Case Report

Fluconazole-Induced Stevens–Johnson Syndrome in a Type 2 Diabetic Male: A Case Report

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ABSTRACT

Background: Stevens–Johnson Syndrome (SJS) is a rare but potentially life-threatening mucocutaneous hypersensitivity reaction, most commonly induced by drugs. Fluconazole, an antifungal agent widely used to treat candidiasis, is infrequently associated with SJS.

Case Presentation: We report a case of a 37-year-old male with Type 2 Diabetes Mellitus admitted with multiple oral ulcers, erythematous genital lesions, and excoriation of skin over hands and feet. He had been diagnosed with oral candidiasis and candidal balanitis five days earlier and was on oral Fluconazole 150 mg daily. On admission, the dose was escalated to 200 mg intravenously and subsequently to 250 mg. Within three days, the patient developed crusted erosions over the lips and buccal mucosa, with erythematous erosions over the genitalia, suggestive of SJS. Fluconazole was immediately withdrawn, and systemic corticosteroid therapy was initiated along with supportive care. The patient showed gradual improvement with re-epithelialization and complete recovery over one week.

Conclusion: This case highlights the rare occurrence of Fluconazole-induced SJS and underscores the importance of early recognition, prompt withdrawal of the offending drug, and multidisciplinary management to prevent morbidity.

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Introduction

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but severe mucocutaneous reactions characterised by widespread epidermal necrosis, detachment, and multisite mucosal involvement [1]. Although their incidence is only 2–7 cases per million persons, they carry high morbidity and mortality [2]. SJS/TEN is primarily triggered by medications, with immune-mediated keratinocyte apoptosis driven by cytotoxic T cells through Fas–FasL, perforin/granzyme, and granulysin pathways; genetic factors such as HLA-B1502 and HLA-B5801 further increase susceptibility [3, 4]. Clinically, symptoms begin 1–3 weeks after exposure and progress from flu-like illness to painful erythematous macules, blistering, and mucosal erosions [5]. Severity is defined by epidermal detachment: <10% body surface area for SJS and >30% for TEN [6]. Early drug withdrawal and supportive care are essential, while systemic therapies show variable evidence [7]. Fluconazole is an uncommon cause, but rare cases have been reported. We describe SJS in a 37-year-old male with type 2 diabetes following fluconazole therapy.

Case Presentation

Patient Information

A 37-year-old male presented with a 5-day history of painful oral ulcers, erythematous genital lesions, and excoriations over the hands and feet. He had been treated at a local clinic for oral candidiasis and candidal balanitis with oral Fluconazole 150 mg once daily. His medical history included type 2 diabetes mellitus (T2DM) for 4–5 years, previously controlled on glimepiride–metformin, which he had stopped several days prior. There was no history of drug allergies, autoimmune diseases, or addictions. He denied fever, malaise, cough, or rash before presentation (Figure 1).

Clinical Findings

On admission, he was alert, oriented, and hemodynamically stable (BP 120/78 mmHg, pulse 82/min, temperature 98.4°F, SpO_2 98%, RR 16/min). Systemic examination of cardiovascular, respiratory, and neurological systems was unremarkable.

