Eur. J. Pediat. Dermatol.
31, 87-90, 2021

A ten-day-old newborn with acute generalized exanthematous pustulosis.

Mai TCC[1], Vo T.T.V.[1], Nguyen T.T.M.[1], Le T.C.N.[1], Nguyen T.T.P.[1], Pham T.N.[2], Mai B.H.A.[1]
[1]Department of Dermatology, Hue University of Medicine and Pharmacy, Hue University, Viet Nam
[2]The Neonatal Unit, Hue University of Medicine and Pharmacy Hospital, Viet Nam

Received: March, 3, 2021; accepted: April, 10, 2021
Published online: April, 19, 2021

Summary Acute generalized exanthematous pustulosis (AGEP) is a rare reaction related to various causes; in most cases, it is a drug-induced reaction. AGEP can occur at any age but is seldom described in children. In this article, we describe an AGEP case in a ten-day-old patient suspected to be caused by erythromycin, cefotaxime and ampicillin. Until now, according to our knowledge, this is the first pulished case of AGEP in a newborn.

Keywords Newborn, skin, ampicillin, cefotaxime, erythromycin.

Abbreviation **AGEP** = acute generalized exanthematous pustulosis.

Acute generalized exanthematous pustulosis (AGEP) is a rare reaction – approximately 5/1,000,000 per year – (1, 11, 12, 13, 14), characterized by numerous, diffuse, acute, nonfollicular, sterile pustules on a background of erythema and usually accompanied by fever and peripheral leukocytosis (1, 13, 14).

Nearly ninety percent of AGEP is due to drugs, of which the most common cause are antibiotics. Leading in this group are beta-lactams and macrolides (11, 15). AGEP has been reported in infants, children, and adults. Nevertheless, it is more common in adults (12). This is our record of an AGEP case in a ten-day-old patient probably caused by erythromycin, cefotaxime and ampicillin. We have been unable to identify any neonatal AGEP cases in the literature.

Case report

A newborn was admitted to the hospital immediately after birth as a result of pneumonia due to inhalation of meconium and early neonatal infection; at this time no skin lesions were observed. He had no family history of psoriasis or any other skin disorders. After ten days applying ampicillin, cefotaxime and two days applying erythromycin, the neonate developed a generalized eruption consisting of multiple pustules. Physical examination (Fig. 1) revealed myriads of small, nonfollicular pustules developing on erythematous plaques on the face. In some areas, they coalesced into larger plaques. The mucous membranes, palms and soles were spared. There was no fever. Nikolsky's sign was negative.

