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# Maculopapular Eruption Secondary to Itraconazole

Tanja Batinac<sup>1</sup>, Gordana Zamolo<sup>2</sup>, Biserka Trošelj-Vukić<sup>3</sup>, Darko Biljan<sup>4</sup>,  
Duška Petranović<sup>3</sup>, Milodar Kujundžić<sup>1</sup>

<sup>1</sup> Department of Dermatovenerology, University Hospital Center »Rijeka«, Rijeka, Croatia

<sup>2</sup> Department of Pathology, School of Medicine, University of Rijeka, Rijeka, Croatia

<sup>3</sup> Department of Internal medicine, University Hospital Center »Rijeka«, Rijeka, Croatia

<sup>4</sup> Department of Dermatovenerology, University Hospital, Osijek, Croatia

## ABSTRACT

*Adverse cutaneous reactions to itraconazole are known to be quite rare. We report a case of maculopapular reaction caused by itraconazole. On the 7<sup>th</sup> day of itraconazole therapy for hand onychomycosis, in a 39-year-old woman pruritus occurred with a subsequent morbiliform, symmetric, maculopapular eruption on the upper torso, neck, trunk and pressure-bearing areas. Eruption progressed, becoming confluent and spreading to extremities. Due to increasing indications for the administration of itraconazole its increased usage as well as the possibility of allergic reactions should be expected even if these are a rare event.*

**Key words:** *adverse drug reaction, itraconazole*

## Introduction

Adverse cutaneous reactions to itraconazole are known to be quite rare and are reported as rash and pruritus<sup>1</sup>, acute generalized exanthematic pustulosis<sup>2</sup>, photosensitivity<sup>3</sup>, acute urticaria and angioedema<sup>4</sup>. Tucker et al. described two patients with maculopapular eruption in his review of 189 patients treated with itraconazole<sup>5</sup>. Here we report a case of maculopapular reaction caused by itraconazole in a young female patient on the 7<sup>th</sup> day of itraconazole therapy.

## Professional Report

A 39-year-old woman began oral treatment with itraconazole, 200 mg twice daily, for hand onychomycosis. She reported no associated illnesses or other medication usage. Her family and personal history were negative and unremarkable for allergy. On the 7<sup>th</sup> day of itraconazole therapy pruritus occurred with a subsequent morbiliform, symmetric, maculopapular eruption on the upper torso, neck, trunk and pressure-bearing areas. Eruption progressed, becoming confluent and spreading to extremities (Figure 1). Laboratory evaluation including im-

munologic workup revealed no abnormalities. Other causes of maculopapular cutaneous reactions were excluded, such as acute viral and bacterial infections, collagen vascular diseases, serum sickness-like reactions. Diagnosis of allergic drug eruption has been suggested. Pathohistology of the skin biopsy showed a focal parakeratosis, dyskeratosis, mild spongiosis and basal cell liquefactive degeneration with lymphocytic exocytosis, a few eosinophils and some red cell extravasation in the dermis, speaking in the favor for diagnosis of adverse drug reaction.

Itraconazole therapy was discontinued and the patient was treated with topical and systemic corticosteroids and systemic antihistamins. The rash resolved during the next few days. Following the rash resolution allergologic testing was suggested but refused by the patient.

## Discussion

Itraconazole is a broad-spectrum oral triazole synthesized in 1980. The mechanism of action is similar to other azoles and is primarily fungistatic. Itraconazole shows less toxicity than the imidazole antifungals. Side



Fig. 1. Maculopapular rash on the back of 39-year-old woman.

effects most frequently reported include nausea, vomiting, abdominal pain, diarrhea, anorexia, headache, dizziness, fatigue, fever and elevation of liver enzymes.

Maculopapular exanthem is the most common type of drug-induced cutaneous reaction. Often, it has a characteristic structure, beginning with the lesions on the upper torso or head and neck<sup>6</sup> lesions becoming confluent, covering large areas of the body in symmetrical pattern, like in our patient.

Firmly establishing a causal reaction between the suspected agent and resulting cutaneous reaction is crucial. Other important factors that contribute to the accurate diagnosis of drug-induced cutaneous reactions are establishing a chronological relation between suspected

drug and the reaction, noting improvement after cessation of the suspected agent. Most drug-induced maculopapular exanthemas usually appear 8–10 days after drug therapy initiation, but can also appear earlier<sup>7</sup> and later, like in our case on the 7<sup>th</sup> day of therapy. Also, it is expected to fade within a similar period of time after medication withdrawal with or without systemic or local corticosteroid therapy.

The pathogenesis of exanthematous drug reactions is not fully understood, although a cytotoxic T-cell-mediated reaction is likely in the majority of cases. The histological features are often subtle but the characteristic changes include lymphocytic exocytosis with mild spongiosis, accompanied by basal cell liquefactive degeneration. In the dermis there is usually a perivascular lymphocytic infiltrate and variable number of eosinophils<sup>8,9</sup>, like in our case.

Reactivation of the rash during re-challenge confirms allergic reaction to suspected drug but in our case we were not able to perform the testing. Confirmation of the medical eruption with challenge test has been performed previously in one case of maculopapular eruption<sup>7</sup> and acute urticaria and angioedema<sup>4</sup>.

Itraconazole has been widely used for onychomycosis and dermatomycosis, especially as »pulse therapy«<sup>10</sup> and some suggested its effectiveness for seborrheic dermatitis and atopic dermatitis as well<sup>11</sup>. Thus, due to increasing indications for the administration of itraconazole its increased usage should be expected, and with that in mind itraconazole induced allergic reactions should be considered as possibility when administering it in dermatology practices.

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T. Batinac MD

Department of Dermatovenerology, University Hospital Center »Rijeka«, Krešimirova 42, 51000 Rijeka, Croatia  
e-mail: tanjabatinac@net.hr

## **MAKULOPAPULOZNI OSIP NAKON TERAPIJE ITRACONAZOLOM**

### **S A Ž E T A K**

Alergijske promjene kože kao posljedica uzimanja itraconazola su rijetke. Prikazan je slučaj makulopapularnog osipa uzrokovanog itraconazolom. Sedmog dana terapije itraconazolom primijenjene radi onihomikoze ruku kod 39-godišnje bolesnice, pojavio se svrbež kože i morbiliformni, simetrični, makulopapulozni osip na koži dekoltea, vrata, trupa i mjestima kompresije. Dolazi do progresije promjena, konfluiranja lezija i širenja na ekstremitete. S obzirom na porast indikacija za terapijsku primjenu itraconazola može se očekivati češća primjena ovoga lijeka kao i pojava alergijskih reakcija premda se rijetko javljaju.