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Case Report / *Olgu Sunumu*

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A Case of Erythema Multiforme Associated with Pustules: Coexistence of Erythema Multiforme Minor and Acute Generalized Exanthamatous Pustulosis

Püstüllerle Birliktelik Gösteren Bir Eritema Multiforme Olgusu: Eritema Multiforme Minör ve Akut Jeneralize Ekzantematöz Püstüloz Birlikteliği

Abstract

Adverse cutaneous drug reactions (ACDRs) can mimic a variety of dermatologic diseases, causing confusion and additional work-up for differential diagnoses. In this report, a case who admitted with non-follicular pustules with extensive targetoid lesions during follow-up is presented. In this case, erythema multiforme (EM)-like lesions were predominant and pustules that were concordant with acute generalized exanthematous pustulosis were thought to be triggered after drug intake. ACDRs can mimic several different infectious and inflammatory entities, and they should be kept in mind in cases accompanied by EM-like lesions with pustules. To our knowledge, EM-like lesions with a small number of pustules are first described in the literature in this case report.

Keywords: Erythema multiforme, acute generalized exanthematous pustulosis, adverse cutaneous drug reaction

Öz

Advers kutanöz ilaç reaksiyonları [adverse cutaneous drug reactions (ACDR)] birçok dermatolojik hastalığı taklit ederek karışıklığa ve ayırıcı tanı için fazladan tetkik yapılmasına neden olabilmektedir. Bu sunumda yaygın targetoid lezyonlar ile birlikte takipte nonfolliküler püstüller ile başvuran bir olgu tanımlanmaktadır. Bu olguda eritema multiforme (EM) benzeri lezyonların ağırlıkta olduğu ve akut jeneralize ekzantematöz püstülozis ile uyumlu olan püstüllerin ilaç alımı sonrası tetiklendiği düşünülmektedir. ACDR'ler çeşitli enfeksiyöz ve enflamatuvar antiteleri taklit edebilirler ve olgularda EM benzeri lezyonlar ve püstüllerin birlikteliğinde ilaç reaksiyonları akla getirilmelidir. Bildiğimiz kadarı ile az sayıda püstül ile birlikte EM benzeri lezyonlar ilk olarak sunulan olguda tanımlanmaktadır.

Anahtar kelimeler: Eritema multiforme, akut jeneralize ekzantematöz püstülozis, advers kutanöz ilaç reaksiyonu

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Introduction

Adverse cutaneous drug reaction (ACDR) is used as a term to define all of the side effects of a drug or its metabolite on skin and its appendages. Drug reactions can mimic a variety of dermatoses with different clinical appereances (1). In this report a patient who presented with extensive erythema multiforme (EM) like lesions and demonstrated non-follicular pustules on follow-up induced after multiple drug intake is described.

Case report

A fourty-three-year-old female patient admitted to outpatient clinic of dermatology for widespread skin eruption that started a few days ago. Medical history revealed that a treatment of amoxicilline/

clavulanic acid, etodolac and acemetacin for an upper respiratory tract infection was given to the patient 12 days ago. She did not have a history of drug reaction or allergy. Elevated targetoid erythematous plaques that extensively distributed on abdomen, back and extremities were noted on dermatologic examination (Figure 1). Conjunctivas, oral and genital mucosa were normal. She had accompanying fever (38.5 °C) and nausea. Depending on drug history and targetoid extensive lesions, the patient was hospitalized with a prediagnosis of EM/EM-like drug eruption. Differential diagnoses included generalized granuloma annulare and subacute cutaneous lupus erythematosus. On laboratory examination, the patient had a high leukocyte count [18.26 10x3/µL (4.4-11.3) with neutrophilia 89.1% (45.5-73.1%)], remaining parameters were unremarkable. Eosinophilia was not present on performed blood smears.

