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Allergic Reaction to Fluoxetine: A Case Report

A. Khallouk, A.K. Rhaouti, A. Boukdir, F. Laboudi, A. Ouanass

Department of Psychiatry, Ar-Razi Psychiatric Hospital, Avicenne University Hospital, Rabat, Morocco

ABSTRACT

Fluoxetine, the first selective serotonin reuptake inhibitor (SSRI), is widely prescribed for depressive and anxiety disorders. Its adverse effects are usually mild and mainly gastrointestinal or neurovegetative. Allergic skin reactions, though exceptional, may be potentially serious. We report a case of an allergic reaction to fluoxetine in a patient treated for major depressive disorder, and we discuss the relevant literature.

Keywords: Fluoxetine, allergic reaction, skin rash, SSRI

Introduction

Fluoxetine, the first SSRI introduced in 1987, remains among the most prescribed antidepressants worldwide. It is indicated in the treatment of depressive disorders, obsessive-compulsive disorder, panic disorder, eating disorders (such as bulimia nervosa), and premenstrual dysphoric disorder [1,2]. Its mechanism of action is based on selective inhibition of serotonin reuptake at the presynaptic level, increasing synaptic serotonin concentration and improving depressive symptoms.

Although fluoxetine is generally considered well tolerated, it can cause various adverse effects, including cutaneous reactions that range from mild to potentially life-threatening.

Since its commercialization, skin reactions have been reported. Literature data estimate that between 4% and 7% of patients treated with fluoxetine develop a rash or urticaria during treatment [5,6]. While most are mild and transient, some may present as severe hypersensitivity syndromes such as Stevens–Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), or DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms), though these remain rare [7–9].

The most common manifestations include maculopapular rashes, urticaria, and, more rarely, angioedema or systemic hypersensitivity reactions [10,11]. The time of onset varies—some reactions occur within hours or days after initiation, others several weeks later, once pharmacokinetic equilibrium is reached [12]. This variability often complicates diagnosis.

From a pathophysiological standpoint, several mechanisms have been proposed. One hypothesis involves peripheral serotonin elevation activating cutaneous receptors responsible for vasodilation and pruritus [13]. Another involves an immune-mediated hypersensitivity reaction, possibly T-cell mediated or related to drug–MHC interactions [14]. The long half-life of fluoxetine (4–6 days) and its active metabolite norfluoxetine (7–15 days) may also explain the persistence or delayed onset of symptoms after discontinuation [15].

Management relies on early recognition, immediate withdrawal of the offending drug, and symptomatic treatment with antihistamines and, if necessary, corticosteroids. Substitution with an antidepressant from another pharmacological class can be considered [16,17].

Here, we present the case of a 38-year-old woman who developed an early allergic skin reaction a few hours after the first fluoxetine dose and discuss related findings from the literature.

Case Report

Ms. C.K., a 38-year-old woman with no relevant medical or psychiatric history, presented with symptoms consistent with a major depressive episode according to DSM-5-TR criteria. The clinical picture included a persistent depressed mood lasting several weeks, marked loss of interest or pleasure (anhedonia), fatigue, insomnia with early awakenings, reduced appetite, and poor concentration, leading to significant psychosocial impairment.

There was no history of allergies, mood episodes, or somatic comorbidities. No alternative diagnosis (brief psychotic disorder, bipolar disorder, substance-related disorder, or medical condition) was retained.

A diagnosis of moderate major depressive disorder was made, and fluoxetine 20 mg/day was initiated.

A few hours after the first dose, the patient developed facial redness with pruritus, followed by a maculopapular erythematous rash on the face and neck. The following day, examination revealed a diffuse rash without mucosal involvement or systemic symptoms (no fever, arthralgia, or airway edema).

A drug-induced allergic reaction to fluoxetine was suspected. The medication was discontinued immediately, and symptomatic treatment with Taraxet® 25 mg/day (antihistamine) was prescribed.

Fluoxetine was replaced by sertraline 25 mg/day, later increased to 50 mg/day.

The rash resolved completely within a few days, without complications. The depressive episode improved progressively under sertraline, with marked mood and functional recovery.

Discussion

SSRIs are widely prescribed antidepressants, but they can induce dermatologic side effects. Reported incidence of fluoxetine-related cutaneous reactions ranges from 4% to 7% [8,9]. Common presentations include maculopapular rashes, urticaria, pruritus, and eczema, while severe cases such as Stevens–Johnson Syndrome SJS, Toxic Epidermal NecrolysisTEN, Drug Reaction with Eosinophilia and Systemic Symptoms DRESS, and leukocytoclastic vasculitis have also been documented [2,4].

Cross-reactivity among SSRIs has been described, suggesting that a patient allergic to one SSRI might also react to another from the same class [2].

