

## **Griseofulvin-induced drug toxicoderma in a child: An unusual case**

### **Abstract**

**Introduction :** Griseofulvin is an antifungal known to be a cause of toxidermias. It is frequently prescribed especially in pediatrics, however it can have serious adverse effects, as we show through an observation.

**Observation :** We present a first case of drug-induced drug eruption type maculo-papular erythema induced by griseofulvin. This is a 10-year-old girl followed for ringworm of the scalp for 1 month, was placed on griseofulvin for 15 days ago. She was hospitalized for febrile rash made up of erythematous, papular and pruritic lesions. She also had ringworm of the scalp. The clinical examination showed a fever of 39 °C, an altered general condition with submandibular lymphadenopathy. Skin examination revealed maculopapular erythema on the face, trunk and limbs with edema of the upper lip. griseofulvin was stopped and replaced by terbinafine, intravenous antihistamine treatment combined with corticosteroid therapy was initiated. The resolution was rapidly favorable.

**conclusion :** Clinicians should be aware of the possibility of an erythema maculopapular-like reaction associated with griseofulvin treatment and consider this possibility when choosing between griseofulvin and newer, more expensive drugs. the molecule of griseofulvin is widely used outside its indications and as the benefit/risk balance then pleads largely against it.

**KEY WORDS :** griseofulvin, serum sickness-like reaction, leather tinea, child

### **Introduction :**

Tinea capitis is a dermatophyte infection of the scalp, most commonly caused by *Trichophyton tonsurans*, sometimes by *Microsporum canis*, and less commonly by other *microsporum* and *Trichophyton* species. Until recently, the mainstay of treatment for all forms of ringworm of the scalp was oral administration of griseofulvin for 6-12 weeks. Adverse effects of griseofulvin include nausea, vomiting, headache, blood dyscrasias, phototoxicity and hepatotoxicity. Griseofulvin can also cause fever, rash, leukopenia, and serum sickness-like reactions. Despite its widespread use, especially in children, it does not [complete sentence](#) There have been no reports in the literature of serum sickness or serum

sickness-like reactions associated with the drug. There was one report of erythema multiforme in 3 adults (2 of whom were HIV-infected). There are several case reports of adverse effects of griseofulvin in association with or precipitating systemic lupus erythematosus. We report this time a case of papular macular exanthema type reaction to griseofulvin in a child.

This type of toxiderma, constituting the majority, presents in the form of a maculopapular erythematous eruption starting at the level of the trunk with a secondary symmetrical extension at the level of the limbs. The clinical appearance may be morbilliform (isolated macules), rubella or scarlatiniform (confluence in sheets) and mimic a viral or bacterial infection. The presence of annular or urticarial lesions can give a polymorphic aspect which, with the confluence of the lesions as well as the presence of blood eosinophilia, is strongly suggestive of the diagnosis. The patient may be subfebrile and suffer from sometimes severe pruritus. The rash begins four to fourteen days after initiation of treatment (“nine-day rash”). After reexposure, drug eruption appears within two to three days with regression within one to two weeks of stopping treatment. Maculopapular rash rarely progresses to more severe drug eruption (erythroderma, Stevens-Johnson syndrome, toxic epidermal necrolysis or drug hypersensitivity syndrome). It is nevertheless necessary to suspend the treatment and to evaluate the alternatives available, avoiding re-exposure as far as possible.

### **Clinical case :**

We report the singular case of drug eruption like maculopapular erythema in a patient treated for ringworm of the scalp after the free and informed consent of her parents. This is a 10-year-old female child, diagnosed with ringworm two weeks ago, She was treated with griseofulvin during two weeks, with a history of herpetic keratitis 3 years ago. She had no known drug sensitivities and no family history of collagen vascular disorders. Vaccinations and developmental milestones were appropriate for his age. She was not taking any other medication.

She was hospitalized for a febrile maculopapular eruption. Physical examination revealed a healthy girl with a weight of 25 kg, an heart rate of 88 beats/min, a Blood pressure of 109/76 mm Hg and a T of 38.7 °C. The lesion was symmetrical in shape and showed two 8 cm papules with little hair in the left parietal and frontal region. Swelling of his lower lip was noted (Figure 1). In addition to an erythematous maculopapular rash on the legs, hands, chest, stomach, and back, excluding the palms or soles (Figure 2).



