

CASE REPORT

A Case of Celecoxib Induced Acute Generalized Exanthematous Pustulosis

Hyun-Tae Shin, M.D., Se-Won Park, M.D., Kyung-Tae Lee, M.D., Hae-Young Park, M.D., Ji-Hye Park, M.D., Dong-Youn Lee, M.D., Ph.D., Joo-Heung Lee, M.D., Ph.D., Jun-Mo Yang, M.D., Ph.D., Eil-Soo Lee, M.D., Ph.D.

Department of Dermatology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Acute generalized exanthematous pustulosis (AGEP) is manifested by rapid development of many sterile, non-follicular pustules on a background of edematous erythema. More than 90 percent of AGEP are induced by medication, mostly antibiotics. Drug patch test can be helpful in the diagnosis of AGEP. This paper reports the first case of celecoxib-induced AGEP confirmed by patch test in Korean literature. (*Ann Dermatol* 23(S3) S380~S382, 2011)

-Keywords-

Acute generalized exanthematous pustulosis, Celecoxib, Patch test

INTRODUCTION

Acute generalized exanthematous pustulosis (AGEP) is an uncommon eruption characterized by acute occurrence of many non-follicular sterile pustules on edematous erythema. More than 90 percent of AGEP are induced by medication and most of them are antibiotics¹. Other etiologic agents include viral infection, mercury and lacquer^{2,3}. Celecoxib is a non-steroidal anti-inflammatory

drug which inhibits cyclooxygenase-2 (COX-2) and prescribed for control of pain. In English literature, three cases of celecoxib induced AGEP had been reported⁴⁻⁶. We report a first case of AGEP induced by celecoxib confirmed by patch test in Korean literature.

CASE REPORT

A 53-year-old Korean woman without any history of allergy and psoriasis presented with disseminated pustules on the face and trunk. The patient had fever and itching. From two weeks before visiting our hospital, she started to take celecoxib for her shoulder pain. Ten days after taking medication, erythematous skin eruption with high fever had developed, and she stopped taking celecoxib. After two days, numerous small pustules developed in these erythematous lesions. Physical examination revealed many tiny non-follicular pustules on the face (Fig. 1A) and trunk (Fig. 1B). The skin lesion was accompanied by leukocytosis ($10.17 \times 10^3/\mu\text{l}$) with elevated neutrophil counts ($8.39 \times 10^3/\text{Ml}$) and C-reactive protein levels (7.32 mg/dl). No microorganism was identified in blood cultures and pustule cultures. Skin biopsy performed on the patient's back revealed subconial pustules, spongiosis in the epidermis, papillary dermal edema and perivascular infiltration of lymphocytes, neutrophils and some eosinophils on papillary dermis (Fig. 2). On admission, the patient was treated with methylprednisolone 40 mg twice a day and improved within seven days. AGEP induced by celecoxib was the most likely suspect. After three months, a drug patch test was performed with celecoxib diluted at 5 percent in normal saline and in petrolatum. To determine whether the constituents of the capsule caused AGEP, constituents of the capsule were diluted at 5 percent in normal saline and in petrolatum; these were also included

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Corresponding author: Dong-Youn Lee, M.D., Ph.D., Department of Dermatology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-dong, Gangnam-gu, Seoul 135-710, Korea. Tel: 82-2-3410-3543, Fax: 82-2-3410-386, E-mail: dylee@skku.edu

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Fig. 1. (A) Numerous tiny non-follicular pustules on the face. (B) A hundred of non-follicular pustules on the back.