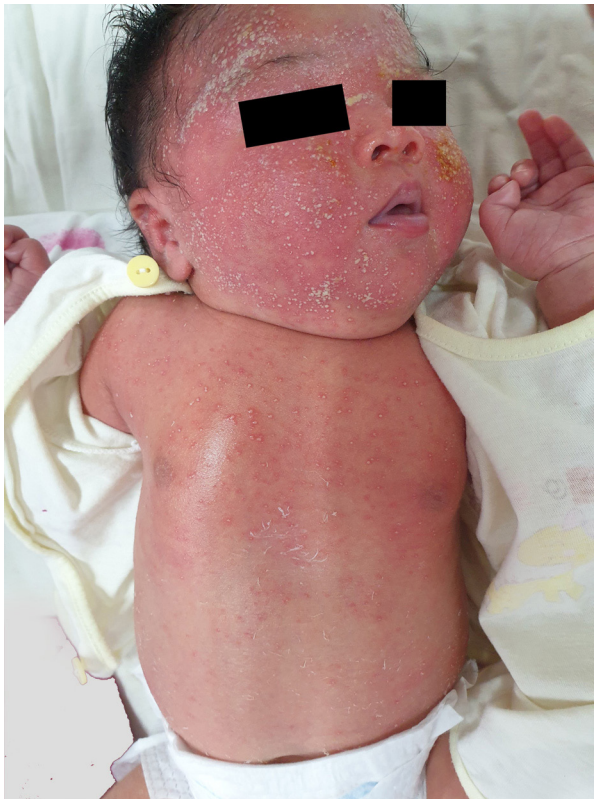

Fig. 1

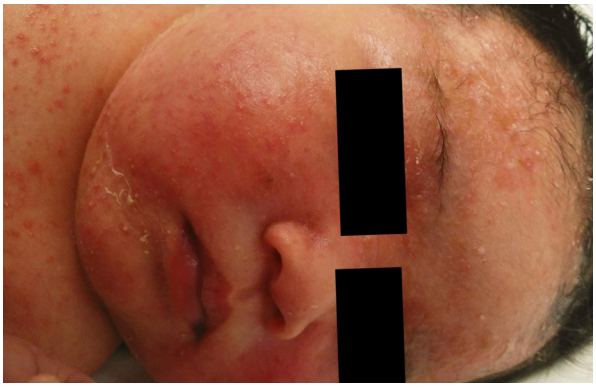

Fig. 2

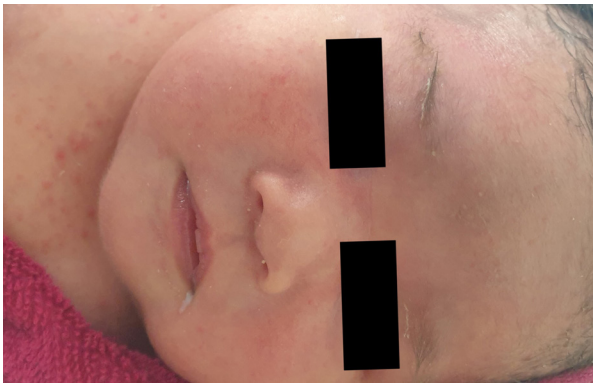

Fig. 3

Fig. 1, 2, 3: AGEP in a newborn: numerous, nonfollicular pustules (Fig. 1). In Fig. 2 you can see the same newborn as in Fig. 1 two days after withdrawal of ampicillin, cefotaxime and erythromycin. In Fig. 3 the same newborn six days after withdraval of the three antibiotics.

Rapid and labored breathing was observed occasionally. His WBCs were 12.77 G/l (n.v. 4-10) with 5.87 x 10^3 neutrophil (n.v. 1.48-7.20 x 10^3). Procalcitonin level was 0.079 ng/ml (n.v. 0-0.05), CRP level was 6.01 mg/l (n.v. 0-5) and AST level was 82.5 U/L (n.v. 0.0-40.0). Hepatic and renal functions, which were performed twice, resulted within normal values. Bacterial cultures of the pustular lesions and daily blood samples were negative. A skin biopsy was not performed due to the patient's age and his parents' disapproval.

The characteristic rash and the typical clinical course led to the diagnosis of AGEP, probably due to ampicillin, cefotaxime and erythromycin. Treatment with those drugs was discontinued and replaced by meropenem, vancomycin, plus a topical combination of fusidic acid and hydrocortisone twice a day and daily diluted 1/10,000 $KMnO_4$ solution wash, resulting in rapid resolution of the rash. In particular, the pustules stopped spreading within one day and began to dry and left scales after two days (Fig. 2). However, the patient still had some small red papules on the face. After six days, there were no lesions on the face and just a few scattered small, red papules and macules remained on the body. After eight days, all cutaneous lesions resolved (Fig. 3). On the other hand, respiratory symptoms remained after two days of the new treatment and started to respond gradually after three days. After 16 days of applying the new treatment, at 29-day-old, the patient recovered totally and was discharged.

Discussion

AGEP is a reaction attributed to a variety of causes; about ninety percent of cases are trigge-

red by drugs. Antibiotics are involved in most cases (11, 15). Other suspected causes such as infections (Cytomegalovirus and Parvovirus B19, *Chlamydia*, and *Mycoplasma pneumoniae*) and mercury have been reported (2, 4, 5, 8, 10).

A study involving 97 patients in the United States revealed that AGEP can occur at any age but its greatest proportion is in adults; the mean age was 56 (12). As far as we know, the youngest patient reported with AGEP was five-month-old, and this patient had no recently received any drugs (7). Another rare infant AGEP case has been reported is a ten-month-old infant; in this case the disease was suspected to be provoked by amoxicillin (9).

Our patient did not underwent a skin biopsy. However, the clinical morphology was very typical for AGEP. According to Euroscar scale, this patient had seven points (table 1), thus he was classified in the group "probable" (12, 13). This patient was hospitalized with neonatal infection and pneumonia. However, two days after changing the antibiotics, the cutaneous lesions began to dry; no new skin lesions appeared; meanwhile, respiratory symptoms did not significantly improve. Moreover, the bacterial culture of pustules and blood samples was negative. Therefore, we thought more about drug-induced AGEP than infection-induced AGEP.

Based on a review of 63 cases from France and a retrospective study conducted in Thailand, beta-lactam and macrolide are the two leading causes of drug-induced AGEP (11, 15). The average time for AGEP to appear is from one to eleven days after drug administration (12). Our patient had AGEP symptoms at the age of ten day, and he had been taking three types of antibiotics: ampicillin, cefotaxime for ten days, and erythromycin for two days. Therefore, we think that our AGEP case was provoked by ampicillin, cefotaxime and erythromycin, but we cannot be sure whether his condition was caused by those drugs acting together or alone.

In this patient, we discounted a superficial primary skin infection, although he had numerous pustules, because these lesions did not turn into superficial erosions and did not have "honey-colored" crusts; additionally, the bacterial culture of the pustules was negative.

Table 1: AGEP validation score of the Euro-SCAR.

