Acute generalized exanthematous pustulosis: A rare side effect of a common over-the-counter drug, Acetylsalicylic acid

Amit Bahuguna

MD, Graded specialist, Skin Department, 92 Base Hospital, India

ABSTRACT

Acute generalized exanthematous pustulosis is an uncommon cutaneous reaction characterized by sudden onset of generalized non-follicular aseptic pustules. It is most often secondary to drugs but causes as varied from viral infection to insect bites are reported. A case report of a 48-year-old male who developed pustular eruptions after taking acetylsalicylic acid is reported here. Clinicians need to be aware of this entity when dealing with pustular rash as this rare side effect of a very common drug is both, easy to miss and easy to manage.

Key words: Acetyl salicylic acid, drug reaction, over-the-counter drugs, pustular eruption

Access this article online

Website: www.idoj.in

DOI: 10.4103/2229-5178.115529

Quick Response Code:

Address for correspondence:
Dr. Amit Bahuguna, Dermatologist, 92 Base Hospital, PIN 901218 C/O 56 APO, India.
E-mail: afmcrocks@yahoo.co.in

INTRODUCTION

Acute generalized exanthematous pustulosis (AGEP) is a cutaneous reaction characterized by sudden onset of numerous non-follicular aseptic pustules that usually begin in intertriginous regions and rapidly progress with widespread erythema.

Historically classified as pustular psoriasis until 1968, when Baker and Ryan described five cases of pustular psoriasis with no history of psoriasis in which the episode of pustular eruption was acute and quickly resolved.[1] In 1980, Beylot *et al.* coined the term *pustuloses exanthématique aiguës généralisés* in French, which translates in English to AGEP.[2]

It is most often secondary to drugs but causes as varied from viral infection to insect bites are reported. Although drugs are the most common cause, an over-the-counter (OTC) drug like acetylsalicylic acid (ASA) is a rare cause, with one case found in literature and a case is reported here.[3]

CASE REPORT

A 48-year-old male patient, with no known comorbidities, presented with complains of mildly itchy rash with fever of two-day duration. The rash started from neck and progressed over two days to involve entire trunk and proximal extremities [Figure 1]. He gave history of taking a tablet of ASA for headache, few hours before development of the rash and fever. He had taken the same drug earlier innumerable times in last 15 years, without any side effects; however, it was a 325 mg tablet this time. There was no history of any other drug intake, previous drug allergy, or insect bite. There was no family or personal history of Psoriasis.

Examination revealed numerous pinhead-sized pustules extensively distributed over upper arms, neck, trunk, and upper thighs over an erythematous background [Figure 2]. The mucous membranes, scalp, palms, and soles were spared. Nails and hair were normal.

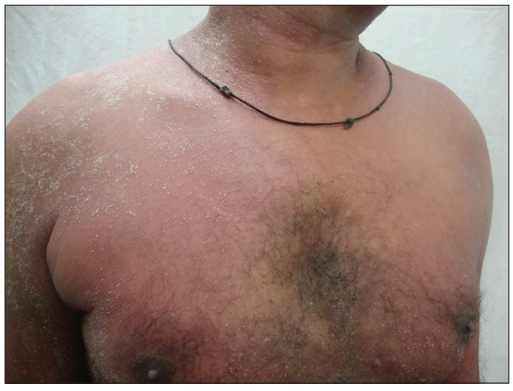

Figure 1: Pinhead sized pustules over neck, shoulder, and upper trunk

His Hb was 14.4 g%; TLC, 10 200/mm^3; DLC - N 78, L 18, M 02, E 02; Platelet count, 244 000/mm^3; and ESR, 30 mm/hr. Liver function tests and urinalysis were within normal limits. No organisms were seen on Gram's stain or isolated on culture of the pustules. Histopathological examination showed subcorneal pustules, a mixed neutrophil-rich interstitial and mid-dermal infiltrate. Tortuous and dilated blood vessels were absent [Figure 3]. The Naranjo Score was 5, which suggested a probable causal association for ASA in this case. The clinicopathological correlation ruled out Pustular Psoriasis, the most common differential diagnosis, in favor of AGEP. He was managed with tapering doses of oral steroids. He responded well and all lesions resolved within 10 days [Figure 4].

DISCUSSION

The use of ASA-like substances in medicine can be traced back to Hippocrates in 400BC, who advocated the use of willow bark extract to relieve the pain of childbirth.[4] ASA is a common analgesic used in the treatment of mild to moderate pain. It has anti-inflammatory and antipyretic properties and acts as an inhibitor of cyclo-oxygenase which results in the inhibition of the biosynthesis of prostaglandins. ASA also inhibits platelet aggregation and this property is the basis of its use in the prevention of arterial and venous thrombosis.