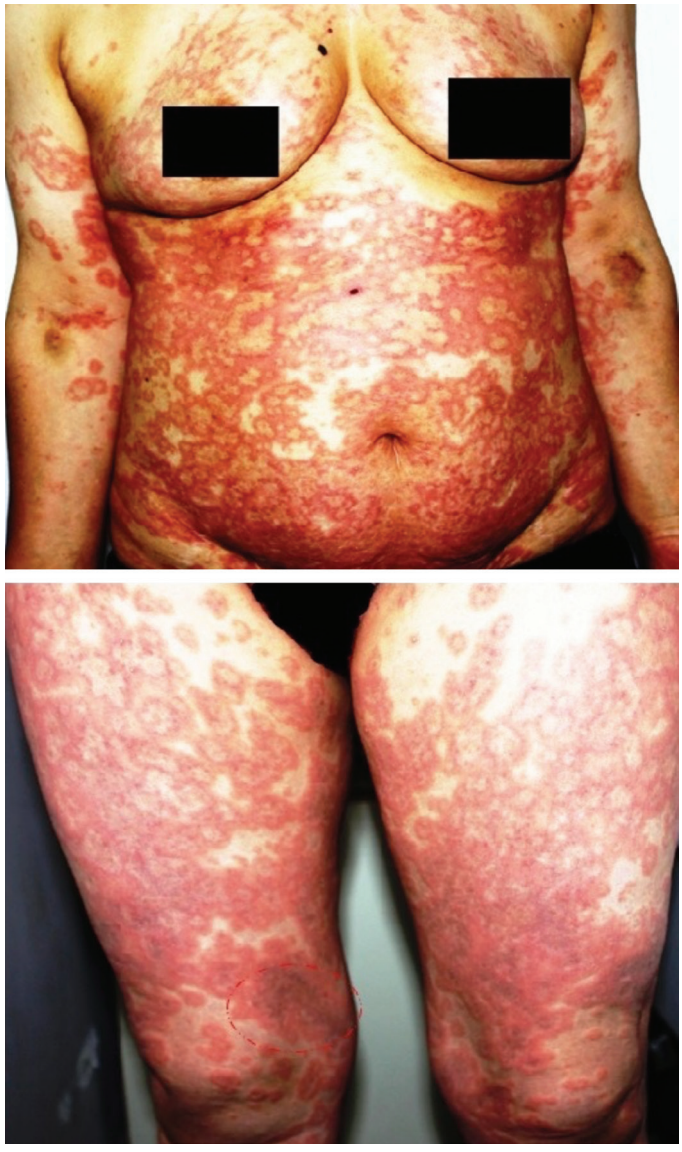

Figure 1. Widespread erythematous targetoid plaques on the trunk and extremities. Red circle: atypic target-targetoid lesion

Antinuclear antibody, cryoglobulin, anti-cardiolipin antibodies were negative and serum immunoglobulin, rheumatoid factor and complement levels were within normal range. Bacterial and fungal cultures were negative. At the third day of hospitalization, the patient developed non-follicular pustules at the edges of edematous targetoid plaques (Figure 2). Acute generalized exanthematous pustulosis (AGEP) and subcorneal pustular dermatosis were included to the differential diagnoses. A biopsy was performed from one of the elevated erythematous plaques. On histopathologic examination, superficial perivascular dermatitis, interface vacuolar degeneration of basal membrane and spongiosis with intraepidermal vesicle formation were observed and interpreted as EM (Figure 3). According to the clinical presentation consisting of EM like lesions with pustules induced after drug intake, final diagnosis was made as EM and AGEP overlap. Short term topical steroid (beclomethasone dipropionate cream twice/day) and systemic anti-histamine (hydroxyzine tablet 3x1 p.o.) therapy was commenced after immediate drug withdrawal. The patient had full recovery in clinical and laboratory aspects in 10 days with this treatment. Informed consent was taken from the patient.

Discussion

EM is an acute, self limited disease which can occur in relapsing episodes. Main triggering factors are assumed

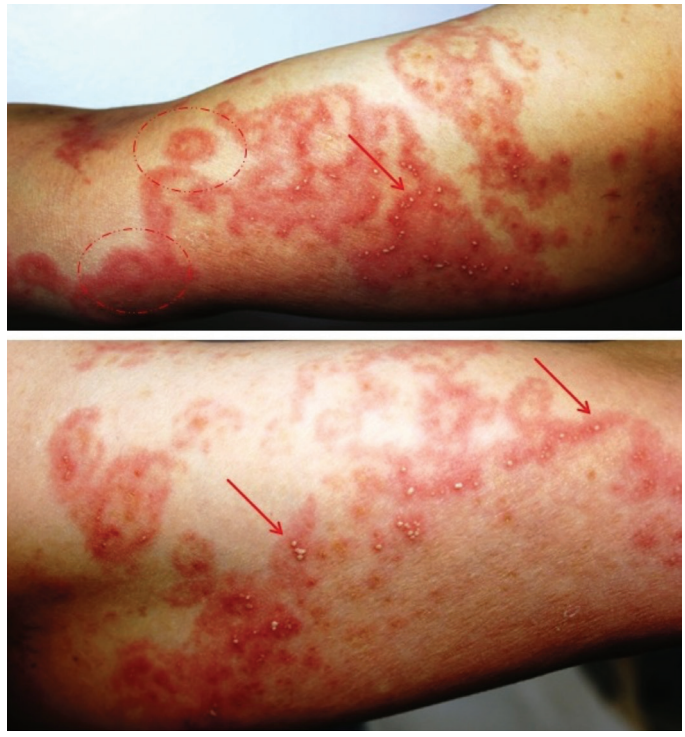

Figure 2. Extensive coalescing annular and targetoid plaques with non-follicular pustules at the edges. Red circle: atypic target-targetoid lesion. Red arrows: pustule formation