**Figure 1**

**A): edema of the lower lip**

**B): generalized maculopapular erythema of the trunk**

**C): ringworm of the scalp**

Biological examinations, including complete blood count, notably the search for hyper-eosinophilia, CRP, renal and hepatic function were carried out to watch for serum involvement, DRESS syndrome or secondary visceral involvement were normal. (Kindly state the meaning in full of all abbreviations used)

Griseofulvin was discontinued and replaced by oral terbinafine 7 mg/day combined with topical sertaconazole nitrate treatment, 1 application twice a day. Antihistamine and steroid anti-inflammatory treatment was initiated to relieve symptoms. Within 5 days, the pruritus disappeared and the maculopapular rash regressed. A good resolution of ringworm of the scalp under terbinafine was noted after a follow-up of one month.



**Figure 2: healing of facial lesions after a 30-day follow-up**

### **Discussion :**

A maculopapular rash is the most frequent drug eruption in children. The drugs most frequently involved are aminopenicillin, sulfonamides, pyrazoles, and anticonvulsants, especially tegretol. (4) The time between drug intake and eruption is generally between 4-14 days. We speak of “9th day erythema”; this drug-induced drug eruption begins on the trunk or

the roots of the limbs, which can gradually spread over a few days. Clinically, it has a polymorphic appearance, isolated macules (morbilliform) in some places, confluent elsewhere in scarlatiniform layers, papules or edematous plaques with sometimes an arciform arrangement, sometimes petechial purpura (legs). Pruritus is frequent, sometimes severe. Moderate fever. Absence of enanthema. Biologically, hyper-eosinophilia is sometimes found on the blood count. (1)

The presence of annular or urticarial lesions can give a polymorphic aspect which, with the confluence of the lesions as well as the presence of blood eosinophilia, is strongly suggestive of the diagnosis. The patient may be subfebrile and sometimes suffer from severe pruritus. After re-exposure, drug eruption appears within two to three days with regression within one to two weeks of stopping treatment.

“Serum sickness is a type III hypersensitivity reaction likely involving complement fixation and deposition of antigen-antibody complexes in small vessels, particularly skin and joints. Clinically, serum sickness usually presents 1 to 12 days after exposure to a foreign substance; sometimes it occurs up to 3 weeks later. Serum sickness is most commonly associated with fever, malaise, and rash. Urticaria accompanied by intense pruritus is a common finding, and edema, arthralgias, myalgias, and gastrointestinal disturbances may also occur. Serum complement levels are usually decreased and anaphylotoxin C3a may be elevated. The disease is usually self-limiting and patients recover in 7 to 10 days. Clinical syndromes that resemble serum sickness but do not meet all diagnostic criteria are called serum sickness-like reactions. These reactions generally occur 7 to 21 days after administration of the offending agent, most often an antibiotic or an anticonvulsant. The clinical manifestations are similar to the full-fledged syndrome. Fever and lymphadenopathy occur less often. On laboratory workup, circulating immune complexes and diminished complement levels are lacking. Symptoms usually go away after stopping the drug”. (2)(3) (5) (7).

Our patient had been taking griseofulvin for 2 weeks before the onset of symptoms, which mainly affected the skin and joints. The clinical progression of its symptomatology, namely fever followed by rash, as well as its temporal relationship to the administration of the antifungal agent were characteristic of drug toxicoderma. However, the biological assessments were normal, so the diagnosis of drug reaction type benign maculopapular erythema was confirmed. The diagnosis was supported by the rapid resolution of symptoms upon discontinuation of treatment

To our knowledge, griseofulvin toxicoderma induced by griseofulvin have been described in the literature only in a few cases.

### **Conclusion :**

Adverse drug reactions are common and potentially serious adverse drug reactions. Identification of suspect drugs and discontinuation of treatment is the first step in patient management

In case of suspicion of severe drug eruption, close monitoring or hospitalization are essential to ensure adequate care.

#### Consent

As per international standard, parental written consent has been collected and preserved by the author(s).

#### Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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