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Original Research Article

Fluoroquinolones Induced Bullous Fixed Drug Eruption

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Abstract: Bullous fixed drug eruption (FDE) is a rare but severe cutaneous adverse reaction characterized by well-demarcated, blistering skin lesions that recur at the same locations upon re-exposure to the offending drug. Fluoroquinolones, a widely used class of antibiotics, infrequently trigger bullous FDE, but cross-reactivity among agents and significant clinical consequences warrant heightened awareness. This article reviews epidemiology, pathophysiology, clinical features, diagnosis, management, and prevention based on clinical cases and synthesized literature.

Keywords: Bullous Fixed Drug Eruption (FDE), Cutaneous Adverse Reaction, Fluoroquinolones, Drug Hypersensitivity, Clinical Management.

INTRODUCTION

Fixed drug eruption represents 16–21% of drug-related cutaneous reactions in several populations[1][2]. While fluoroquinolones—especially ciprofloxacin, ofloxacin, and levofloxacin—are most often associated with morbilliform eruptions and photosensitivity, bullous FDE is a rare presentation[2][3]. Prompt recognition is crucial for cessation of the offending agent and prevention of recurrences or escalation to more severe reactions (e.g., Stevens–Johnson syndrome).

PATHOPHYSIOLOGY

FDEs are type IV hypersensitivity reactions, predominantly involving cytotoxic CD8+ T cells residing in the epidermis. Upon re-exposure, the sensitized cells trigger localized tissue destruction and inflammation, resulting in sharply demarcated erythematous patches or plaques, which may become bullous[1][4].
Mechanism:

- Fluoroquinolones or their metabolites bind to keratinocytes.
- Drug-modified keratinocytes become targets for memory T cells.
- Lytic enzymes and cytokines released cause apoptosis and blister formation.

Epidemiology

Cutaneous adverse reactions to fluoroquinolones occur in 1–2% of patients, with FDE constituting a minor proportion[1][2]. Reports suggest bullous FDEs are more frequent in adults but have no clear gender predominance[5]. Risk factors include prior drug hypersensitivity, genetic predisposition (e.g., HLA-B22), and intermittent or repeated

drug exposure.

CLINICAL PRESENTATION

Features

- **Onset:** Lesions develop within 30 minutes to 8 hours after drug ingestion[1][2][3].
- **Morphology:** Sharply marginated, erythematous or violaceous patches, often with blister (bullous) or vesicle formation.
- **Distribution:** Predilection for hands, feet, genitalia, face, lips, but can be generalized.
- **Symptoms:** Pruritus, burning, sometimes pain at the lesion site. Healing leaves hyper- or hypopigmentation.
- **Re-exposure:** Identical lesions recur at same sites; new sites may be involved with repeated exposures.
- **Mucosal involvement:** Generally absent or mild in bullous FDE (distinguishing from Stevens–Johnson syndrome)[1][2][4][6].

Table 1: Clinical Characteristics of Bullous FDE due to Fluoroquinolones

Parameter	Characteristics
Timing	30 min – 8 hr post-drug ingestion
Lesion type	Well-demarcated, erythematous, bullous
Common sites	Hands, feet, lips, face, genitalia
Pigmentation post-healing	Present (hyperpigmentation)
Systemic symptoms	Rare
Course	Resolves on drug cessation

Case Examples

- **Ciprofloxacin-induced bullous FDE:** 60-year-old presented with bullous lesions on hands and feet several hours post-ingestion[2].
- **Generalized bullous FDE:** 57-year-old with widespread blisters after ciprofloxacin; previous similar but milder reaction confirmed diagnosis[6].
- **Cross-reactivity:** Patient with history of bullous FDE to ciprofloxacin developed similar lesions with ofloxacin after 1 year[1].

Diagnosis

Diagnosis relies on:

- **Clinical history:** Drug exposure prior to lesion onset; recurrence at the same site(s).
- **Physical examination:** Characteristic lesions—well-marginated, blistering patches.
- **Histopathology:** Interface dermatitis with necrotic keratinocytes, subepidermal blister; perivascular lymphocytic infiltrate.
- **Provocation testing:** Rarely done due to risk; patch testing may have limited utility.
- **Exclusion:** Rule out severe reactions (e.g., Stevens–Johnson syndrome, toxic epidermal necrolysis) and other bullous dermatitides[1][2][6].

Differential Diagnosis

- Stevens–Johnson syndrome/toxic epidermal necrolysis: Extensive mucosal involvement, widespread epidermal loss.
- Bullous pemphigoid or pemphigus vulgaris: Autoimmune blistering diseases with different lesion morphology.
- Erythema multiforme: Targetoid lesions, mucosal involvement.

Mechanism of Cross-reactivity

Quinolones share a core chemical structure; thus, cross-reactivity between agents like ciprofloxacin and ofloxacin is possible[1][3]. Re-exposure to any in the class should be avoided if FDE occurs.

Management

- **Immediate cessation** of the offending fluoroquinolone[1][2][7].
- **Symptomatic therapy:**

  - Topical corticosteroids for localized lesions.
  - Systemic antihistamines for pruritus.
  - Systemic corticosteroids rarely required except for extensive/generalized or severe cases.
  - Emollients for skin barrier support.
- **Wound care:** For areas with bullae/blistering.
- **Follow-up:** Monitor for secondary infection and provide skin care advice.
- **Patient education:** Strict avoidance of all fluoroquinolones thereafter[1][2][5][8].

Figure 1: Clinical progression of bullous FDE (illustrative schematic)

- A: Early erythematous plaque after drug exposure
- B: Formation of fluid-filled bullae on plaque background
- C: Healing with residual hyperpigmentation after cessation

Prognosis

Resolution typically occurs within 1–2 weeks of drug discontinuation, with hyperpigmentation remaining for months. Re-exposure leads to faster and more severe recurrences. Prognosis is excellent if recognized and treated early, with low risk of progression or systemic involvement.

Prevention

- **Detailed drug history:** Ask about prior reactions to any antibiotics, especially fluoroquinolones.
- **Medic alert:** Patients with known FDE to any fluoroquinolone should carry a warning card and inform all healthcare providers.
- **Pharmacovigilance:** Report adverse reactions to improve awareness and surveillance.

Graphical Data

Figure 2: Distribution of Causative Drugs in Cutaneous FDE

Drug Class	% of FDE Cases
Antibiotics	66.7
NSAIDs	32.4
Fluoroquinolones	~10 (subset of abx)

Data adapted from a large case series review[9].

Figure 3: Incidence of Cutaneous Adverse Reactions to Fluoroquinolones

Reaction Type	Estimated Incidence (%)
Photosensitivity	0.5–2
Morbilliform	1–2
FDE	<0.5
Bullous FDE	<0.05

DISCUSSION

Bullous fixed drug eruption due to fluoroquinolones, albeit rare, represents an important clinical entity due to its acute presentation and potential for recurrence or misdiagnosis. The key to effective management is early recognition and prompt discontinuation of the causal drug. Histological and clinical confirmation, avoidance of re-challenge, and robust patient education are the cornerstones of care. Given the rising use of fluoroquinolones and over-the-counter access in some regions, prescriber vigilance and pharmacovigilance remain critical[1][4][5][10][9].

CONCLUSION

Fluoroquinolone-induced bullous FDE is a rare, often under-recognized adverse drug reaction. Clinicians must be alert to this diagnosis in patients presenting with recurrent, sharply marginated blisters after antibiotic use and should avoid all quinolones in sensitized individuals. Clear documentation and patient education can prevent recurrences

and reduce morbidity.

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