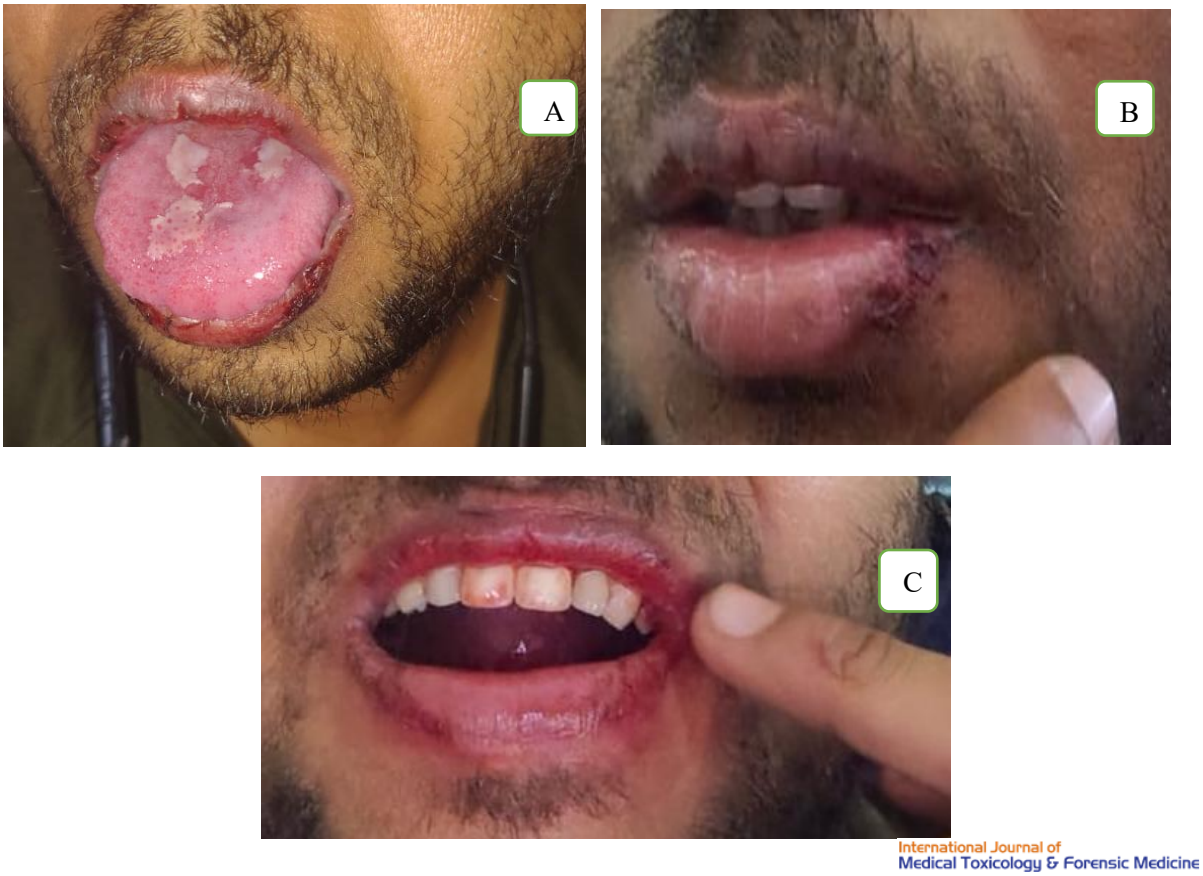

Figure 1. Clinical presentation of mucocutaneous lesions in the patient. A. Diffuse ulcerations and erythematous erosions over the dorsal surface of the tongue, with crusting and fissuring along the oral commissures. B. Crusted erosions and deep fissures at the corners of the lips, consistent with mucosal involvement of Stevens–Johnson Syndrome. C. Extensive erythema and raw erosive areas along the inner lip mucosa and vermilion border, with marked tenderness and bleeding points.

Table 1. Timeline of Clinical Course and Management.

