles are primarily composed of drug-specific CD4 T cells and keratinocytes, which release large quantities of a potent neutrophilic cytokine called CXCL8. This cytokine leads to neutrophil chemotaxis into the vesicles, transforming them into sterile pustules [6].

There are few reports in the literature of AGEP during pregnancy, and most are related not only to pregnancy but also to the consumption of food and medications. It is known that during pregnancy, necessary immunological changes occur to prevent maternal rejection of genetically different fetal tissues. These changes increase innate cellular immunity, leading to the recruitment of various cells associated with Th2-type immunity. Thus, the gestational state makes women more susceptible to inflammatory dermatoses [5].

Regarding diagnosis, a validation scoring system for AGEP from the EuroSCAR study group seeks to assist in the diagnosis using clinical, laboratory, and histopathological criteria (Table 1) [3,7]. Considering these criteria, the diagnosis of AGEP is defined in the reported case. The treatment of AGEP consists primarily of symptom control and discontinuation of the causative agent, as the clinical presentation is usually benign and self-limited. As the clinical presentation includes fever, leukocytosis, and pustules, an incorrect diagnosis of bacterial infection is often made. It is important to emphasize that the pustules are sterile, and antibiotic use should be reserved for cases of secondary infection. Although corticosteroids, both topical and systemic, are empirically used, and clinical experience suggests a reduction in disease duration, their use is questioned, as there is not enough scientific evidence in the literature to support their use [6]. In addition to this measure, the use of disinfectant solutions during the pustular phase and moisturizers during the desquamative phase seem to be beneficial for symptom control [1].

Table 1: AGEP diagnostic score, proposed by the EuroScar group.

	Morphology	Score
Pustules	Typical Compatible Insufficient	+2 +1 0
Erythema	Typical Compatible Insufficient	+2 +1 0
Distribution	Typical Compatible Insufficient	+2 +1 0
Postpostular desquamation	Yes No/Insufficient	+1 0
	Course	Score
Mucosal involvement	Yes No	-2 0
Acute onset (< 10 days)	Yes No	0 -2
Resolution (≤ 15 days)	Yes No	0 -4
Fever > 38ºC	Yes No	+1 0
PMN > 7000/mm³	Yes No	+1 0
	Histopathology	Score
Other diseases		-10
Not significant/no pathological examination		0
Polymorphonuclear exocytosis		+1
No subcorneal and/or intraepidermal spongiosis or unspecified, pustule with papillary edema or subcorneal and/or intraepidermal spongiosis or unspecified, pustules, without papillary edema		+2

Subcorneal and/or intradermal spongiform pustule with papillary edema		+3
Interpretation (Score) 0: not AGEP; 1-4: AGEP is possible; 5-7: AGEP is likely; 8-13: AGEP is set;		
*Typical: typical morphology; **Compatible: non-typical morphology, but strongly suggestive; ***Insufficient: injuries cannot be judged (due to the advanced stage of development); AGEP: Acute Gestational Exanthematous Pustulosis; PMN: polymorphonuclear. Source adapted: Sideroff et al. [3] Histopathology		

Conclusion

Considering the rarity of this condition and the extensive differential diagnosis, it is essential to have an understanding of the etiology, clinical manifestations, and treatment of AGEP. This knowledge is particularly crucial because appropriate and early treatment can prevent maternal and fetal morbidity and mortality.

References

1. Jesse Szatkowski, Robert A Schwartz. Acute generalized exanthematous pustulosis agep a review and update. J Am Acad Dermatol. 2015; 73: 843-848.
2. Lorena Amaral Batista Leite, Eve Grillo Carvalho, Lorena Luana Batista, et al. Acute generalized exanthematous pustulosis in a 9-year-old child. Residência pediátrica. 2019; 9: 319-321.
3. Sidoroff A, Halevy S, Bavinck JN, et al. Acute generalized exanthematous pustulosis agep a clinical reaction pattern. J Cutan Pathol. 2001; 113-119.
4. Laurence Feldmeyer, Kristine Heidemeyer, Nikhil Yawalkar. Acute generalized exanthematous pustulosis: pathogenesis, genetic background, clinical variants and therapy. Int J Mol Sci. 2016; 17: 1214-1222.
5. Alicia Minerva López López, Ana Laura Shiguetomi Sifuentes, Samuel Amezcua Gudiño, et al. Pustulosis exantemática generalizada aguda asociada al embarazo. Piel. 2018; 10: 623-625.
6. Halevy, sima. Acute generalized exanthematous pustulosis pathogenesis genetic background clinical variants and therapy. Current opinion in allergy and clinical immunology. 2009; 322-328.
7. Sidoroff A, Dunant A, Viboud C, et al. Risk factors for acute generalized exanthematous pustulosis agep results of a multinational case-control study euroscar. BJD. 2007; 989-996.

© 2023 Dandhara De Lima CA, et al. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License