Despite being a common over the counter drug, ASA has its fair share of adverse drug reactions (ADRs).[5] Although most are very mild to be of much concern, rare severe ADRs which are mostly on long-term therapeutic consumption also occur, such as the occurrence of gastrointestinal ulcerations, nephrotoxicity, hepatotoxicity, and even renal cell cancer.[6]

Cutaneous drug reactions occur with a frequency of 1% to 8% and can be higher for certain classes of drugs.[7] The problem of ADRs is compounded by the fact that even rampantly used OTC drugs can lead to severe ADRs.

ADRs can range from mild morbilliform eruptions to more severe forms such as drug hypersensitivity syndrome, toxic epidermal necrolysis, anaphylaxis, and AGEP.

In 1980, Beylot *et al.* introduced the term "*pustuloses exanthematiques aigues generalizes"* which was reported in

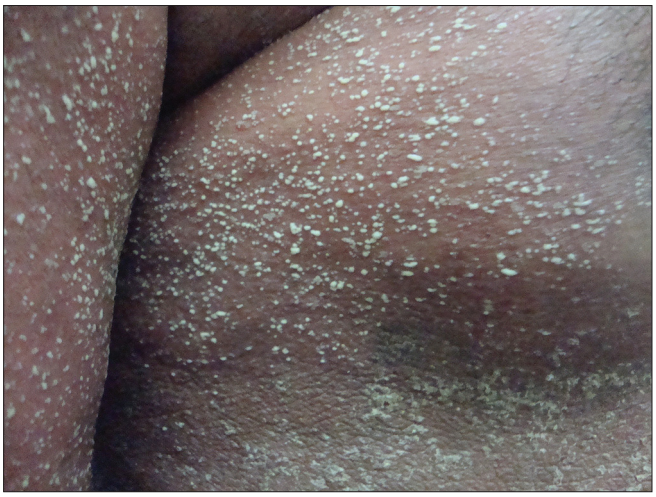

Figure 2: Pustules over an erythematous background

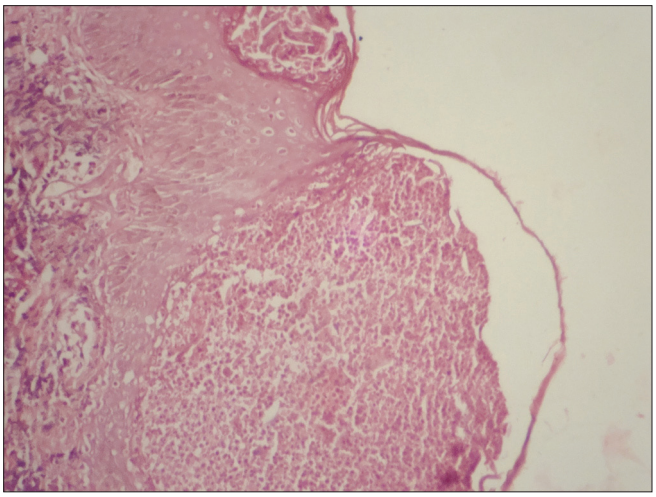

Figure 3: Subcorneal pustule in H & E section at 40x

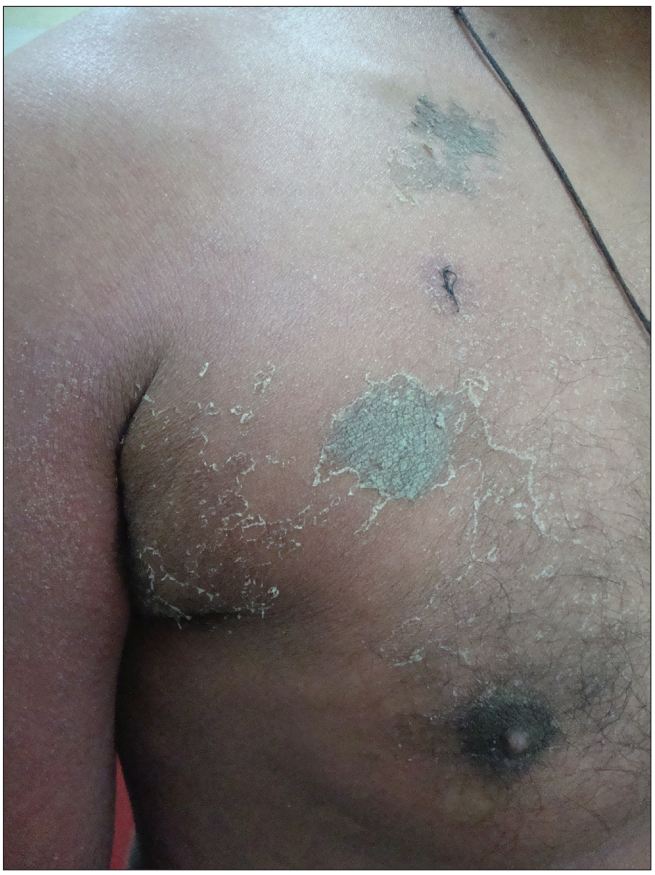

Figure 4: Pustules resolved with exfoliation

English literature as AGEP.[2] In 1991, Roujeau *et al.* described AGEP as an acute pustular dermatosis distinct from pustular psoriasis and stressed systemic drugs as its main cause.

