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### Authors

Lai, Olivia  
Hsu, Sylvia

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**Letter**

**Fixed drug eruption related to fluconazole**

Olivia Lai<sup>1</sup>, Sylvia Hsu<sup>2</sup>

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<sup>1</sup>USC Keck School of Medicine

<sup>2</sup>Baylor College of Medicine

**Correspondence:**

Sylvia Hsu  
Baylor College of Medicine  
shsu@bcm.edu

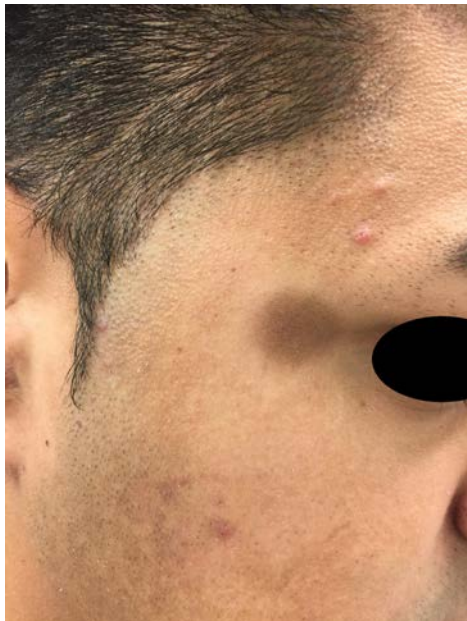
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**Abstract**

Fixed drug eruption (FDE) is a type of cutaneous drug reaction that occurs at the same sites upon re-exposure to specific medications. Herein we discuss the case of a 23-year-old man with a FDE to fluconazole.

**Case synopsis**

A 23-year-old man presented with complaints of erythematous/edematous plaques in his right axilla and over his right lateral eyebrow area. He said that the plaques always appeared within 24 hours after he took his monthly dose of 300 mg of fluconazole for treatment of recurrent tinea versicolor. He denied taking any other prescription or over-the-counter medications. Physical exam revealed hyperpigmented round patches on the right temple (Figure 1) and right proximal ventral arm (Figure 2). He was diagnosed with FDE related to fluconazole and his antifungal medication was switched to itraconazole 400 mg, with resolution of the FDE.



## Discussion

The skin is commonly affected by adverse drug eruptions [1]. Approximately 2-3% of patients who are taking drugs experience drug-induced cutaneous reactions [2]. Drug-induced exanthems are the most common type of drug-induced cutaneous reaction and account for approximately 90-95% of all drug eruptions [2,3].

Fixed drug eruption (FDE) is the next most common type of drug eruption. The incidence of FDE varies widely depending on the population studied, with the incidence being as high as 22% in one cohort of pediatric patients in North India who were suffering from drug eruptions [4,5]. One study that examined 450 pediatric and adult patients with FDE found that the mean age for both male and female patients was approximately 30 years old [6].

Fixed drug eruption is most frequently associated with antibacterial sulfonamides, antibiotics, nonsteroidal anti-inflammatory agents, analgesics, antimalarials, barbiturates, oral contraceptives, and food coloring [2,7]. Oral antifungals are not a common cause of FDE, but there are rare reports of FDE related to fluconazole [8].

The most typical diagnostic characteristic for FDE is the repeated recurrence of lesions at the same sites upon exposure to the offending drug(s) [4]. Acute lesions most commonly appear 30 minutes to 8 hours after drug exposure. However, lesions can develop for up to two weeks after exposure [2]. Lesions can occur anywhere on the skin and/or the mucosal membranes. Certain drugs cause lesions more often in specific sites [4]. For example, one study showed that tetracyclines preferentially cause FDE on the genitalia ( $p < 0.001$ ) [9]. Overall, the sites commonly affected by FDE are the genitalia, lips, perianal area, feet, and hands. FDE can also occur, albeit rarely, on sites that have experienced trauma [2].

The most common type of FDE is the pigmented FDE. These eruptions are so named because they leave behind areas of post-inflammatory hyperpigmentation upon healing [4]. Pigmented FDE typically presents with one or several well-demarcated macules that may coalesce into plaques. These macules have a violaceous center with erythematous margins, and bullae may or may not occur [4]. Burning sensations and/or pruritus may occur. Systemic symptoms usually are not present [2]. Other, rarer forms of FDE exist. These include generalized FDE, erythema multiforme-like FDE, toxic epidermal necrolysis-like FDE, nonpigmenting FDE, linear FDE, wandering FDE, and bullous FDE [2,4]. The differential diagnosis for FDE may include conditions such as bullous pemphigoid, erythema multiforme, Stevens-Johnson syndrome/toxic epidermal necrolysis, herpes simplex, contact dermatitis, and phytophotodermatitis [2,4,7].

Fixed drug eruption may be caused by a delayed type IV hypersensitivity reaction, but the exact pathogenetic mechanism for FDE is still unclear [10]. Histopathological examination of FDE generally reveals a lichenoid tissue reaction and pigmentary incontinence (leakage of melanin into the papillary dermis owing to melanocyte damage). Other features include a lymphocytic perivascular infiltrate in the mid-upper dermis, dermal melanophages, damage to the basal keratinocytes, dyskeratotic cells in the epidermis, and broader epidermal necrosis. FDE can be diagnosed through systemic (oral) and topical (patch testing) provocation tests [2,7].

Management of FDE mainly consists of discontinuation and avoidance of the offending drug and other cross-reactive drugs. Inflammatory lesions typically resolve within 7-10 days after the offending drug is discontinued. Symptomatic treatment for FDE targets pruritus. Treatment options include medium to high potency topical corticosteroids applied twice daily for 7-10 days and oral antihistamines such as hydroxyzine or diphenhydramine. Patients suffering from generalized FDE and systemic symptoms may be treated with a short 3-5 day course of moderate dose systemic corticosteroids (e.g. prednisone 0.5–1 mg/kg/day) [2,7].

In this case report, we present a case of a pigmenting FDE due to fluconazole, a drug that is not commonly associated with FDE. Physicians should understand how to properly diagnose and manage this relatively common dermatological condition, which can be caused by a wide variety of offending drugs.

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