Date / Day	Clinical Findings	Management
03-10-25	Diagnosed with oral candidiasis and candidal balanitis	Fluconazole 150 mg OD initiated
08-10-25 (Day 1)	Admitted with oral and genital lesions	IV Fluconazole 200 mg OD; Inj Methylprednisolone 60 mg IV; mouth paint; PPI; sucralfate; insulin therapy
09-10-25 (Day 2)	Worsening oral ulcers; genital discomfort	Fluconazole increased to 250 mg IV; Azithromycin 500 mg OD; antihistamine; Rebamipide
10-10-25 (Day 3)	Crusted erosions over the lips, buccal mucosa, and genital erosions. Dermatology: SJS suspected	Fluconazole discontinued; Inj dexamethasone BD × 3 days; Inj Pheniramine maleate BD; Chlorhexidine mouthwash; topical therapy.
11-10-25 (Day 4)	No fresh lesions; stable vitals; gradual improvement	Continued IV Methylprednisolone 40 mg OD; Insulin glargine 18 U HS; supportive oral and skin care
12-10-25 (Day 5)	Oral ulcers are improving; no new complaints	Added a laxative for constipation
13-10-25 (Day 6)	Marked improvement; 2 episodes of loose stools	Switched to oral steroids (Tab Prednisolone 10 mg 2 tabs × 3 days than 1 tab × 3 days); Tab Bilastine 20 mg BD; continued topical and oral care.
14-10-25 (Day 7)	Oral ulcers healed; minimal residual hypopigmentation on palms	Discharged on tapering corticosteroids and supportive medications; advised strict avoidance of Fluconazole and azoles

Oral examination revealed multiple shallow erosions, crusting over the lips, and extensive ulcerations involving the buccal mucosa and tongue. Genital examination showed erythematous, tender erosive lesions with excoriation. The dorsum of both hands and feet exhibited superficial excoriations and mild erythema. No ocular involvement or epidermal detachment was noted initially.

Diagnostic Assessment

Differential diagnoses included aphthous ulcers, fixed drug eruption, erythema multiforme, and Stevens–Johnson Syndrome (SJS). The temporal association with Fluconazole, progression of mucosal involvement, and rapid improvement after drug withdrawal supported a diagnosis of fluconazole-induced SJS.

Laboratory Findings

CBC and renal function tests were normal. Random blood glucose was 235 mg/dL; HbA1c 6.5%. Liver function tests showed mildly reduced globulin with an elevated A/G ratio. Urine examination revealed trace albumin, positive ketones, and mild pyuria. Viral markers (HBsAg, HIV-1 & 2, VDRL, HCV) were non-reactive. Endoscopy showed LA Grade A esophagitis and mild gastritis.

Causality, Severity, and Preventability Assessment

Causality assessment using the Naranjo Adverse Drug Reaction Probability Scale scored 8 (Table 2), indicating a probable adverse reaction to Fluconazole.

Table 2. Naranjo Adverse Drug Reaction Probability Scale Assessment for Fluconazole-Induced SJS.

Question	Answer	Score
1. Are there previous conclusive reports on this reaction?	Yes	+1
2. Did the adverse event appear after the suspected drug was administered?	Yes	+2
3. Did the adverse reaction improve when the drug was discontinued, or a specific antagonist was given?	Yes	+1
4. Did the adverse reaction reappear upon re-administration of the drug?	Not done	0
5. Are there alternative causes that could have caused the reaction?	No	+2
6. Did the reaction reappear when a placebo was given?	Not applicable	0
7. Was the drug detected in blood (or other fluids) in toxic concentrations?	No	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	Yes	+1
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	No	0
10. Was the adverse event confirmed by objective evidence?	Yes	+1
Total Score	8 (Probable ADR)	

According to Hartwig and Siegel's severity scale, the event was classified as Level 6 (Severe ADR) due to hospitalization and need for intensive drug withdrawal and systemic therapy. Schumock and Thornton's criteria categorized the reaction as probably preventable.

Therapeutic Interventions

The primary intervention was the immediate cessation of Fluconazole. Systemic corticosteroids (IV Medrol, later tapered to oral prednisolone), antihistamines, topical mucosal and skin care, oral mucosal protectants, gastrointestinal prophylaxis, hydration, and glycemic management were provided. Supportive treatments included Rebagen for mucosal repair and Cremaffin Plus for constipation.

Follow-Up and Outcomes

By Day 7, the patient had significant healing of oral and genital erosions, complete pain relief, and stable blood glucose levels. He was discharged with tapering steroids and advised lifelong avoidance of fluconazole and azole antifungals.

At the two-week follow-up, he showed complete mucosal healing with improved post-inflammatory hypopigmentation over both palms (Figure 2).

