Case Report
JCAM

Low Dose Methotrexate Induced Perilesional Bullous Erythema in Plaque Type Psoriasis

Plak Tip Psöriazisde Düşük Doz Metotreksat ile İndüklenen Perilezyonel Büllöz Eritem

Perilesional Bullous Erythema

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Özet

Kemoterapi ile indüklenen büllöz tip akral eritem, metotreksat ile ve daha sıklıkla sitozin arabinozid ile bildirilmiştir. Ancak metotreksat ile ilişkili perilezyonel büllöz eritem daha önce bildirilmemiştir. Burada, biyopsi ile kanıtlanmış jeneralize plak tip psöriazisi olan 64 yaşında bir erkek hastada 15 mg/hafta dozda metotreksat tedavisi sonrası büllöz perilezyonel eritem gelişimi sunuldu. Hastada tedavinin ilk 3 günü içerisinde psöriaziform plakları çevreleyen simetrik, iyi sınırlı, ağrılı, eritemli perilezyonel büllöz lezyonlar gelişti. Lezyonlar güçlü topikal kortikosteroidlere ve ıslak pansumanlara yanıtsız idi. Üç hafta sonra topikal kortikosteroidler kesildi ve metotreksat dozu 10 mg/haftaya azaltıldı. Büllöz perilezyonel eritemin devamı nedeniyle, anti-inflamatuar yanıt için kına ekstresi "Lawsonia inermis" içeren bir topikal bitkisel tedavi başlandı. Lezyonlar giderek iyileşti ve iki hafta içerisinde rezidüel hiperpigmentasyon ile tama yakın geriledi. Metotreksat ile tedavi olan psöriatik olgularda, nadir olarak perilezyonel büllöz eritemin görülebileceği ve metotreksat tedavisinin kesilmesinin gerek olmadığını düşünmekteyiz.

Anahtar Kelimeler

Büllöz Lezyon; Eritem; Lawsonia Bitkisi; Metotreksat; Psöriazis

Abstract

The bullous variant of chemotherapy-induced acral erythema has been reported with methotrexate and more frequently cytosine arabinoside. However, perilesional bullous erythema in association with methotrexate hasn't been reported before. Herein, we presented a 64-year-old male patient, a biopsy proven case of generalized plaque psoriasis, who developed a bullous perilesional erythema after a single oral dose of 15 mg/week methotrexate. The patient developed symmetrical, well-demarcated, painful, erythematous perilesional bullous lesions surrounding these psoriasiform plaques within 3 days of receiving the medication. The lesions were unresponsive to the potent topical corticosteroids and wet dressings. After 3 weeks the topical corticosteroids were discontinued and methotrexate dose was reduced to 10 mg/week. As a result of the permanency of the bullous perilesional erythema, a topical herbal therapy including a henna extract "Lawsonia inermis" was started for an anti-inflammatory response. The lesions gradually improved and resolved almost completely with residual hyperpigmentation within two weeks. We believe that, perilesional bullous erythema may be seen rarely in psoriatic patients treated with methotrexate and there is no need for discontinuation of methotrexate therapy.

Keywords

Bullous Lesion; Erythema; Lawsonia Plant; Methotrexate; Psoriasis

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Introduction

Chemotherapy-induced acral erythema (CIAE) is characterized with a painful erythema of the palms and soles which occurs following chemotherapy due to cytarabine, paclitaxel, mercaptopurine, doxorubicin and fluorouracil [1]. The bullous variant had been reported in relation to methotrexate (MTX) and more frequently cytosine arabinoside treatment [1-3]. The reaction usually begins with palmoplantar dysesthesia, causing symmetrical erythema with well-demarcated borders and blistering and eventual desquamation that remains limited to the palms and soles [1,4]. To the best of our knowledge, up to now almost fifteen case reports of bullous acral erythema (AE) due to MTX have been published, but this is the first case of MTX induced perilesional bullous erythema [2,3,5-7].

Case Report

A 64-year-old man with a biopsy proven case of plaque type psoriasis for 15 years was unresponsive to topical treatments of corticosteroids, calcipotriol and PUVA. Therefore oral methotrexate 15 mg/week, with 5 mg of folinic acid per day was prescribed after the routine blood examinations. His other medical and drug history were unremarkable. On the dermatological examination; several demarcated, erythematous psoriasiform squamous plaques were present on both shins and elbows. No other chemotherapeutic or immunosuppressive agents were additionally administered. The patient developed symmetrical, well-demarcated, painful, erythematous perilesional bullous lesions surrounding these psoriasiform plaques within 3 days of receiving the medication (Figure 1). His palms and soles were



Figure 1. Well-demarcated, painful, erythematous perilesional bullous lesions surrounding these psoriasiform plaques within 3 days of receiving the medication.

spared and no mucosal lesions were noted. His blood count, liver and kidney function tests and urine analysis were all normal. No systemic side effects were observed.