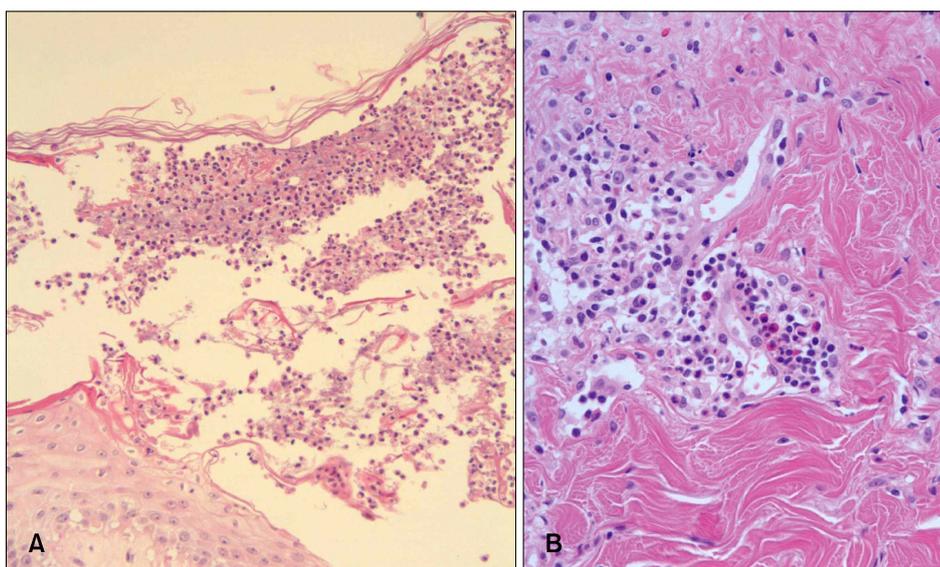


Fig. 2. (A) Subcorneal pustules in the epidermis (H&E, $\times 200$). (B) Perivascular infiltration of lymphocytes and eosinophils in the upper dermis (H&E, $\times 400$).

in patch test. At the same time, several other antibiotics and non-steroidal anti-inflammatory drugs were tested, but sulfonamide drugs were not included. To rule out false-positive reactions, two healthy persons were also tested. The patient showed strong vesicular reaction to celecoxib diluted at 5 percent in normal saline (Fig. 3) and erythematous reaction to celecoxib diluted at 5 percent in petrolatum. The result for other drugs was negative. It was concluded that celecoxib was the cause of AGEF.

DISCUSSION

When Baker and Ryan⁷ reported 104 cases of pustular psoriasis in 1968, they found five patients who had no

history of psoriasis, rapidly progressing and with quick improvement. In 1980 Beylot et al.⁸ introduced the term AGEF.

AGEF is a rare and severe pustular reaction of drug eruption characterized by acute, extensive, non-follicular pustules, accompanied by high fever and leukocytosis. Mild oral mucous membrane involvement may occur in approximately 20 percent of AGEF. Pustules resolve spontaneously within a few (~ 4 to 10) days and are followed by postpustular, pin-point desquamation. Undoubtedly, AGEF is improved by discontinuing the culprit medication and antibiotics are unnecessary unless there are signs of infection. Because AGEF is a self-limiting disease, systemic steroid treatment is not always required¹.



Fig. 3. Strong vesicular reaction to celecoxib diluted at 5% in normal saline after 48 hours.

Currently, several mechanisms of AGEP have been proposed. Britschgi et al.⁴ suggested the involvement of a drug-specific T cell, which produces interleukin (IL)-8 and IL-5. The other mechanisms are the formation of antigen-antibody complex by viral infection or medication that causes activating of the complement system².

Drug patch tests can be helpful in the defining the cause of AGEP⁹. Based on the fact that the patch test shows positive results, AGEP is considered as a delayed type of hypersensitivity reaction. However, the usefulness of the drug patch test is dependent on the tested drug. Because of the possibility of false negative results, the drug patch test should be performed with high concentrations of the commercialized form of the medication. Thirty percent is the maximum concentration possible to get a uniform dilution in petrolatum or in water. In drug patch tests for celecoxib with concentration higher than 10 percent, irritant reactions were reported⁹. To avoid false positive results by irritation, the patch test was performed with celecoxib diluted at 5 percent in normal saline and petrolatum and two healthy persons were also tested. The patient showed positive result and the two healthy persons showed negative results.

Celecoxib, a selective COX-2 inhibitor, is a non-steroidal anti-inflammatory drug for the reduction of pain. A number of skin adverse effects of celecoxib have been reported, including urticaria, anaphylaxis, angioedema, ery-

thema multiforme, fixed drug eruption, vasculitis, Stevens-Johnson syndrome, sweet's syndrome, toxic epidermal necrolysis, and AGEP⁵. Since celecoxib contains a sulfonamide substituent, it has the potential for cross-reacting with other sulfonamide antibiotics. However, some authors disagree as to the presence of structural differences between sulfonamide antibiotics with aromatic amines and other sulfonamide containing drugs with non-aromatic amines^{5,6}. In the case, the cross reaction had not been evaluated.

To the authors' knowledge, this is the first report of celecoxib-induced AGEP confirmed by patch test in Korean literature. Drug patch tests can be helpful in the defining the cause of AGEP, but there is no standardization for the test. Therefore, a sufficient literature review is essential for drug patch tests.

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