Most cases of AGEP (90%) have been described in association with the intake of drugs, in particular antibacterial agents such as Aminopenicillins and Macrolides.[8] In a few cases, the etiology of AGEP appears to be a viral infection, ingestion of chromium picolinate, lacquer chicken, or a hypersensitivity reaction to mercury.[9]

The etiopathogenesis of AGEP is still obscure. Although initially it was considered a type III hypersensitivity reaction, today most believe it to be a type IV delayed hypersensitivity reaction.[9] Positive skin patch test results and short time between introduction of the drug and onset of the eruption support this hypothesis.

Britschgi *et al.*[10] suggested a T-cell-mediated mechanism wherein the drug presentation elicits a drug-specific CD4+ AND CD8+ T cell activation and release of neutrophil-attracting factors such as chemokine CXCL8, IL-4, IL-5, resulting in neutrophilic and eosinophilic rich inflammation. The granulocyte-macrophage colony-stimulating factor and interferon" are also secreted because of T-cell activation.[10,11] This was supported by positive patch tests and lymphocyte transformation tests.[11] The release of inflammatory cytokines such as interferon " may stimulate keratinocytes to secrete IL-8 and other factors. The cytotoxic T cells are involved in local tissue destruction and neutrophils create the sterile pustules.[11,12]

The diagnosis is mostly with clinicopathological correlation as there is no single definitive and confirmatory diagnostic test for AGEP. The first step in management of AGEP like any other drug reaction is to discontinue the offending drug. Although the condition is mostly self limiting, still topical as well as oral and injectable steroids are often prescribed.[1]

Clinicians need to be aware of this entity when dealing with pustular rash as this rare side effect of a very common drug is both, easy to miss and easy to manage.

REFERENCES

1. Momin SB, Del Rosso JQ, Michaels B, Mobini N. Acute generalized exanthematous pustulosis: An enigmatic drug-induced reaction. Cutis 2009;83:291-8.
2. Beylot C, Bioulac P, Doutre MS. Acute generalized exanthematic pustuloses (four cases). Ann Dermatol Venereol 1980; 107: 37–48.
3. Ballmer-Weber BK, Widmer M, Burg G. Acetylsalicylsaure-induzierte generalisierte Pustulose. Schweiz Med Wochenschr 1993;123:542-6.
4. Miner J, Hoffhines A. The discovery of aspirin's antithrombotic effects. Tex Heart Inst J 2007;34:179-86.
5. Boullata JI, McDonnell PJ, Oliva CD. Anaphylactic Reaction to a Dietary Supplement Containing Willow Bark. Ann Pharmacother 2003;37:832-5.
6. McCredie M, Pommer W, McLaughlin JK, Stewart JH, Lindblad P, Mandel JS, *et al*. International renal-cell cancer study II. Analgesics. Int J Cancer 1995;60:345-9.
7. Arroyo MP, Heller P, Pomeranz MK. Generalized pustules in a healthy woman. J Drugs Dermatol 2002;1:63-5.
8. Roujeau JC. Neutrophilic drug eruption. Clin Dermatol 2000;18:331-7.
9. Machet L, Martin L, Vaillant L. Acute generalized exanthematic pustulosis. Ann Dermatol Venereol 2001;128:73-9.
10. Britschgi M, Steiner UC, Schmid S, Depta JP, Senti G, Bircher A, *et al*. T-cell involvement in drug-induced acute generalized exanthematous pustulosis. J Clin Invest 2001;107:1433-41.
11. Britschgi M, Pichler WJ. Acute generalized exanthematous pustulosis: A clue to neutrophil-mediated inflammatory processes orchestrated by T cells. Curr Opin Allergy Clin Immunol 2002;2:325-31.
12. Beltraminelli HS, Lerch M, Arnold A, Bircher AJ, Haeusermann P. Acute generalized exanthematous pustulosis induced by the antifungal terbinafine: Case report and review of the literature. Br J Dermatol 2005;152:780-3.

Cite this article as: Bahuguna A. Acute generalized exanthematous pustulosis: A rare side effect of a common over-the-counter drug, Acetylsalicylic acid. Indian Dermatol Online J 2013;4:231-3.

Source of Support: Nil, **Conflict of Interest:** None declared.