The histopathological examination of the punch biopsy material taken from the bullous lesion showed acantholysis, subepidermal bullae with keratinocyte necrosis, apoptosis, vacuolar changes along the basal cell layer and lymphocytic inflammatory infiltration in the upper dermis. Direct immunofluorescent staining was negative for C3 and Ig G. Serum C3 and Ig G antibodies detected by indirect immunofluorescent study were also negative. He was diagnosed with MTX induced perilesional bullous erythema. Written informed consent was obtained from the patient for publication of this brief case report and accompanying images.

The patient was first treated with potent topical corticosteroids and wet dressings without any response for 3 weeks intermittently. After one month the topical corticosteroids were discontinued and methotrexate dose was reduced to 10 mg/week and a topical henna extract (Kapederm® cream) 6 times a day was started for an anti-inflammatory response. The lesions gradually improved and resolved almost completely with residual hyperpigmentation within two weeks (Figure 2). No cessation of



Figure 2. The lesions gradually improved and almost resolved completely within two weeks with topical herbal therapy including a henna extract "Lawsonia inermis".

the treatment was required. His pain completely resolved and no recurrence was noted in 10 months follow up.

Discussion

On the contrary that CIAE is also called as a "palmoplantar erythrodysesthesia syndrome" or "chemotherapy-induced syringosquamous metaplasia" caused by the toxicity of the chemotherapeutic agents concentrated in the eccrine sweat glands, the sparing of the palmoplantar areas was very unusual in this case [4]. This reminds us another possible etiopathogenic mechanism like the presence of an associated local inflammatory receptor in the psoriatic plaque lesions that links the systemic toxic agent causing a bullous reaction. But on this occasion, we should have expected more severe cases of chemotherapy induced bullous erythema after the intralesional injection of MTX in plaque type psoriasis. We believe that the present new entity may be re-named as not CIAE but "chemotherapy induced perilesional bullous erythema in an erythema multiforme like pattern". However, furthermore similar cases are also needed to be investigated. In this case we also excluded the diagnosis of autoimmune bullous diseases, as a result of the lack of the histopathological findings and negativity of the direct and indirect immunofluorescent tests.

In the prior reported cases of MTX induced bullous AE including this case the lesions appeared rapidly within the first 24-72 hours [2]. It is usually dose dependent and mostly appears with bolus high-dose infusions or long-term low-dose infusions [4]. As we know, CIAE due to oral, low dose (15 mg/week) and short-term MTX treatment was very unusual.

The patients with CIAE usually recover without complications [1,4]. Response to dose reduction is expected but not to folinic acid. Interestingly, our patient was almost completely ameliorated with topical use of henna in two weeks without cessation of the MTX therapy. "Henna" is a dye extracted from the dried leaves and skin of branches of a bush-like plant from lythracea

family called “Lawsonia inermis” which is used in eastern cultures and in rural areas of Turkey. So far anti-microbial, anti-inflammatory, anti-oxidant and immunomodulatory effects of henna have been reported in rats [8].

In a previous case series including 10 patients with hand and foot syndrome (HFS) due to capacitabine chemotherapy remarkable and rapid clinical improvements were also reported after using topical henna like in our case [9]. Of those patients with Grade 3 HFS, in four; complete response, in two; regression to grade 1 level were reported. The complaints of the other four patients with grade 2 HFS were also fully recovered after the first week of outpatient visit [9]. In an animal model, it was also demonstrated that “Lawsonia inermis” extracts are capable of promoting wound healing activity [10]. Enhanced wound contraction, tensile strength, increased hydroxyproline content in histological observations suggest that “Lawsonia inermis” has potential in the management of wound healing and these invite further studies. The sudden dramatic improvement of this patient with topical henna suggests us that it might act as an anti-inflammatory agent.

In conclusion, the clinical improvement in this case might be a spontaneous resolution seen in CIAE reactions, or it might be due to elimination of another unknown causative agent. The reduction of the MTX dose from 15 to 10 mg/week might also play a role in improvement of the lesions in this case. We also approved to emphasize that the improvement of the lesions suggests that topical henna might act as an anti-inflammatory agent.

We believe that, perilesional bullous erythema may be seen rarely in psoriatic patients treated with MTX and there is no need for discontinuation of MTX therapy.

Competing interests

The authors declare that they have no competing interests.

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