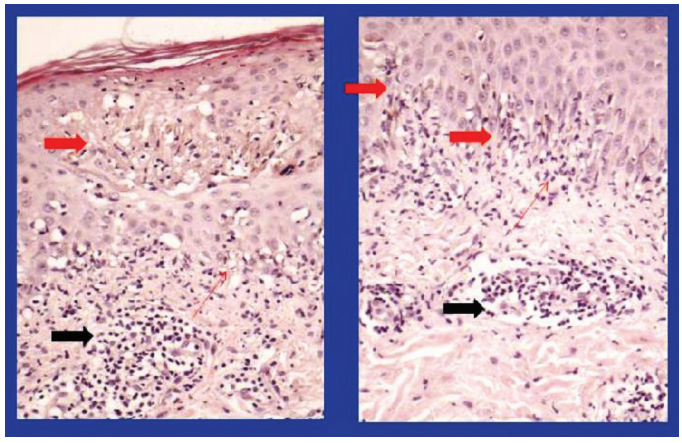

Figure 3. H&E stain x40 magnification. bold red arrow; spongiosis and lymhocyte exocytosis in the epidermis, light red arrow; vacuolar degeneration at the basal membrane, black arrow; superficial perivascular mononuclear cell infiltration

to be herpes simplex viral infections and drugs which initiate type IV hypersensitivity reaction in predisposed individuals (1,2). Approximately 50% of EM cases are considered to be induced by drugs (2). Most common triggering drugs are sulfanomides, anticonvulsant drugs; barbiturates, carbamazepine, phenytoin, antibiotics; ampiciline as in our case, tetracyclines, cephalosporine, trimetoprime+sulphametoksazole, rifampicine, isoniacide, and nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirine, phenylbutazone and piroxicam (1,2). EM-like drug eruptions are induced by the abnormal metabolization of offending drug. Individuals who have different genetic features for drug metabolism show deficiency in detoxification of reactive drug metabolites. These metabolites are believed to act as haptens and induce immunologic reactions binding to epithelial proteins (1,2). EM is generally subdivided into minor and major forms according to the mucosal involvement, distribution and severity of the disease. EM minor cases are due to recent herpes virus infections where characteristic acral target lesions appear. EM major cases are generally due to preceding drug intake and can present with target and/or targetoid lesions. At disease onset, erythematous papules appear and transform into pathognomonic target or so called iris lesions which consists of 3 different shades of circles where the darkest part is located at the center. Drug induced EM is characterised with atypical or targetoid lesions which may not demonstrate this full configuration but resemble it by its annular or ring shaped apperance. AGEP which is later recognized as a distinct antity is characterized with non-follicular sterile pustules generally induced after drug intake or infections (3). AGEP can also present with purpura, oedema, bullae and mucosal erosions. In severe forms, it is also known to overlap with toxic epidermal necrolysis (1-4). To our knowledge only one case was described in the literature who presented with EM major and AGEP (3). The clinics of this case was dominated with lesions concordant with AGEP but also rare targetoid lesion were observed leading to a suspicion of AGEP-EM major overlap.

Amoxicilline/clavulanic acid and NSAID usage induced atypical target/targetoid lesions which were histopathologically consistent with EM in our case. The drugs also induced fever, leukocytosis and non-follicular pustules concordant with AGEP simultaneously in the same patient. Although AGEP is known to overlap with other ACDRs, predominant EM like lesions with few pustules was first to be defined in our case. By the presentation of this case, we would like to remind that ACDRs may overlap with each other mimicking several different infectious and inflammatory diseases. The rapid improvement of our patient with drug withdrawal and treatment consisting of systemic antihistamines and topical corticosteroids supported the diagnosis of ACDR. Although the exact inciting agent of ACDR was not able to be defined because of multiple drug intake of the patient, further investigations including drug patch testing can be performed for the identification of the causative drug. For persistant cases with targetoid lesions accompanied with pustules lineer IgA dermatosis, subcorneal pustular dermatose, IgA pemphigus and other neutrophilic dermatoses should be kept in mind. Such cases should also be evaluated by laboratory parameters, cultures for bacteriologic investigations and histopathologic examination including "immunofloresence" studies (1,3,5).

Hypersensitivity reactions to antibiotics and NSAIDs are commonly reported. Nonimmediate hypersensitivity reactions are classically known as maculopapular exanthems in which specific T lymphocytes may play a role (6). In selected cases, skin drug testing including patch tests, intradermal tests and drug provocation tests can be used for diagnosis. Nonimmediate reactions are generally assessed by delayed-reading skin tests, patch tests, and drug provocation tests and these tests have been well validated mainly for β-lactam antibiotics but less for other classes of antibiotics, NSAIDs and anticonvulsant drugs (6,7).

Ethics

Informed Consent: It was a taken from the patient.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.D., E.K., A.K., Concept: S.D., Design: S.D., Data Collection or Processing: S.D., E.K., Analysis or Interpretation: S.D., E.K, A.K., F.A., Literature Search: S.D., E.K., A.K., F.A., Writing: S.D., E.K., A.K., F.A.

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