

# Fixed drug eruption induced by ibuprofen gel

## İbuprofen jel ile indüklenen fiks ilaç erüpsiyonu

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### ABSTRACT

Fixed drug eruption is a common cutaneous reaction which may be seen in reaction to several medications. For the etiological evaluation of fixed drug eruption, topical provocation with patch testing on sites of previous lesions is frequently applied. Bullous fixed drug eruption mimicking toxic epidermal necrolysis due to a topical agent has not been previously reported. Here we describe a case of generalized bullous fixed drug eruption due to ibuprofen gel.

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**Key words:** Fixed drug eruption, ibuprofen gel, toxic epidermal necrolysis

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### INTRODUCTION

Fixed drug eruption (FDE) is a distinctive cutaneous eruption characterized by solitary or multiple, round/and or oval, edematous, dusky-red patches, accompanied by burning and/or itching. Some cases may show the formation of vesicles, bullae and denuded skin which may be confused with erythema multiforme, Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)<sup>[1-3]</sup>. Skin reactions

### ÖZET

Fiks ilaç erüpsiyonu çeşitli ilaçlara bağlı olarak ortaya çıkan sık görülen bir ilaç reaksiyonudur. Fiks ilaç erüpsiyonunun etyolojik değerlendirilmesinde daha önceki lezyonların gelişim yerlerine uyan bölgelerde yama testi ile provokasyon sıklıkla yapılmaktadır. Bugüne kadar topikal bir ilaca bağlı olarak ortaya çıkan ve toksik epidermal nekrolizisi taklit eden fiks ilaç erüpsiyonu bildirilmemiştir. Burada ibuprofen jele bağlı jeneralize büllöz ilaç reaksiyonu gelişen bir olgu sunulmaktadır.

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**Anahtar kelimeler:** Fiks ilaç erüpsiyonu, ibuprofen jel, toksik epidermal nekroliz

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to ibuprofen include urticaria, angioedema, contact dermatitis, and photosensitivity<sup>[4-6]</sup>. Potentially severe drug reactions such as TEN has also been reported in association with ibuprofen<sup>[7,8]</sup>. Kanwar et al. analysed 98 cases of FDE who were subjected to oral provocation test<sup>[6]</sup>. In only six of them ibuprofen was confirmed as the responsible drug. Although a number of drugs have been implicated in the development of FDE, there is no previous observation of bullous FDE induced by ibuprofen gel.

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## CASE REPORT

A 77-year-old woman presented with a two day history of widespread, tender, scattered blisters on erythematous-purplish base. The patient stated that lesions had appeared within five hours of applying topical ibuprofen on her knees with a sensation of burning (Figure 1). Shortly after the development of the skin lesions, similar ones had occurred symmetrically on her extremities, genital and intertriginous sites with bulla formation. She had applied ibuprofen gel intermittently during the last one year with no side effects. The patient denied taking any other drug in the preceding days. She had a previous history of a generalized maculopapular drug eruption after taking naproxen sodium six years ago. The patient stated that she did not use oral ibuprofen, previously. Physical examination revealed extensive purplish-livid patches covering almost 30% of the total body surface. Multiple well-circumscribed patches studded with flaccid bullae were observed on the left side of the face, arms, dorsal aspects of the feet, lower parts of the breasts, lower abdomen, inguinal folds and gluteal regions (Figure 2). Pseudo-Nikolsky's sign was positive. The mucous membranes were not involved. Histopathological examination of a biopsy specimen showed full-thickness necrosis of epidermal keratinocytes with subepidermal clefting. There was a sparse superficial perivascular mixed inflammatory infiltrate containing few eosinophils and lymphocytes. The



Figure 1. Symmetrical well-circumscribed erythematous-purplish patches on the knees.

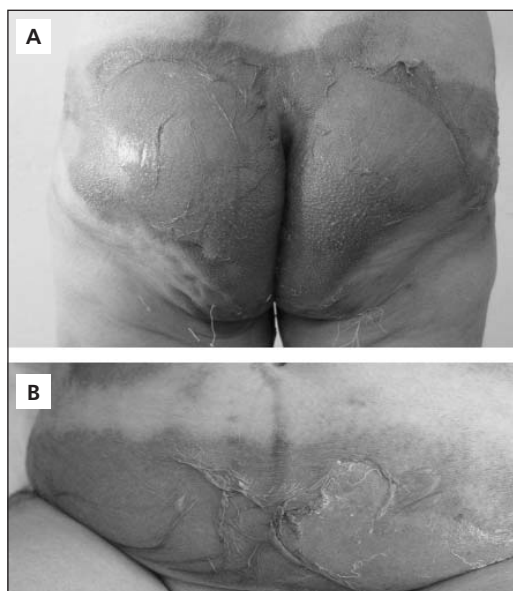


Figure 2. Large erythematous-purplish patches with wide-spread bullae and epidermal sloughing on the abdominal and gluteal regions.