Criteria	*Description*	*S.*
Morphology		
• Pustules	Typical, myriad small nonfollicular and sterile pustules developed on erythematous background	+2
• Erythema	Typical, diffuse	+2
• Distribution	Typical, on the face, trunk and limbs	+2
• Desquamation post pustulation	Yes	+1
Course		
• Mucosal involvement	No	0
• Acute start (<10 days)	Yes	0
• Resolution (<15 days)	Yes	0
• Fever ≥ 38 ºC	No	0
• Polymorphonuclear neutrophils ≥ 7000/mm^3	No	0
Histopathology	No	0
Total		7
Legenda: S. = score.		

The diagnosis of candidiasis was also excluded by the clinical features and course of the disease. We also ruled out pustular psoriasis because none of his family members had psoriasis, and we observed rapid clinical response after drug discontinuation.

Drug-induced AGEP is a self-limiting reaction and can disappear spontaneously within two weeks after withdrawal of offending drugs. Its therapy is symptomatic including control of pruritus and skin inflammation. In fact, depending

on the affected area, mild to moderate potency topical steroids are recommended (3, 6, 13). In conclusion, AGEP may occur in neonates and the symptoms are similar to children and adults. Clinicians need to consider this diagnosis, especially in newborns using medications.

Conflicts of interest

The Authors declare that they have no conflicts of interest.

Address to:
Mai Ba Hoang Anh, M.D.
Department of Dermatology
Hue University of Medicine and Pharmacy
6 Ngo Quyen st
Hue city, Viet Nam
Fax: 84.234.3826269

References

1) Alniemi D.T., Wetter D.A., Bridges A.G. et Al. 2017. Acute generalized exanthematous pustulosis: clinical characteristics, etiologic associations, treatments, and outcomes in a series of 28 patients at Mayo Clinic, 1996-2013. *Int. J. Dermatol*. 56 (4): 405-14.
2) Belhadjali H., Mandhouj S., Moussa A. et Al. 2008. Mercury-induced acute generalized exanthematous pustulosis misdiagnosed as a drug-related case. *Contact Dermatitis* 59 (1): 52-4.
3) Britschgi M., Steiner U.C., Schmid S. et Al. 2001. T-cell involvement in drug-induced acute generalized exanthematous pustulosis. *J. Clin. Invest*. 107 (11): 1433-41.
4) Calistru A.M., Lisboa C., Cunha A.P. et Al. 2012. Acute generalized exanthematous pustulosis to amoxicillin associated with parvovirus B19 reactivation. *Cutan. Ocul. Toxicol*. 31 (3): 258-61.
5) Chamlin S., Metry D. (2009). Acute generalized exanthematous pustulosis associated with asymptomatic *Mycoplasma pneumoniae* infection. *Arch. Dermatol*. 145 (7): 848-9.
6) De A., Das S., Sarda A. et Al. 2018. Acute generalised exanthematous pustulosis: an update. *Int. J .Dermatol*. 63 (1): 22-9.
7) Ersoy S., Paller A.S., Mancini A.J. 2004. Acute generalized exanthematous pustulosis in children. *Arch. Dermatol*. 140 (9): 1172-3.
8) Haro-Gabaldón V., Sánchez-Sánchez-Vizcaino J., Ruiz-Avila P. et Al. 1996. Acute generalized exanthematous pustulosis with cytomegalovirus infection. *Int. J. Dermatol*. 35 (10), 735–7.
9) Her Y., Kil M.S., Park J.H. et Al. 2009. Acute generalized exanthematous pustulosis in a 10-month-old infant. *Korean J. Dermatol*. 47 (11): 1321-3.
10) Manzano S., Guggisberg D., Hammann C., Laubscher B. 2006. Acute generalized exanthematous pustulosis: first case associated with a *Chlamydia pneumonia*e infection. *Arch. Pediatr.* 13 (9): 1230-2.
11) Roujeau J.C., Bioulac-Sage P., Bourseau J.C. et Al. 1991. Acute generalized exanthematous pustulosis. Analysis of 63 cases. *Arch. Dermatol*. 127 (9): 1333-8.
12) Sidoroff A., Dunant A., Viboud C. et Al. 2007. Risk factors for acute generalized exanthematous pustulosis (AGEP)—results of a multinational case-control study (EuroSCAR). *Br. J. Dermatol*. 157 (5): 989-96.
13) Sidoroff A., Halevy S., Bacinck J.N. et Al. 2001. Acute generalized exanthematous pustulosis (AGEP) – A clinical reaction pattern. *J. Cutan. Pathol*. 28 (3): 113-9.
14) Speeckaert M.M., Speeckaert R., Lambert J., Brochez L. 2010. Acute generalized exanthematous pustulosis: an overview of the clinical, immunological and diagnostic concepts. *Eur. J. Dermatol*. 20 (4): 425-33.
15) Thienvibul C., Vachiramon V., Chanprapaph K. 2015. Five-year retrospective review of acute generalized exanthematous pustulosis. *Dermatol. Res. Pract*. 2015: 260928.