Figure 2. Sharply demarcated hypopigmented macules over the thenar and hypothenar regions, consistent with post-inflammatory hypopigmentation during SJS.

Discussion

In this case, the patient developed widespread mucosal and cutaneous erosions within three days of fluconazole dose escalation. The short latency, absence of alternative high-risk drugs, and rapid improvement after discontinuation strongly support Fluconazole as the causative agent, consistent with timelines described in previous reports [8]. The underlying mechanism is believed to involve a T-cell–mediated type IVc hypersensitivity reaction leading to keratinocyte apoptosis, mediated by Fas–FasL and cytotoxic granules. Reactive metabolites, genetic susceptibility involving HLA alleles, and variations in cytochrome P450 metabolism may contribute to idiosyncratic reactions [9].

Although fluconazole-induced Stevens–Johnson syndrome has been reported only rarely, this case adds unique clinical value to the existing literature. First, the reaction occurred shortly after administration of a standard therapeutic dose without prior sensitization, emphasizing that even routine dosing can precipitate severe cutaneous adverse reactions. Second, the patient had type 2 diabetes mellitus, a comorbidity rarely highlighted in previous reports, which may influence immune dysregulation and susceptibility to severe drug hypersensitivity. Third, the clinical course demonstrated a favourable and relatively rapid recovery following early withdrawal of the offending agent and prompt supportive management. These features collectively distinguish this report from previously published cases of fluconazole-associated SJS.

Causality assessment using the Naranjo algorithm yielded a "probable" score, and severity grading classified the reaction as severe, requiring hospitalization and systemic therapy. Diabetes mellitus, present in this patient, may alter immune and metabolic responses and is associated with increased risk of fungal infections and prolonged antifungal exposure.

Systemic corticosteroids remain a debated therapy; however, in this early, rapidly progressive presentation, short-course intravenous steroids led to marked improvement, as noted in selected reports [10]. The role of systemic corticosteroids in the management of SJS remains controversial. Current guidelines offer mixed recommendations. The British Association of Dermatologists notes insufficient evidence to support the universal use of corticosteroids but allows consideration in early, rapidly progressing cases [11]. Several observational studies and meta-analyses suggest that early administration (within 24–48 hours of onset) may reduce progression and shorten hospital stay; however, other studies report no significant benefit and raise concerns about secondary infections and delayed wound healing [12]. In our case, systemic corticosteroids were administered briefly and tapered, leading to rapid improvement. This aligns with the modern trend toward individualized decision-making based on disease severity, comorbidities, and risk–benefit assessment.

Supportive care, including wound management, hydration, electrolyte correction, glycemic control, and infection prevention, was essential for recovery. Post-inflammatory hypopigmentation observed during follow-up is a typical sequela of SJS [13].

Fluconazole-induced SJS remains exceedingly rare, but similar cases with comparable latency, clinical presentation, and response to drug withdrawal have been documented. Cross-reactivity among azole antifungals is not fully understood. Although some patients tolerate alternative azoles, recurrence has been reported; hence, complete avoidance of the azole class is advisable.

Overall, this case highlights the need for vigilance even with commonly prescribed antifungals. Early withdrawal of the offending drug, timely initiation of appropriate therapy, and thorough documentation of drug allergy are crucial to preventing recurrence and ensuring patient safety.

Conclusion

Fluconazole, though generally considered a safe antifungal agent, can rarely cause severe cutaneous adverse drug reactions such as Stevens–Johnson Syndrome. In this case, the rapid onset of mucocutaneous lesions after dose escalation, absence of alternative etiologies, and prompt improvement following drug withdrawal support fluconazole as the causative agent. Early recognition, immediate discontinuation of the offending drug, and timely initiation of supportive measures and systemic corticosteroids were key to the patient's favorable outcome. Clinicians should remain vigilant for SJS even with commonly used medications, ensure accurate documentation of drug allergies, and counsel patients to avoid future exposure to azole antifungals.

Conflicts of Interest

The authors report there are no competing interests to declare.

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