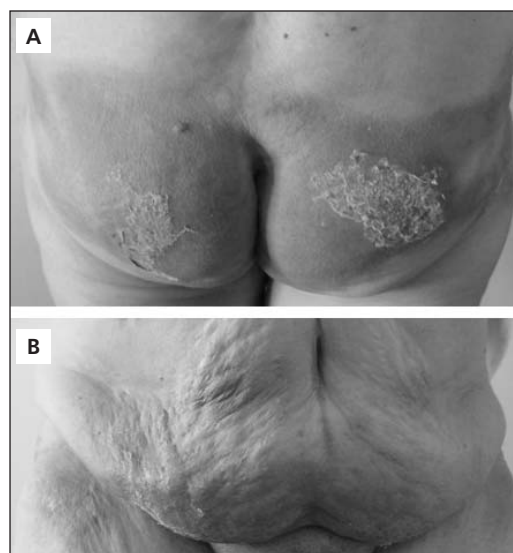


Figure 3. Re-epithelisation of the lesions located on the abdominal and gluteal regions after one week of systemic corticosteroid therapy.

patient was diagnosed as having ibuprofen-induced generalized bullous FDE. We initiated oral prednisolone (1 mg/kg/day) therapy. The bullae, and eroded areas disappeared after one week, leaving a dusky-brown residual hyperpigmentation (Figure 3).

## DISCUSSION

FDE due to ibuprofen has been rarely described. FDE constitutes 10% of all adverse drug reactions. The main presentation of FDE consists of sharply defined, rounded, large, purplish-livid patches. A diagnostic hallmark is the reappearance of the lesions over the previously affected sites, when the offending drug is re-used<sup>[9]</sup>. Vesicles and hemorrhagic bullae with crusting may also develop. Generalized bullous FDE is rare, but may be severe. Distribution of the lesions in bullous FDE is often symmetrical with a predilection for the extremities, genital and intertriginous sites<sup>[10]</sup>.

The degree of sensitization of the individual to a particular drug determines the first development of FDE. This incubation period may run from a few weeks to several years. Our patient has been applying ibuprofen gel off and on for the past one year without any reaction. The interval between last and previous administration was one month. The lesions had appeared within five hours after applying ibuprofen gel on her knees. Within hours after the occurrence of the lesions on the exposure site, generalized bullous lesions developed on exposed and non-exposed sites of the body.

Generalized bullous FDE may be clinically misdiagnosed as SJS or TEN<sup>[2,3,10]</sup>. Histopathological differentiation may also be challenging since all three disease may show epidermal changes varying from a few scattered necrotic keratinocytes to full-thickness epidermal necrosis. In FDE, a mixed inflammatory infiltrate containing not only lymphocytes but also neutrophils and eosinophils is present around both the superficial and deep plexus. In SJS and TEN, the infiltrate is mainly lymphohistiocytic and tends to be located around the superficial plexus<sup>[3,11]</sup>. However mucosal involvement is hallmark of TEN and the disease presents with marked constitutional symptoms with lesions covering more than 30% of the body surface. In our patient, although the dermatopathologic findings were more compatible with TEN, sparing of mucosal sites, mild constitutional symptoms and lesions which covered less than 30%

of body surface, led us to consider generalized bullous FDE as the diagnosis. The distribution of the lesions was also at the common sites of bullous FDE and the rapid healing of the lesions with marked residual hyperpigmentation was also consistent with bullous FDE.

This is the first report of topical ibuprofen induced generalized bullous FDE. Widespread distribution of the lesions can be explained by potential systemic absorption of ibuprofen gel. Although patch testing could have provided sufficient proof of ibuprofen gel being the culprit agent, the value of patch testing in FDE is not well established and taking into account the severity of the lesions, we considered it unethical to perform patch testing.

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