The pathogenesis remains unclear but is likely multifactorial—combining immune-allergic mechanisms and pharmacologic skin effects. Increased extracellular serotonin in the skin may play a role, as serotonin regulates microcirculation, vascular permeability, inflammation, and pruritus. Serotonin receptors (5-HT2, 5-HT7) are expressed in keratinocytes, endothelial cells, and sensory nerve endings, potentially explaining local hypersensitivity [2,12].

Delayed-type hypersensitivity (Type IV) mediated by T-cells can cause benign maculopapular eruptions. In more complex presentations (with eosinophilia, arthralgia, or organ involvement), systemic hypersensitivity is suspected.

The latency period varies widely—from hours (as in this case) to several weeks after steady-state plasma levels are achieved [3]. The long half-life of fluoxetine (1–3 days) and norfluoxetine (up to two weeks) can prolong reactions even after discontinuation.

Here, the rapid regression within days suggests a mild allergic reaction responding well to antihistamines.

Similar cases have been reported: urticaria and angioedema (Tuman et al., 2017), maculopapular rash (Gupta & Garg, 2016), and dermatitis due to weekly fluoxetine formulation (Gupta et al., 2002). Pediatric and food-related reactions, particularly with chocolate, have also been noted (Muzenda &Grimwade, 2023).

Table 1. Summary of Reported Fluoxetine-Induced Skin Reactions

Variable	Beer et al., 1994 [13]	Cederberg et al., 2004 [7]	Gupta & Garg, 2016 [4]	Tuman et al., 2017 [3]	Muzenda&Grimwade, 2023 [6]	Present Case (2025)
Age / Sex	F/44	Adult (unspecified)	Adultfemale	Adult (unspecified)	M/16	F/38
Indication	Likelydepression	Depressionunder SSRI	Major depressiveepisode	Depression / otherpsychiatric indication	Depressivedisorder	Major depressiveepisode
Initial Dose	Not specified	20 mg/day	20 mg/day	Not specified	20 mg/day	20 mg/day
Onset	Variable	Not specified (chocolate interaction)	5 days	Few days	4 weeks	Few hours after 1st dose
Type of Skin Reaction	Pruritic rash + eosinophilia + arthralgia (systemic)	Pruritus + rash (food-related)	Maculopapular rash, localized→generalized pruritus	Urticaria + angioedema	Generalizedurticaria	Maculopapular erythematous rash (face/neck) + pruritus
SystemicInvolvement	Present (arthralgia, eosinophilia)	None	None	Facial edema (angioedema)	None	None

Therapeutic Management	Drug withdrawal + corticosteroids	Withdrawal + diet modification	Withdrawal + antihistamines	Withdrawal + antihistamines	Withdrawal of fluoxetine	Withdrawal + antihistamines (Taraxet® 25 mg/day)
Antidepressant Switch	Not specified	Not specified	Paroxetine 12.5 mg/day	Not specified	Not specified	Sertraline 25 → 50 mg/day
Outcome	Rechallenge positive → confirmedcausality	Resolution after drug + diet withdrawal	Resolution in 1 week (+ transient hyperpigmentation)	Rapid resolution	Resolutionin 10 days	Complete resolution in few days
Clinical Notes	First systemichypersensitivity report	Rare food interaction	Earlybenign rash	Immediatereaction withangioedema	Delayed reaction at steady state	Very early mild cutaneous reaction

Diagnosis and Management

Diagnosis of SSRI-induced skin reactions relies on a detailed drug history, clinical examination, and exclusion of alternative causes. In selected cases, patch testing or oral challenge tests may help confirm diagnosis, but these must be conducted under strict medical supervision.

Management typically involves immediate drug discontinuation. Mild reactions respond to oral antihistamines or topical corticosteroids, while severe cases may require systemic corticosteroids, hospitalization, or IV immunoglobulins.

Patients should be informed about possible cross-reactivity among SSRIs and alternative pharmacologic options.

In clinical practice:

Patients treated with SSRIs—especially fluoxetine—should be informed of early warning signs of allergic skin reactions (pruritus, rash, edema), even within hours of initiation.

Discontinue the medication immediately if such symptoms occur, start appropriate symptomatic therapy (antihistamines for mild cases; systemic corticosteroids for severe ones), avoid re-exposure to fluoxetine, and monitor closely when introducing another SSRI due to potential cross-reactivity [2].

In delayed or severe cases, referral to allergy specialists for patch testing or supervised challenge is warranted.

Conclusion

Although rare, fluoxetine-induced cutaneous reactions are clinically significant and require increased vigilance. They may appear anytime during treatment, from the first hours to several weeks, and vary in severity from benign rashes to severe systemic hypersensitivity syndromes.

Our case illustrates a very early, mild cutaneous reaction resolving rapidly after drug discontinuation and antihistamine therapy. Successful switching to another SSRI (sertraline) highlights the benefit of individualized therapeutic adjustment.

Reported cases include delayed urticaria, maculopapular rashes, eosinophilia-associated hypersensitivity, and rare food interactions, underscoring the diversity of underlying mechanisms. Early recognition, appropriate management, and pharmacovigilance reporting remain key to improving patient safety.

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